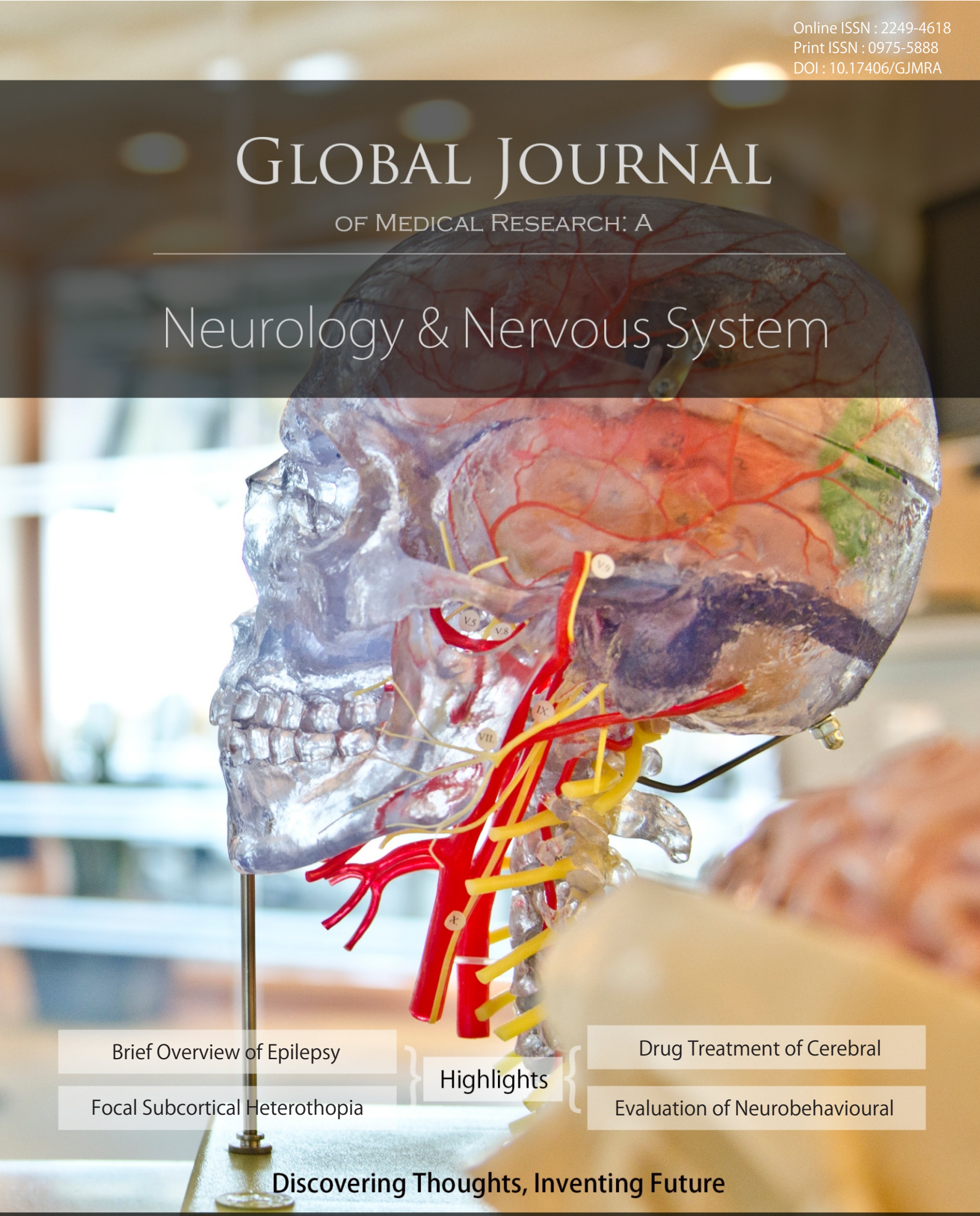
Online ISSN : 2249-4618
Print ISSN : 0975-5888
DOI : 10.17406/GJMRA

Global Journal

of Medical Research: A

Neurology & Nervous System



Brief Overview of Epilepsy

Focal Subcortical Heterothopia

Highlights

Drug Treatment of Cerebral

Evaluation of Neurobehavioural

Discovering Thoughts, Inventing Future

VOLUME 16 ISSUE 1 VERSION 1.0

© 2001-2016 by Global Journal of Medical Research, USA

Volume 16 Issue 16 was originally issued as A1

Global Journal of Medical Research: A
Neurology and Nervous System

Volume 16 Issue 16
Originally issued as A1

Global Journal of Medical Research: A Neurology and Nervous System

Volume 16 Issue 1 (Ver. 1.0)

Open Association of Research Society

© Global Journal of Medical Research . 2016.

All rights reserved.

This is a special issue published in version 1.0 of "Global Journal of Medical Research." By Global Journals Inc.

All articles are open access articles distributed under "Global Journal of Medical Research"

Reading License, which permits restricted use. Entire contents are copyright by of "Global Journal of Medical Research" unless otherwise noted on specific articles.

No part of this publication may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopy, recording, or any information storage and retrieval system, without written permission.

The opinions and statements made in this book are those of the authors concerned. Ultraculture has not verified and neither confirms nor denies any of the foregoing and no warranty or fitness is implied.

Engage with the contents herein at your own risk.

The use of this journal, and the terms and conditions for our providing information, is governed by our Disclaimer, Terms and Conditions and Privacy Policy given on our website http://globaljournals.us/terms-and-condition/menu-id-1463/

By referring / using / reading / any type of association / referencing this journal, this signifies and you acknowledge that you have read them and that you accept and will be bound by the terms thereof.

All information, journals, this journal, activities undertaken, materials, services and our website, terms and conditions, privacy policy, and this journal is subject to change anytime without any prior notice.

Incorporation No.: 0423089
License No.: 42125/022010/1186
Registration No.: 430374
Import-Export Code: 1109007027
Employer Identification Number (EIN):
USA Tax ID: 98-0673427

Global Journals Inc.

*(A Delaware USA Incorporation with "Good Standing"; **Reg. Number: 0423089**)*

Sponsors: Open Association of Research Society
Open Scientific Standards

Publisher's Headquarters office

Global Journals® Headquarters
945th Concord Streets,
Framingham Massachusetts Pin: 01701,
United States of America
USA Toll Free: +001-888-839-7392
USA Toll Free Fax: +001-888-839-7392

Offset Typesetting

Global Journals Incorporated
2nd, Lansdowne, Lansdowne Rd., Croydon-Surrey,
Pin: CR9 2ER, United Kingdom

Packaging & Continental Dispatching

Global Journals
E-3130 Sudama Nagar, Near Gopur Square,
Indore, M.P., Pin: 452009, India

Find a correspondence nodal officer near you

To find nodal officer of your country, please email us at *local@globaljournals.org*

eContacts

Press Inquiries: *press@globaljournals.org*
Investor Inquiries: *investors@globaljournals.org*
Technical Support: *technology@globaljournals.org*
Media & Releases: *media@globaljournals.org*

Pricing (Including by Air Parcel Charges):

For Authors:
22 USD (B/W) & 50 USD (Color)
Yearly Subscription (Personal & Institutional):
200 USD (B/W) & 250 USD (Color)

Integrated Editorial Board
(Computer Science, Engineering, Medical, Management, Natural Science, Social Science)

John A. Hamilton,"Drew" Jr.,
Ph.D., Professor, Management
Computer Science and Software Engineering
Director, Information Assurance Laboratory
Auburn University

Dr. Henry Hexmoor
IEEE senior member since 2004
Ph.D. Computer Science, University at Buffalo
Department of Computer Science
Southern Illinois University at Carbondale

Dr. Osman Balci, Professor
Department of Computer Science
Virginia Tech, Virginia University
Ph.D. and M.S. Syracuse University, Syracuse, New York
M.S. and B.S. Bogazici University, Istanbul, Turkey

Yogita Bajpai
M.Sc. (Computer Science), FICCT
U.S.A. Email:
yogita@computerresearch.org

Dr. T. David A. Forbes
Associate Professor and Range Nutritionist
Ph.D. Edinburgh University - Animal Nutrition
M.S. Aberdeen University - Animal Nutrition
B.A. University of Dublin- Zoology

Dr. Wenying Feng
Professor, Department of Computing & Information Systems
Department of Mathematics
Trent University, Peterborough,
ON Canada K9J 7B8

Dr. Thomas Wischgoll
Computer Science and Engineering,
Wright State University, Dayton, Ohio
B.S., M.S., Ph.D.
(University of Kaiserslautern)

Dr. Abdurrahman Arslanyilmaz
Computer Science & Information Systems Department
Youngstown State University
Ph.D., Texas A&M University
University of Missouri, Columbia
Gazi University, Turkey

Dr. Xiaohong He
Professor of International Business
University of Quinnipiac
BS, Jilin Institute of Technology; MA, MS, PhD,. (University of Texas-Dallas)

Burcin Becerik-Gerber
University of Southern California
Ph.D. in Civil Engineering
DDes from Harvard University
M.S. from University of California, Berkeley
& Istanbul University

Dr. Bart Lambrecht
Director of Research in Accounting and Finance Professor of Finance
Lancaster University Management School
BA (Antwerp); MPhil, MA, PhD (Cambridge)

Dr. Carlos García Pont
Associate Professor of Marketing
IESE Business School, University of Navarra
Doctor of Philosophy (Management), Massachusetts Institute of Technology (MIT)
Master in Business Administration, IESE, University of Navarra
Degree in Industrial Engineering, Universitat Politècnica de Catalunya

Dr. Fotini Labropulu
Mathematics - Luther College
University of Regina Ph.D., M.Sc. in Mathematics
B.A. (Honors) in Mathematics
University of Windso

Dr. Lynn Lim
Reader in Business and Marketing
Roehampton University, London
BCom, PGDip, MBA (Distinction), PhD, FHEA

Dr. Mihaly Mezei
ASSOCIATE PROFESSOR
Department of Structural and Chemical Biology, Mount Sinai School of Medical Center
Ph.D., Etvs Lornd University
Postdoctoral Training,
New York University

Dr. Söhnke M. Bartram
Department of Accounting and Finance Lancaster University Management School Ph.D. (WHU Koblenz)
MBA/BBA (University of Saarbrücken)

Dr. Miguel Angel Ariño
Professor of Decision Sciences
IESE Business School
Barcelona, Spain (Universidad de Navarra)
CEIBS (China Europe International Business School).
Beijing, Shanghai and Shenzhen
Ph.D. in Mathematics
University of Barcelona
BA in Mathematics (Licenciatura)
University of Barcelona

Philip G. Moscoso
Technology and Operations Management
IESE Business School, University of Navarra
Ph.D in Industrial Engineering and Management, ETH Zurich
M.Sc. in Chemical Engineering, ETH Zurich

Dr. Sanjay Dixit, M.D.
Director, EP Laboratories, Philadelphia VA Medical Center
Cardiovascular Medicine - Cardiac Arrhythmia
Univ of Penn School of Medicine

Dr. Han-Xiang Deng
MD., Ph.D
Associate Professor and Research Department Division of Neuromuscular Medicine
Davee Department of Neurology and Clinical Neuroscience Northwestern University Feinberg School of Medicine

Dr. Pina C. Sanelli
Associate Professor of Public Health
Weill Cornell Medical College
Associate Attending Radiologist
NewYork-Presbyterian Hospital
MRI, MRA, CT, and CTA
Neuroradiology and Diagnostic Radiology
M.D., State University of New York at Buffalo,School of Medicine and Biomedical Sciences

Dr. Roberto Sanchez
Associate Professor
Department of Structural and Chemical Biology
Mount Sinai School of Medicine
Ph.D., The Rockefeller University

Dr. Wen-Yih Sun
Professor of Earth and Atmospheric SciencesPurdue University Director
National Center for Typhoon and Flooding Research, Taiwan
University Chair Professor
Department of Atmospheric Sciences, National Central University, Chung-Li, TaiwanUniversity Chair Professor
Institute of Environmental Engineering, National Chiao Tung University, Hsin-chu, Taiwan.Ph.D., MS The University of Chicago, Geophysical Sciences
BS National Taiwan University, Atmospheric Sciences
Associate Professor of Radiology

Dr. Michael R. Rudnick
M.D., FACP
Associate Professor of Medicine
Chief, Renal Electrolyte and Hypertension Division (PMC)
Penn Medicine, University of Pennsylvania
Presbyterian Medical Center, Philadelphia
Nephrology and Internal Medicine
Certified by the American Board of Internal Medicine

Dr. Bassey Benjamin Esu
B.Sc. Marketing; MBA Marketing; Ph.D Marketing
Lecturer, Department of Marketing, University of Calabar
Tourism Consultant, Cross River State Tourism Development Department
Co-ordinator , Sustainable Tourism Initiative, Calabar, Nigeria

Dr. Aziz M. Barbar, Ph.D.
IEEE Senior Member
Chairperson, Department of Computer Science
AUST - American University of Science & Technology
Alfred Naccash Avenue – Ashrafieh

President Editor (HON.)

Dr. George Perry, (Neuroscientist)
Dean and Professor, College of Sciences
Denham Harman Research Award (American Aging Association)
ISI Highly Cited Researcher, Iberoamerican Molecular Biology Organization
AAAS Fellow, Correspondent Member of Spanish Royal Academy of Sciences
University of Texas at San Antonio
Postdoctoral Fellow (Department of Cell Biology)
Baylor College of Medicine
Houston, Texas, United States

Chief Author (HON.)

Dr. R.K. Dixit
M.Sc., Ph.D., FICCT
Chief Author, India
Email: authorind@computerresearch.org

Dean & Editor-in-Chief (HON.)

Vivek Dubey(HON.)
MS (Industrial Engineering),
MS (Mechanical Engineering)
University of Wisconsin, FICCT
Editor-in-Chief, USA
editorusa@computerresearch.org

Sangita Dixit
M.Sc., FICCT
Dean & Chancellor (Asia Pacific)
deanind@computerresearch.org

Suyash Dixit
(B.E., Computer Science Engineering), FICCTT
President, Web Administration and
Development , CEO at IOSRD
COO at GAOR & OSS

Er. Suyog Dixit
(M. Tech), BE (HONS. in CSE), FICCT
SAP Certified Consultant
CEO at IOSRD, GAOR & OSS
Technical Dean, Global Journals Inc. (US)
Website: www.suyogdixit.com
Email: suyog@suyogdixit.com

Pritesh Rajvaidya
(MS) Computer Science Department
California State University
BE (Computer Science), FICCT
Technical Dean, USA
Email: pritesh@computerresearch.org

Luis Galárraga
J!Research Project Leader
Saarbrücken, Germany

Contents of the Issue

i. Copyright Notice
ii. Editorial Board Members
iii. Chief Author and Dean
iv. Contents of the Issue

1. Grey Matter Focal Subcortical Heterothopia-A Case Report. *1-3*
2. A Brief Overview of Epilepsy. *5-10*
3. Drug Treatment of Cerebral Vasospasm after Subarachnoid Hemorrhage Following Aneurysms. *11-20*
4. Evaluation of Neurobehavioural and Cognitive Changes Induced by Carbamazepine and/or Phenytoin in Wistar Rats. *21-26*
5. Epilespy and Enuresis of Teenagers and Young Adults: Attitudes, Practices and Knowledge in Togo. *27-30*

v. Fellows
vi. Auxiliary Memberships
vii. Process of Submission of Research Paper
viii. Preferred Author Guidelines
ix. Index

Global Journal of Medical Research: a
Neurology and Nervous System
Volume 16 Issue 1 Version 1.0 Year 2016
Type: Double Blind Peer Reviewed International Research Journal
Publisher: Global Journals Inc. (USA)
Online ISSN: 2249-4618 & Print ISSN: 0975-5888

Grey Matter Focal Subcortical Heterothopia-A Case Report

By Mihaela Lungu

Abstract- The article presents the case of a 40-year old patient, diagnosed with partial epileptic seizures since he was one year old. He also presented a psychomotor delay and spastic left palsy. For a long time, the diagnosis was infant encephalopathy. In 2014, during an MRI investigation, a large, right-side, pseudo-tumoral, temporo-parietal heterothopia was found. This heterothopia also presented a posterior agenesis of the corpus callosum. The grey matter focal heterothopia explained the cause of the epileptic seizures.

Keywords: heterothopia, seizures, cognitive impairment.

GJMR-A Classification : NLMC Code: WL340



Strictly as per the compliance and regulations of:



© 2016. Mihaela Lungu. This is a research/review paper, distributed under the terms of the Creative Commons Attribution-Noncommercial 3.0 Unported License http://creativecommons.org/licenses/by-nc/3.0/), permitting all non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

Grey Matter Focal Subcortical Heterothopia-A Case Report

Mihaela Lungu

Abstract- The article presents the case of a 40-year old patient, diagnosed with partial epileptic seizures since he was one year old. He also presented a psychomotor delay and spastic left palsy. For a long time, the diagnosis was infant encephalopathy. In 2014, during an MRI investigation, a large, right-side, pseudo-tumoral, temporo-parietal heterothopia was found. This heterothopia also presented a posterior agenesis of the corpus callosum. The grey matter focal heterothopia explained the cause of the epileptic seizures.

Keywords: heterothopia, seizures, cognitive impairment.

I. Introduction

The grey matter heterothopia (GMH) is a brain malformation caused by abnormal neuronal migration. This impairment of neuronal migration takes place during the third to fifth month of gestation.

In these cases, a subset of neurons fails to migrate from the vicinity of the ventricle into the developing cerebral cortex. So, they form nodules that line the ventricular surface: "normal neurons in abnormal locations". The neurons fail to climb to the end of their ladder correctly and are permanently situated in the wrong location.

Classically, GMH is a X-linked dominant disorder, more frequent in females. The patients present intelligence varying from normal to borderline mental retardation. Other related pathology include epilepsy, cardiovascular defects or coagulopathy. This disorder is usually associated with premature lethality in males, who have a high risk of aortic pathology.

Periventricular heterothopias is related to chromosome 5. Its incidence is unknown. It is caused by mutations in ARFGEF2 and FLNA genes. The FLNA gene provides instructions for producing the protein filaminin-A, which helps building the network of protein filaments-cytoskeleton, that gives structure to cells and allows them to change shape and move ()

In GMH, results are impaired. FLNA protein cannot perform this function, disrupting the normal migration of neurons, during the development of the brain. GMH is associated with mutations in the Filanin-A gene (FLN1, FLNA, ABP-280), ARFCEF2 gene and, in some individual cases, a chromosomal rearrangement in 5P151. Syndactily and mental retardation are also associated with N.H. (1)

GMH may also be caused by infection or trauma.

Macroscopically, GMH can be divided into:

1. Nodular heterothopias:

-subependymal heterothopias- most common
-subcortical heterothopias.

2. Diffuse heterothopias: band heterothopias (double cortex heterothopias, X-linked lissencephaly), laminar heterothopias, lissencephaly - types 1 and 2. (1)

a) Focal subcortical GMH (FSCGMH)

Clinical presentation: most commonly, patients present epileptic seizures such as partial seizures, progressing towards drug resistant epilepsy in the second decade of life. Additionally there are also some associated development delays or mental retardation. GMH are more frequent in patients with other congenital central nervous system anomalies, such as the agenesis of the corpus callosum, Chiari II malformation and pachygyria.

FSCGHM forms distinct nodules in the white matter, in a specific area. Patients present fixed neurologic deficits and develop partial epilepsy, between the ages of 6 and 10.

Management of the patient presenting GMH is based on symptomatic treatment, including antiepileptic drugs and surgical therapy for cardiovascular defects (most often persistence of Botallo's duct and aortic valvulopathy.)

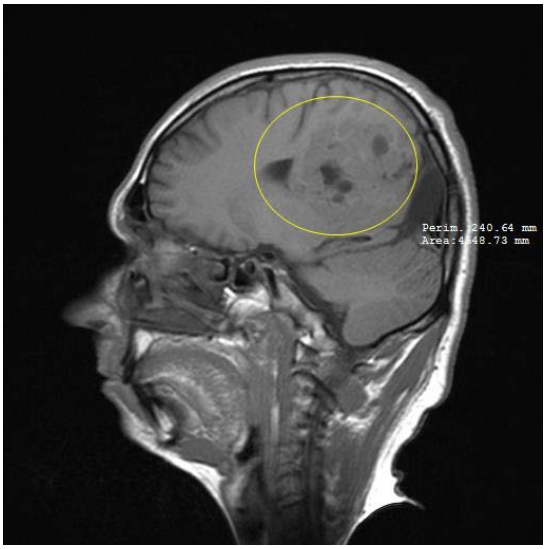
II. Case Report

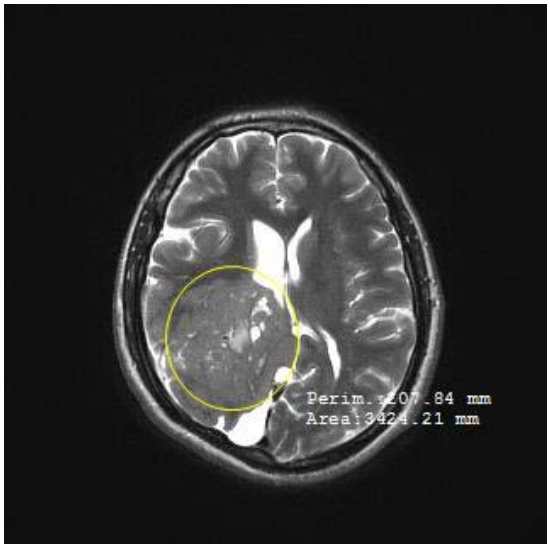
This article aims to present a case of a 40 year old male who was admitted to our clinic for recurrent epileptic seizures, associated with cognitive impairment and a spastic left palsy. The seizures started since when he was 20 years old, with focal sensory and motor seizures. The frequency of these episodes at the beginning is unknown.

Subsequently, the frequency of the seizures escalated to 6 episodes per week. Various antiepileptic drugs were employed, consisting in levetiracetamum, carbamazepinum, valproic acid, phenitoinum, oxcarbazepinum. With this schedule, the patient still had 2-3 seizures per week.

Author: Department of Neurology, Galati Emergency Hospital, Romania.
e-mails: mihaelalungu17@yahoo.com, micalungu@gmail.com

© 2016 Global Journals Inc. (US)





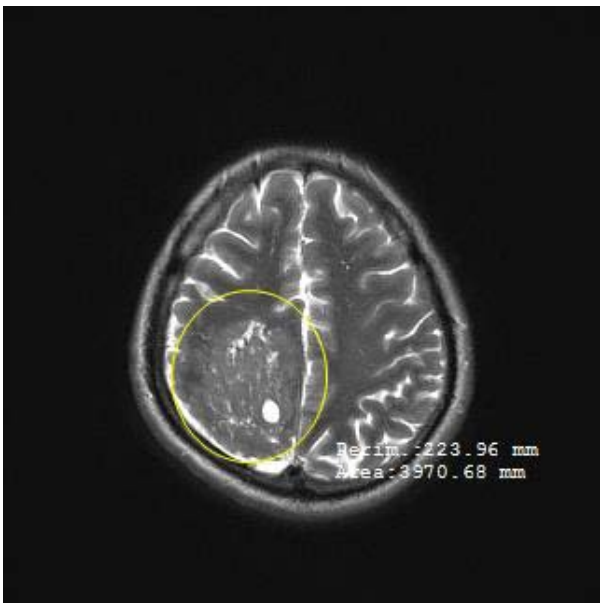
a) Clinical and paraclinical examinations

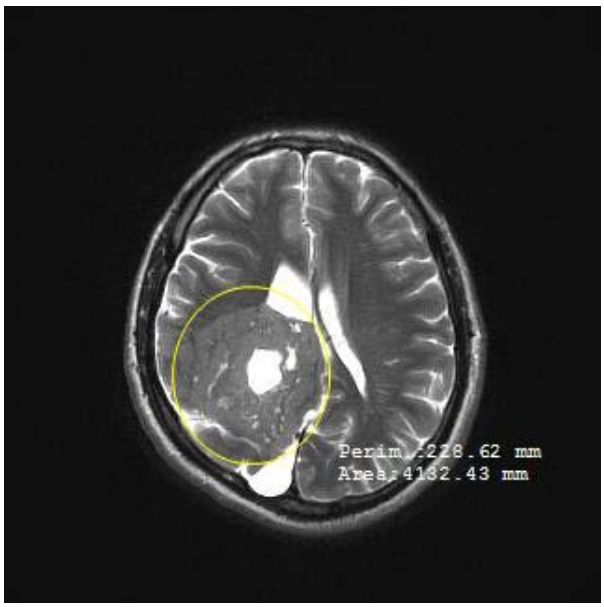
The personal and heredo-colateral history were unremarkable. The neurological examination shows bradylalia, bradipsychia, spastic left palsy - MRC of 3/5 and the pshychological examination shows a mild cognitive impairment.

b) Interpretation of the cerebral MRI

The brain MRI using Gadolinium shows a conglomerate of nodular grey matter, with bands of white matter, alternately disposed, located in the right parietal lobes, spanning from the ventricular walls to the cortex surface. The nearby parietal and temporal cortexes show an underdeveloped gyrus and inadequate thickness.

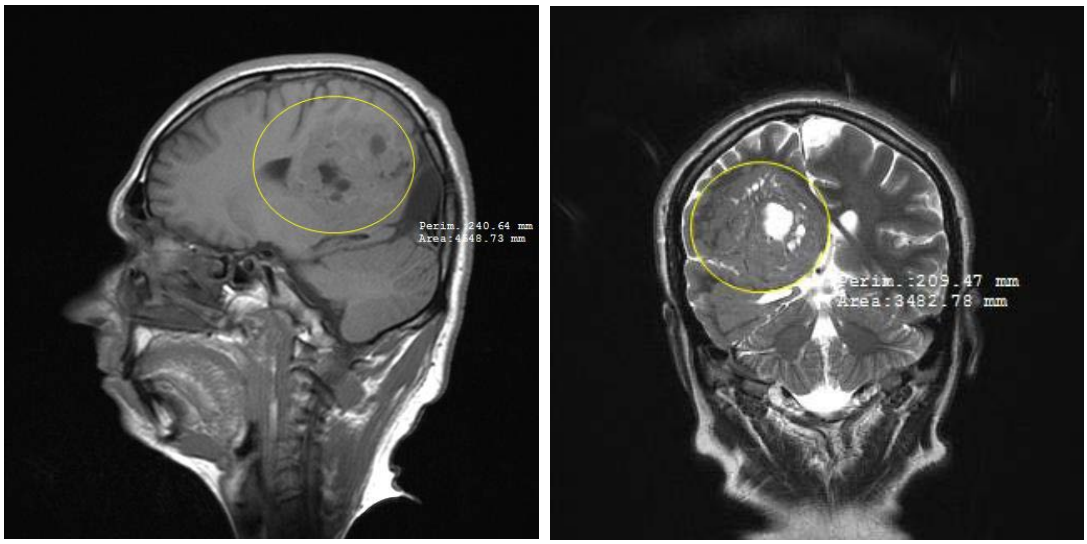
The corpus callosum has posterior agenesis and the lateral ventricle is imprinted.



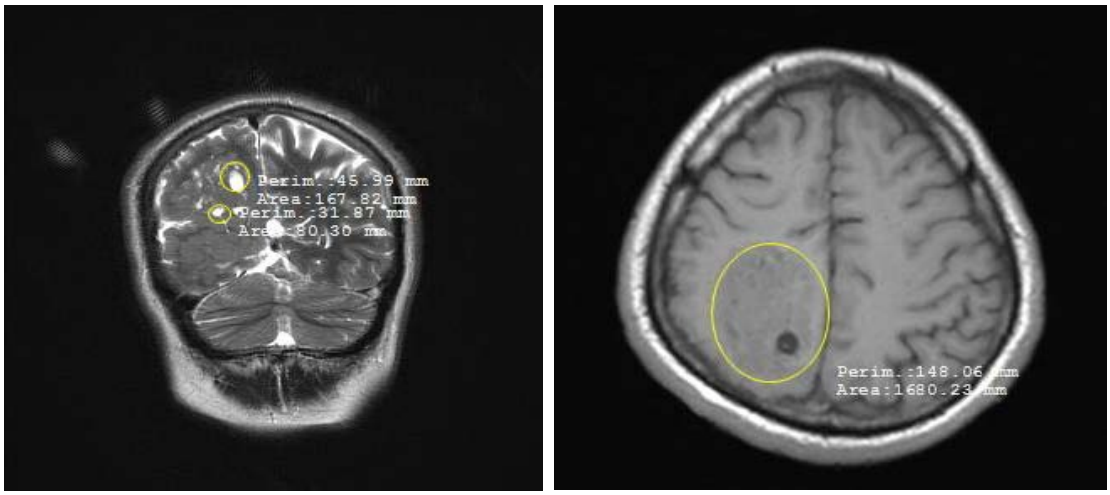


No signal modifications are present within the cerebral parenchyma. Ventricular system appears normal in size. Arterial vascular paths from the base of the scull present normal MRI flow.

© 2016 Global Journals Inc. (US)



Lateral venous sinuses are normal in appearance.



There are no more modifications of the brain tissue. The ventricular system is normal. The arteries and dural venous sinuses appear normal.

Conclusion: Giant right sided temporo-parietal pseudotumoral heterothopia.

Treatment and evolution:

The current scheme contains the following drugs: Levetiracetamum (2000 mg daily) and Carbamazepinum (800 mg daily).

The patient still has partial motor-sensorial seizures, with a frequency of 2-3 episodes per week, mainly during the day.

The psychological examination shows a mild cognitive impairment.

The mental abilities have remained at the same level since 2014, when he was first diagnosed.

III. Conclusions

The case presented in the article shows the fact that the GMH has special clinical aspects- seizures, cognitive impairment, focal neurological palsy, but characteristic aspects of the cerebral MRI, which reveals the cortical malformations.

The diagnosis was established after a long period of time, only due to MRI examination.

The patient is still monitored in order to determine the possible changes of treatment.

The case is isolated in the family.

Bibliography

1. Adams and Victor `s Principles of Neurology- Tenth Edition, 2014, McGraw-Hill Education, USA, pg.1007-1008
2. Hufschmidt A., Lucking C.H.- Neurologie integral, de la symptom la tratament, Editura Polirom, Bucuresti, 2002, pg.199
3. Neurology- J. Cambier, M. Masson, H. Dehen, 11-edition, Masson, Paris, 2004, pg.475
4. Subcortical Band Heterotopia Syndrome in children-comparison of two case reports- Sanda Nica, Magdalena Sandu, Raluca Teleanu, Romanian Journal of Neurology, vol.XII, No.3, 2013, pg. 152-155.

© 2016 Global Journals Inc. (US)

This page is intentionally left blank

© 2016 Global Journals Inc. (US)

Global Journal of Medical Research: a
Neurology and Nervous System
Volume 16 Issue 1 Version 1.0 Year 2016
Type: Double Blind Peer Reviewed International Research Journal
Publisher: Global Journals Inc. (USA)
Online ISSN: 2249-4618 & Print ISSN: 0975-5888

A Brief Overview of Epilepsy

By Vikash Kumar Chaudhari, Pushpendra Kumar, Vijay Yadav, Devender Pathak & Zeashan Hussain

Abstract- Epilepsy is a group of neurological diseases characterized by epileptic seizures. Epileptic seizures are episodes that can vary from brief and nearly undetectable to long periods of vigorous shaking. In epilepsy, seizures tend to recur, and have no immediate underlying cause while seizures that occur due to a specific cause are not deemed to represent epilepsy. The cause of most cases of epilepsy is unknown, although some people develop epilepsy as the result of brain injury, stroke, brain tumors, and substance use disorders.

Keywords: *epilepsy, neurological disease, seizures.*

GJMR-A Classification : *NLMC Code: WL 385*



Strictly as per the compliance and regulations of:



© 2016. Vikash Kumar Chaudhari, Pushpendra Kumar, Vijay Yadav, Devender Pathak & Zeashan Hussain. This is a research/ review paper, distributed under the terms of the Creative Commons Attribution-Noncommercial 3.0 Unported License http://creativecommons.org/licenses/by-nc/3.0/), permitting all non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

A Brief Overview of Epilepsy

Vikash Kumar Chaudhari [α], Pushpendra Kumar [σ], Vijay Yadav [ρ], Devender Pathak [ω] & Zeashan Hussain [¥]

Abstract- **Epilepsy is a group of neurological diseases characterized by epileptic seizures. Epileptic seizures are episodes that can vary from brief and nearly undetectable to long periods of vigorous shaking. In epilepsy, seizures tend to recur, and have no immediate underlying cause while seizures that occur due to a specific cause are not deemed to represent epilepsy. The cause of most cases of epilepsy is unknown, although some people develop epilepsy as the result of brain injury, stroke, brain tumors, and substance use disorders.**

Keywords: epilepsy, neurological disease, seizures.

I. Introduction

Epilepsy is very common disorder or a group of neurological diseases, characterized by seizures[1,2] which take various forms and result from episodic neuronal discharges, the forms of the seizure depending on the part of the brain affected. Epilepsy affects 0.5% of the population. Often there is no recognizable case although it may develop after brain damage, such as trauma, infection or tumor growth or other kind of neurological disease, including various inherited neurological syndromes. Epilepsy is treated mainly with drug through brain surgery may be used for several cases [3,4]. Current antiepileptic drugs are effective in controlling seizures in about 70% of patients [5,6,7].

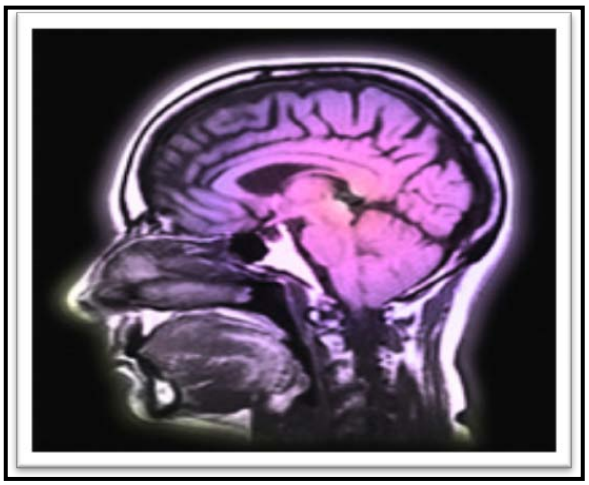


Fig. 1 : Brain

Author α ¥: Department of Pharmacy, Mahatma Gandhi Institute of Pharmacy, Lucknow-227101, Uttar Pradesh, India.
e-mail: vikashk464@gmail.com
Author σ ω: Pharmacy College Saifai, UP RIMS & R, Saifai, Saifai, Etawah-206130, Uttar Pradesh, India.
Author ρ: Department of Pharmacy, Dr. Bhim Rao Ambedkar University, Agra-282004, Uttar Pradesh, India.

Anticonvulsants act to prevent the spread of the neuronal excitation by mechanisms that are not fully understood, but which can be roughly divided in to those which involve stabilizing effect on excitable cell membranes, and those which involves enhanced functional activity of neurotransmitters such as gamma amino butyric acid (GABA), which then act to inhibit spread of seizure activity by blocking synaptic transmission at some point. Status epilepticus is potentially fatal, and is a medical emergency requiring swift and effective treatment to minimize the risk of brain damage. [3,5]

The term epilepsy refers to a disorder of brain function characterized by the periodic and unpredictable occurrence of seizures. Seizures can be "nonepileptic." When evoked in a normal brain by treatments such as electroshock or chemical consultants or "epileptic" when occurring without evident provocation. [6,8]

Epilepsy is a chronic disorder of the Central Nervous System (CNS) with a prevalence rate between 3 and 6 per thousand populations.

II. Types of Epilepsies [8,9]

Generalized Seizure:

a) *Generalized tonic-clonic seizures (GTC, major epilepsy, grand mal)*

Commonest, lasts 1-2min. the usual sequence is aura, cry and unconsciousness-tonic spasm of all body muscles clonic- jerking followed by prolonged sleep and depression of all CNS functions.

b) *Absence seizures (Minor epilepsy, Petit mal)*

Prevalent in children, lasts about ½ min. Momentary loss of consciousness, patient apparently freezes, stares in one direction, no muscular component or little bilateral jerking. EEG shows characteristic 3 cycle per second spike and wave pattern.

c) *Atonic seizures (A Kinetic epilepsy)*

Unconsciousness with relaxation of all muscles due to excessive inhibitory discharges. Patient may fall.

d) *Myoclonic seizures*

Shock-like momentary contraction of muscles of a limb or whole body.

e) *Infantile spasms (Hypsarrhythmia)*

Seen in infants. Probably not form of epilepsy. Intermittent muscle spasm and progressive mental deterioration. Diffuse changes in the inter seizure EEG are noted.

© 2016 Global Journals Inc. (US)

III. Partial Seizures

a) Simple partial seizures (SPS, Cortical focal epilepsy)

Last ½-1min. often secondary. Convulsions are confined to a group of muscles or localized sensory disturbance depending on the area of cortex involved in the seizure, without loss of consciousness.

b) Complex partial seizures (CPS, Temporal lobe epilepsy, Psychomotor)

Attacks of bizarre and confused behavior and purposeless movements, emotional changes lasting 1-2 min along with impairment of consciousness. An aura often proceeds. The seizure focus is located in the temporal lobe.

c) Simple partial or complex partial seizures secondarily generalized

The partial seizure occurs first and evolves in to generalized tonic-clonic seizures with loss of consciousness.

IV. General Mechanism of Action of Antiseizure Drugs

Order to bring normal balance between excitery and inhibitory postsynaptic potential, antiseizure drugs may use one or more of the following mechanisms.

a) Enhancement of GABA-mediated inhibition

The drug may act directly on the GABA-receptor-chloride channel complex (e.g., benzodiazepines, barbiturates) and inhibit the metabolism of GABA (e.g., vigabatrin, valproate) or increase the release of GABA (e.g., gabapentin).This mechanism provides protection against generalized and focal seizures.

b) Suppression of rapid repetitive firing

This mechanism of action of antiseizure drugs (Phenytoin, carbamazepine, valproate and lamotrigine). Involves the prolongation and the closing of inactivation gate of Na+ channels, thus reducing the ability of neurons to fire at high frequencies.This mechanism provides protections against maximal electric shock in animals and focal seizures in humans.

c) Reduction of current through T-type Ca++ channels

A low threshold Ca++ current (T- type) governs oscillatory response in thalamic neurons. Reduction of this current by antiseizure drugs (e.g, ethosuximide, dimethadione and valproate) explains the mechanism of action against absence seizures.

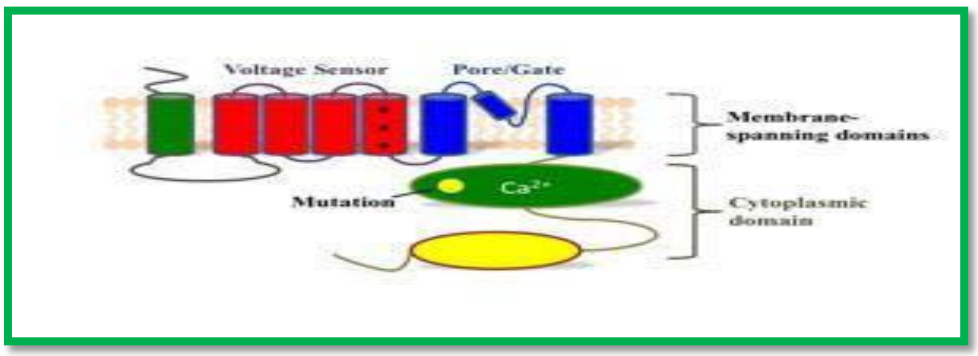


Fig. 2 : Ca++channels

d) Reduction of excitatory glutaminergic neurotransmission

Some antiseizure drugs (e.g., Phenobarbital, topiramate) block the AMPA receptor and some (Felbamate, remacemide, an investigational drug) block NMDA receptors. The understanding of these basic mechanisms has resulted in the development of many new antiseizure drugs.

V. Diagonosis [10,11]

a) The electroencephalogram (EEG)

The EEG is central to the diagnosis of epilepsy. To record the brain's electrical rhythms, a number of electrodes (usually 22) are placed against the scalp, arranged in a fixed pattern. They may be held in place by a rubber cap device, or, if longer recordings are required, they can be secured by an adhesive chemical (collodion) the modern EEG machine now allows the recording of information from all leads simultaneously. The brain's rhythms can be traced out on folding chart paper, or recorded on videotape. Routinely, brain rhythms are recorded for about 30 minutes.

© 2016 Global Journals Inc. (US)

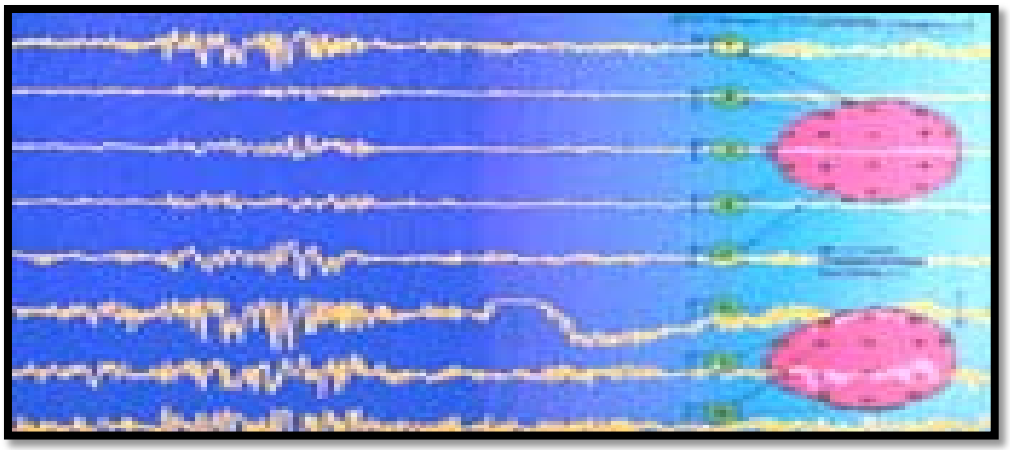


Fig. 3 : EEG

b) CT Scanning

Computerized Tomography (CT) is a procedure which allows the radiologist to study images of the brain, as if the brain could be "sliced". In this way, the brain can be examined to exclude tumors, strokes and other localized abnormalities which may have given rise to seizures.

c) MRI Scanning

Introduced in the 1980s, MRI (magnetic resonance imaging) uses a strong magnet instead of x-rays to take pictures of the brain. It is one of the best and most precise mechanisms for examining the brain, so it is extremely common for doctors to use MRI for diagnosis in epilepsy. It allows them to look at nerve tissue, the flow of blood and spinal fluid and any tumors or other localized changes or injuries.

d) Scanning with Radioisotopes

It is here that radioisotope scanning comes into its own. For this purpose, two types of scanning may be used:

- SPECT (Single Photon Emission Tomography)
- PET (Positron Emission Tomography)



Fig. 4 : MRI Scanning

VI. General Causes of Epilepsy

The causes of epilepsy are summarized in three general etiological groups.

The first one is the threshold, which determines the susceptibility of individual brains to generate seizures in response to epileptogenic perturbations. This will determine what is called PRIMARY or IDIOPATHIC epilepsy, when it is not the result of some other brain abnormality. They are usually benign and often remit spontaneously or after uninterrupted pharmacological treatment with antiepileptic drugs (AED). The duration between onset and remission can vary from 2 to 12 years.

The second group is related to a specific epileptogenic abnormality, which could be an acquired lesion of the brain, congenital malformations of the brain or genetic disorders other than epilepsy. These SECONDARY or SYMPTOMATIC epilepsies are very common in developing countries, where they are responsible for the difference in terms of *prevalence and prognosis*. Risk factors are dominated by poor perinatal care, head trauma, and intracranial infection, including parasitic infestations (such as neurocysticercosis,

© 2016 Global Journals Inc. (US)

neuromalaria), and these are far more common than in industrialised countries. Their control requires, in addition to AED, specific care of the aetiology (medical and/or neurosurgical).

The third group is represented by epileptic disorders that are probably symptomatic, but the causes have not been identified with existing diagnostic means, and therefore they are called CRYPTOGENIC (which means hidden cause)with a high suspicion of a genetic (but non identifiable) factor.

VII. Treatment[11,12]

The goal for individual patients is no seizures and minimal side effects and the job of the physician is to aid the patient to find the best balance between the two during the prescribing of anticonvulsants.

Table 1 : Classification of anticonvulsant drugs

Category	Drugs	Use
Aldehyde	Paraldehyde	Status Epilepsy
Aromatic allylic alcohol	Stiripentol	Myoclonic epilepsy
Barbiturates	Phenobarbital, Methylphenobarbital, Barbexaclone	Status Epilepsy
Benzodiazepines	Clobazam, Clonazepam, Diazepam, Midazolam, Lorazepam	Status Epilepsy
Carbamates	Carbamazepine, Oxcarbamazepine	Status Epilepsy
Fatty acids	Valproic acid, Divalproex, Progabide, Tiagabine	Absence seizures
Fructose derivative	Topiramide	Pentylenetetrazol clonic seizures
GABA Analogue	Gabapentine, Pregabaline	Simple partial seizures
Hydantoin	Ethotoin, Phenytoin, Mephentoin, Fosphenytoin	Simple and complex partial seizures
Oxazolidinedione	Paramethadione, Trimethadione, Ethadione	Simple partial seizures
Pyrimidinediones Succinimide	Primidone Phensuccimide Mesuccimide	Simple partial seizures Absence seizures
Triazine	Lamotrigine	Generalised tonic-clonic seizures
Valproylamides	Valpromide, Valnoctamide	Myoclonic and atonic seizures

Devices:

The vagus nerve stimulator (VNS) is a device that sends electric impulses to the left vagus nerve in the neck via a lead implanted under the skin. It was FDA approved in 1997 as an adjunctive therapy for partial-onset epilepsy.

© 2016 Global Journals Inc. (US)

Table 2 : Acute side effects

Antiepileptic drugs	Concentration dependent	Idiosyncratic	Chronic side effects
Carbamazepine	Diplopia Dizziness Drowsiness Nausea Unsteadiness Lethargy	Blood dyscrasias Rash	Hyponatremia
Ethosuximides	Ataxia Drowsiness GI distress Unsteadiness	Blood dyscrasias	Behaviour changes headache
Felbamate	Anorexia Nausea Vomiting Insomnia	Aplastic anaemia Acute hepatic failure	Not established
Lamotrigene	Diplopia	Rash	Not established
Levetiracetam	Sedation Dizziness Ataxia Nausea	Not established	Not established
Oxcarbazepine	Sedation	Rash	Hyponatremia
Phenobarbitol	Ataxia Hyperactivity Headache Sedation	Blood dyscrasias	Sedation Behavior change, Moodchange
Phenytoin	Ataxia Nystagmus Dizziness Sedation Visual blurring	Blood dyscrasias Rash	Cerebellar syndrome Hirsutism
Primidone	Nausea Sedation Unsteadiness	Blood dyscrasias Rash	Behaviour change Connective tissue disorders
Tigabine	Diziness Nervousness Depression	Not established	Not established
Valproic acid	GI upset Sedation Unsteadiness Thrombocytopenia	Acute hepatic failure Acute pancreatits	Polycystic ovary-like syndrome Alopecia

VIII. Surgical Treatment

Epilepsy surgery is an option for patients whose seizures remain resistant to treatment with anticonvulsant medications who also have symptomatic localization-related epilepsy; a focal abnormality that can be located and therefore removed. The goal for these procedures is total control of epileptic seizures although anticonvulsant medications may still be required.

The most common surgeries are the resection of lesions like tumors or arteriovenous malformations which, in the process of treating the underlying lesion, often result in control of epileptic seizures caused by these lesions.

IX. Other Treatment

a) Ketogenic diet

A high fat, low carbohydrate diet developed in the 1920s, largely forgotten with the advent of effective anticonvulsants, and resurrected in the 1990s. The mechanism of action is unknown. It is used mainly in the treatment of children with severe, medically-intractable epilepsies.

b) Electrical stimulation

Methods of anticonvulsant treatment with both currently approved and investigational uses. A currently approved device is vagus nerve stimulation (VNS). Investigational devices include the responsive neurostimulation system and deep brain stimulation.

c) Vagus nerve stimulation (VNS)

The VNS (US manufacturer = Cyberonics) consists of a computerized electrical device similar in size, shape and implant location to a heart pacemaker that connects to the vagus nerve in the neck. The device stimulates the vagus nerve at pre-set intervals and intensities of current. Efficacy has been tested in patients with localization-related epilepsies demonstrating that 50% of patients experience a 50% improvement in seizure rate.

Case series have demonstrated similar efficacies in certain generalized epilepsies such as Lennox-Gastaut syndrome. Although success rates are not usually equal to that of epilepsy surgery, it is a reasonable alternative when the patient is reluctant to proceed with any required invasive monitoring, when appropriate pre surgical evaluation fails to uncover the location of epileptic foci, or when there are multiple epileptic foci.

d) Responsive neurostimulator system (RNS)

(US manufacturer Neuropace) consists of a computerized electrical device implanted in the skull with electrodes implanted in presumed epileptic foci within the brain. The brain electrodes send EEG signal to the device which contains seizure-detection software. When certain EEG seizure criteria are met, the device delivers a small electrical charge to other electrodes near the epileptic focus and disrupt the seizure. The efficacy of the RNS is under current investigation with the goal of FDA approval.

e) Deep brain stimulation (DBS)

(US manufacturer Medtronic) consists of a computerized electrical device implanted in the chest in a manner similar to the VNS, but electrical stimulation is delivered to deep brain structures through depth electrodes implanted through the skull. In epilepsy, the electrode target is the anterior nucleus of the thalamus. The efficacy of the DBS in localization-related epilepsies is currently under investigation.

© 2016 Global Journals Inc. (US)

References Références Referencias

1. BS Chang, DH Lowenstein. Epilepsy. *N. Engl. J. Med*, 2003, 349 (13): 1257–66.
2. Fisher, Robert S, Acevedo C, Arzimanoglou A, Bogacz, A, Cross JH, Elger CE, Engel J, Jr, Forsgren L, French JA, Glynn M, Hesdorffer DC, Lee BI, Mathern GW, Moshe SL, Perucca E, Scheffer IE, Tomson T, Watanabe M, Wiebe S. (April 2014). ILAE Official Report: A practical clinical definition of epilepsy. *Epilepsia*, 2014, 55 (4): 475–82.
3. Epilepsy. Fact Sheets. Worl Health Organization. *October 2012*. Retrieved January 24, 2013.
4. Fisher R, Van Emde Boas W, Blume W, Elger C, Genton P, Lee P, Engel J. Epileptic seizures and epilepsy: definitions proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE). *Epilepsia, 2005*, 46(4): 470–2.
5. Longo, Dan L. Seizures and Epilepsy. Harrison's principles of internal medicine, 18th ed. 2012, McGraw-Hill. pp. 3258.
6. Pandolfo M. Genetics of epilepsy. *Semin Neurol*, 2001, 131(5): 506-18.
7. Eadie MJ. Shortcomings in the current treatment of epilepsy. Expert Review of Neurotherapeutics, 2012, 12 (12): 1419–27.
8. Commission on Classification, International League Against Epilepsy (1981) Proposed provisions of clinical and electroencephalographical classification of epileptic seizures. *Epilepsia* 22, 489-501.
9. Engel J Jr. Report of the ILAE classification core group. *Epilepsia*, 2006, 47, 1558-1568.
10. Engel J. A proposed diagnostic scheme for people with epileptic seizures and with epilepsy: report of the ILAE Task Force on Classification and Terminology. *Epilepsia*, 2001, 42, 796-803.
11. Shorvon S. The etiologic classification of epilepsy. *Epilepsia*, 2011, 52, 1052-1057.
12. Luders H, Amina S, Baumgartner C. Modern technology calls for a modern approach to classification of epileptic seizures and the epilepsies. *Epilepsia*, 2012, 53, 405-411.

© 2016 Global Journals Inc. (US)

Global Journal of Medical Research: a
Neurology and Nervous System
Volume 16 Issue 1 Version 1.0 Year 2016
Type: Double Blind Peer Reviewed International Research Journal
Publisher: Global Journals Inc. (USA)
Online ISSN: 2249-4618 & Print ISSN: 0975-5888

Drug Treatment of Cerebral Vasospasm after Subarachnoid Hemorrhage Following Aneurysms

By Yong-fei Liu, Han-Cheng Qiu, Juan Su & Wei-Jian Jiang

Third Military Medical University

Abstract- Cerebral vasospasm (CVS) is a common and severe complication of aneurysmal subarachnoid hemorrhage (aSAH). Despite the improvement in treatment of aSAH, CVS complicating aSAH has remained the main cause of death. CVS begins most often on the third day after the ictal event and reaches the maximum on the 5th–7th postictal days. Several therapeutic modalities have been employed to prevent or reverse CVS. The aim of this review is to emphatically introduce some kind of pharmacological agent for vasospasm.

Keywords: cerebral vasospasm, subarachnoid hemorrhage, aneurysms, drug treatment.

GJMR-A Classification : NLMC Code: R743.35



Strictly as per the compliance and regulations of:

© 2016. Yong-fei Liu, Han-Cheng Qiu, Juan Su & Wei-Jian Jiang. This is a research/review paper, distributed under the terms of the Creative Commons Attribution-Noncommercial 3.0 Unported License http://creativecommons.org/licenses/by-nc/3.0/), permitting all non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

Drug Treatment of Cerebral Vasospasm after Subarachnoid Hemorrhage Following Aneurysms

Yong-fei Liu [α], Han-Cheng Qiu [σ], Juan Su [ρ] & Wei-Jian Jiang [ω]

Abstract- Cerebral vasospasm (CVS) is a common and severe complication of aneurysmal subarachnoid hemorrhage (aSAH). Despite the improvement in treatment of aSAH, CVS complicating aSAH has remained the main cause of death. CVS begins most often on the third day after the ictal event and reaches the maximum on the 5th–7th posticta l days. Several therapeutic modalities have been employed to prevent or reverse CVS. The aim of this review is to emphatically introduce some kind of pharmacological agent for vasospasm.

Keywords: cerebral vasospasm, subarachnoid hemorrhage, aneurysms, drug treatment.

I. Introduction

Posthemorrhagic cerebral vasospasm (PHCV) is a major cause of death and permanent disability in patients with aneurysmal subarachnoid hemorrhage (aSAH), which may account for almost 50% of the deaths among those surviving in the initial ictus[1]. Despite the improvement in the treatment of aSAH with reduced mortality by almost 50% over the last 20 years[2], angiographic Cerebral vasospasm (CVS) is very common, affecting up to 70% of aSAH patients, which has a predictable time course: delayed onset between day 3 and 5, maximal narrowing between day 5 and 14, and then gradual resolution over week 2–4. Nearly half of these patients, about 30% of all aSAH survivors, will develop a delayed ischemic neurological deficit (DIND), also called symptomatic CVS [1]. The incidence of symptomatic CVS varies between 17% and 48%[3-5]. Although endovascular devices and treatment techniques are continuously developing, these minimally invasive procedures still carry treatment-specific risks. At present drug treatment is still the main therapeutic choice, and this review mainly introduces the recent development of drug treatment.

Author α: The New Era Stroke Care and Research Institute, The Rockets Army General Hospital of PLA, Beijing 100088, China. Third Military Medical University, Chongqing 400038, China.
Author σ ρ: The New Era Stroke Care and Research Institute, The Rockets Army General Hospital of PLA, Beijing 100088, China.
e-mail: cjr.jiangweijian@vip.163.com, sujuan919@126.com
Author ω: New Era Stroke Care and Research Institute, The Rockets Army General Hospital of PLA, Beijing 100088, China.
e-mail: cjr.jiangweijian@vip.163.com

II. Materials and Methods

An extensive literature search through the PubMed, Embase and SciFinder database was performed without language restrictions using the following terms: (cerebral vasospasm) AND (aneurysm subarachnoid hemorrhage) AND (drug OR medicine OR pharmacon) AND (review OR animal experimental OR clinical trial). At present, the most commom drugs for preventing and treating cerebral vasospasm were classified into the following drugs: calcium channel blocker, fasudil, magnesium, statins, hormones, phosphoiesterase inhabitor, endothelin-1 antagonists, nitric oxide, heparin and fibrinolysis.

a) Calcium channel blocker (CCB)

i. *Nimodipine*

Nimodipine is a dihydropyridine agent that blocks voltage-gated calcium channels and has a dilatory effect on arterial smooth muscle. It is the only FDA-approved agent for vasospasm with a half-life of about 9 hours [6]. Its beneficial effect on CVS derives most likely from its neuroprotective properties compared to arterial smooth muscle cell relaxation [7]. Nimodipine may achieve favorable results in angiographic response and clinical outcomes as well as low complication rate. In addition, nimodipine may reduce the risk of secondary cerebral ischemia after aneurysmal haemorrhage. Safety and effectiveness of nimodipine was recently shown in a meta-analysis conducted in 2011, in which administration of nimodipine was contributed to a significant prevention of CVS after aneurysm rupture ($p<0.00001$) [8].

Oral administration of 60mg nimodipine every 4 hours over a period of 21 consecutive days is recommended by the current guidelines of the American Stroke Association [9,10]. Some experts have proposed the scheme of 30mg oral nimodipine every 2h is more conducive to alleviate vasospasm, especially for the patients with low blood pressure [11]. But its efficiency and safety is needed to be evaluated. Intra-arterial (IA) nimodipine infusion is an effective and safe treatment for symptomatic CVS [12,13]. In 2009, one prospective randomized clinical trial showed no difference in ischemia prevention and prognosis improvement between intravenous (IV) and oral administration of

© 2016 Global Journals Inc. (US)

nimodipine [14]. In 2011, Onal et al. [15] performed an experiment in rabbits to investigate the comparative effects of nimodipine administrated by several pathways, and their study showed that selective IA administration of nimodipine and intrathecal injection (IT) of nimodipine were better than IV and oral administration for chronic vasospasm following SAH.

Recently a group of randomized controlled experiments showed that topical administration of nimodipine did not significantly improve cerebral blood flow (CBF) following SAH [16]. These findings were not consistent with our previous data which demonstrated that the topical administration of nimodipine significantly alleviated CVS following aSAH detected by transcranial Doppler (TCD).

During the actual clinical practice, we have used nimodipine as the treatment of aSAH, which was common for vascular spasm. The unresolved issue is to determine how nimodipine improves aSAH outcomes and its mechanism of limiting delayed cerebral ischemia (DCI). In the future more fundamental research is needed to clarify the mechanism of nimodipine.

ii. *Nicardipine*

Nicardipine is a dihydropyridine agent that selectively inhibits calcium ion inflow into the smooth muscle, which is a potent antihypertensive drug. Due to regional selectivity in cerebrovascular smooth muscle, nicardipine has also been investigated in the treatment of vasospasm following aSAH. However, earlier studies showed that nicardipine may be associated with a poor outcome and mortality in patients with CVS.

IA nicardipine is most commonly used in the treatment of CVS after subarachnoid hemorrhage (SAH) mode, which also brings various complications, including pulmonary oedema, prolonged hypotension and renal failure. Interestingly, given those complications caused by nicardipine and the results of many studies that nicardipine does not improve poor outcomes of CVS, its use in clinical practice is controversial. It should be cautious to use IA nicardipine as the treatment of vasospasm, and physicians should be ready to manage the potential severe adverse effects.

In 2005, Hoh et al.[17] revealed significant improvement in TCD velocity studies ($p<0.01$) and improved clinical outcomes in 42% of the patients four days after IA nicardipine treatment, and no drug-related complications were reported. A recent meta-analysis by Huang et al. suggested that the risk of poor outcomes (death, vegetative state, or dependency) was reduced by nicardipine in patients after aneurysmal SAH[18]. In 2011, a review of randomized controlled trials and meta-analyses in the literature revealed that nimodipine demonstrated benefit following aSAH, however, other calcium channel blockers, including nicardipine, did not provide unequivocal benefit[8].

Nicardipine is a second-generation dihydropyridine-type CCB that was developed approximately 30 years ago. Therefore, nicardipine may act in neuroprotection as a preventive factor of the CVS due to its vasodilator property and a peculiar cerebrovascular profile[18]. However, considering individual differences of the patients and hypotension complication, clinical application of nicardipine is still limited. Therefore, additional large Phase III trials are required before this therapeutic approach can be introduced into routine use. Modification of the presented conclusion may be justified after publication of the prospective multicentre clinical trials.

iii. *Verapamil*

Like nimodipine, the CCB verapamil also blocks voltage-gated calcium inflow into the smooth muscle cells of the artery. However, verapamil has been used to treat coronary vasospasm in a long time according to the literatures. Its use in the treatment of refractory coronary spasm is safe and effective, which is also advantageous in availability and low price[19, 20]. Alana et al.[21] prospectively studied the subjects with vasospasm scheduled for cerebral angiography with possible IA injection of verapamil, and their results refuted earlier reports that suggested IA verapamil was not associated with systemic hemodynamic effects. Mikeladze et al.[22] reported a female case which had selective IA administration of verapamil for the treatment of CVS after severe subarachnoid parenchymal hemorrhage due to the internal carotid artery bifurcation aneurysm, and the result showed good clinical outcomes.

Although verapamil is a CCB, it is not selective to cerebral vasculature. There is a controversy as to the systemic hemodynamic effects of IA verapamil. Some studies have indicated no effect of IA verapamil on systemic blood pressure or heart rate [23]. In contrast, Stuart et al. have demonstrated significant reduction in mean arterial blood pressure several hours after IA injection of verapamil in their retrospective study [20]. Although IA administration of verapamil can theoretically alleviate CVS, its clinical application is limited. Moreover, duration of the pharmacological effects of IA verapamil on the cerebral circulation remains unknown. More research is required to evaluate its benefits in preventing delayed ischemic neurological deficits (DINDs) following SAH.

b) Fasudil

Fasudil hydrochloride is a Rho kinase inhibitor, which has inhibitory effect on protein phosphorylation. It has been reported that various protein kinases, such as protein kinase C, light chain kinase and Rho-kinase, may play a critical role in the signal transduction pathway of CVS [24]. Thereby fasudil is contributed to a unique and effective anti-CVS effect without significantly lowering blood pressure. Preoperatively prophylactic

© 2016 Global Journals Inc. (US)

use of anti-spasm drugs significantly reduces intraoperative and postoperative complications [25].

Juan Liu et al. [26] investigated the role of fasudil in preventing CVS in extracranial carotid artery stenting. They retrospectively analyzed 178 patients with unilateral carotid angioplasty and stenting (CAS) who were given IV fasudil hydrochloride during the perioperative period. The results showed that local CVS was absent in 80.9 % patients, asymptomatic vasospasm was observed in 17.4 % patients and symptomatic vasospasm in 1.7 % patients via DSA imaging.

Shin-ichi Satoh et al.[27] used canine and rat model to verify validation effect of fasudil in the treatment of vasospasm and proved the effectiveness. It was suggested that hydroxyfasudil was contributed to the potency of fasudil to prevent CVS and hyperviscosity, and the potential utility of hydroxyfasudil as a therapeutic agent for patients with SAH was also suggested. However, Naraoka M et al.[28] employed the double-hemorrhage rabbit model to investigate whether the combination treatment, consisting of pitavastatin as an inhibitor of RhoA and fasudil as an inhibitor of Rho-kinase, prevented CVS. And the results showed the cross-sectional area of basilar artery were significantly increased only by the combination treatment, and the separate use of fasudil or pitavastatin had no significant effect.

Liu Guang Jian et al. [29] conducted a systematic assessment and meta-analysis on fasudil, which demonstrated that occurrence of CVS and cerebral infarction was greatly reduced by fasudil in SAH patients, and clinical outcomes of the patients (as assessed by the Glasgow Outcome Scale) were significantly improved. Due to the limited number of samples and trials, the conclusion still requires further verification by large randomized controlled clinical trials.

c) Magnesium

Magnesium sulfate is first used in pre-eclamptic pregnant women to reduce uterine smooth muscle contractions. It is a noncompetitive calcium antagonist with several important vascular and potentially neuroprotective effects [30]. Magnesium has the effect of vasodilatation by blocking the voltage-dependent calcium channel and decreasing glutamate release as well as the entry of calcium into the cell [31]. In addition, magnesium also attenuates the effect of various potent vasoconstrictors, such as endothelin 1, and blocks the formation of reactive oxygen species [32].

These potential effects of magnesium on vasodilation and consequent neuroprotection have driven some investigators to study the role of magnesium in preventing CVS and DCI after SAH. Maintenance of a normal magnesium level is reasonable, but the use of a continuous magnesium infusion does not seem to be supported by the evidence [33]. A trial published showed a trend toward an increase in percentage of patients attaining favorable neurological outcomes in the magnesium sulfate group [34]. However, in 2013, one meta-analysis showed that magnesium did not increase the probability of good neurologic outcomes (risk ratio [RR], 1.02; 95% confidence interval [CI], 0.97-1.07; P = .49; 12 trials, n = 2345) or decrease the risks of cerebral infarction [35]. Another randomized controlled trial showed that the patients with a higher serum magnesium concentration had a reduced incidence of vasospasm indicated by angiography, but it was not statistically significant [36]. In 2015, a randomized controlled trial revealed continuous cisternal irrigation with magnesium sulfate solution from Day 4 to Day 14 significantly inhibited CV in patients with aSAH, however, no improvement was found in reducing the incidence of DCI and functional outcomes [37].

The effect of magnesium sulfate in the treatment of aASH is not definite. Early studies have shown that magnesium sulfate is contributed to better outcomes of aASH, but the recent studies demonstrate that magnesium sulfate treatment has no significant effect. Therefore, further research focusing on clinical effect, dosage and side effects, etc., is required in the future.

d) Statins

Statins were discovered in Japan by Kuroda and Akira in 1971[38]. The initial aim was to isolate microbial metabolites capable of inhibiting 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, the main enzyme responsible for the synthesis of cholesterol. Later, some authors found statins had not only cholesterol-lowering effects but also some pleiotropic effects (eg., downregulation of inflammation, upregulation of endothelial and nitric oxide synthesis) [39]. Statins are HMG-CoA reductase inhibitors, which seem to have an important role in vasospasm prevention. The proposed mechanism of the action of statins involves induction of NO pathway and dilation of cerebral vessels, thereby leading to improved cerebral blood flow[40].

In 2005, two small randomized placebo-controlled studies with a total of 119 patients who received either pravastatin or simvastatin showed a reduction of cerebral artery narrowing, less delayed cerebral ischaemic events and an improvement in functional patient outcomes. DINDs were significantly reduced in patients treated with simvastatin. Although many studies have shown that early statins treatment is effective for CVS, its wide use in clinical practice is controversial. In 2010, a randomized, double-blind, placebo-controlled pilot study of simvastatin and a systematic review revealed no significantly beneficial effect of statins in patients with aSAH[41]. In 2013, another trial showed that simvastatin had benefit in reduction of clinical vasospasm and mortality as well as

© 2016 Global Journals Inc. (US)

improvement of functional outcomes, but it was not statistically significant[42]. Recently, meta-analyses for patients with SAH show no benefits of statins-use to reduce the incidence of vasospasm, which was quite different from the results of previous meta-analysis [43,44]. However, whether statin therapy after subarachnoid hemorrhage vasospasm is effective or not remains to be confirmed.

e) Hormones

i. *Erythropoietin (EPO)*

EPO is a 165-amino acid sialoglycoprotein. There are few studies on EPO treatment in aSAH, and most aim at anemia treatment after SAH. Early animal studies and in-vitro experiments have suggested that EPO has a neuroprotective role in cerebral ischaemia [45].

A growing body of evidence has been accumulated regarding the employment of EPO in the management of CVS. However, the mechanism of EPO action to decrease occurrence of vasospasm remains poorly understood. Several different mechanisms such as inflammation limitation, apoptosis inhibition, oxidative damage limitation, and neurogenesis upregulation have been postulated to explain EPO's neuroprotective action [46,47].

In 2010, one review revealed that the use of EPO may not necessarily reduce the incidence of vasospasm after SAH, but it may reduce the severity and its eventual outcome [46]. In 2013, a randomized controlled animal study suggested that timely EPO application in SAH was sufficient to prevent delayed proximal CVS, but the doses were insufficient to improve microcirculation or show directly neuroprotective effect [48].

EPO treatment in CVS after SAH still stays in the animal experiment level, and a large number of prospective clinical studies are lack. Although the number of patients investigated is smaller, this treatment approach may be a promising option in the acute phase of aSAH.

ii. *Estrogen*

Estrogen, specifically 17β-estradiol (E2), possesses powerful vasodilatory, anti-inflammatory, and neuroprotective properties. Though its current use remains limited to in-vivo animal models of experimental SAH, E2 has potential therapeutic implications for ameliorating the DINDs which follow aneurysmal SAH [49]. Derived from cholesterol, E2 is a powerful vasodilator with the potential to prevent or reverse the vasoconstriction which occurs in CVS. Some experiments have shown that estrogen promotes vasodilatation by three mechanisms: (1) attenuating the up-regulation of endothelin-1 receptors after SAH as cited above [50]; (2) inducing the up-regulation of L-type calcium ion channels of smooth muscle cells; (3) decreasing SAH-induced inducible nitric oxide synthase (iNOS) expression, and normal endothelial nitric oxide synthase (eNOS) expression [51].

It is suggested that E2 may have neuroprotective properties as follows (1) E2 decreases expression of the critical proinflammatory cytokine, tumor necrosis factorα(TNFα), by reducing activity of c-JunN-terminal kinase (JNK) [52]; (2) E2 increases expression of the antioxidant thioredoxin (Trx) in a cGMP-dependent manner[53]. Trx decreases oxidation damage and inhibits apoptosis; (3) Neuroglobin (Ngb) is a protein which regulates neuronal oxygen homeostasis by binding to oxygen with a higher affinity than hemoglobin[54]. Recently, we found that, in neurones, Ngb was pivotal for hormone-induced anti-apoptotic effects against H2O2 toxicity, which may protect brain tissue from oxidative inflammatory injury[55], while E2 increased Ngb expression. (4) E2 has been found to exert antiapoptotic effects through upregulation of adenosine A2a receptor (A2aAR) and extracellular signal-regulated kinases 1 and 2 (ERK1/2) expression[56]. (5) The current in vivo evidence presented by Kao et al. [57] implicates Akt signaling pathway in E2-mediated neuroprotection.

Estrogen possesses powerful vasodilatory, anti-inflammatory, and neuroprotective properties, but its current use in CVS remains limited to animal models of experimental SAH. E2 has been successfully used in clinical treatment of CVS and DCI following SAH, but a lot of clinical studies are also required to provide robust evidence[49].

f) Phosphodiesterase Inhibitors

i. *Milrinone*

Milrinone is a phosphodiesterase III inhibitor that affects cyclic adenosine monophosphate (cAMP) pathways with both inotropic and vasodilatory effects. Its first use in CVS after intracranial aneurysm rupture dated back to 2001 [58]. IA milrinone is a safe and effective treatment of CVS after aSAH. A study investigating the effects of milrinone in 14 patients reported a significant improvement of vasospasm assessed by angiographic control ($p<0.0001$) [59].

The specific mechanism of milrinone is unclear. Many authors agree it can improve cerebral microcirculation, without changing cardiac output. Some authors also propose milrinone acts through anti-inflammatory pathway to alleviate CVS[24]. Saurabh et al.[60] reported a patient with severe vasospasm who was treated with continuous IA administration of nimodipine combined with milrinone and excellent result was achieved. Thus they proposed higher dose of these drugs may be used to effectively control severe CVS.

Although it has been showed that continuous IA injection of milrinone, especially combined with other drugs, is effective in relieving CVS, the side effect of hypotension makes its clinical application very limited.

© 2016 Global Journals Inc. (US)

This risk is to thwart the favorable vasodilatory effect on cerebral blood flow. More prospective studies are needed to study which dose is safe and the most effective to patients.

ii. *Papaverine*

Like milrinone, papaverine is a phosphodiesterase inhibitor. The use of papaverine as a vasodilator was instigated by the observation during surgery that papaverine, when applied directly on the arterial wall, relieved arterial vasospasm during aneurysm surgery. For a long time, papaverine has been widely employed in IA vasodilator therapy procedures. However, in the current clinical practice, it is infrequently used given concerns about potential neurotoxicity, including transient or permanent monocular blindness, mydriasis, transient hemiparesis, seizures, gray matter necrosis, cardiac dysfunction, respiratory arrest[61], increased intracranial pressure and irreversible brain tissue damage[62]. IV administration of papaverine is not favorable for CVS because of its vasodilatory effect on the peripheral vasculature and the transient nature of its efficacy [63].

Complications of papaverine make its use in clinical practice very limited. Since papaverine relieves spasm more obviously, some surgeons still use it to ease CVS during operation. Future clinical use of papaverine to treat CVS, and what dose of papaverine can maximize its effect with minimum complications still need further research.

iii. *Cilostazol*

Cilostazol is an anti-platelet drug. It inhibits phosphodiesterase activity of platelet and vascular smooth muscle, thereby increasing its anti-platelet effect and vasodilator effect of cAMP concentration. A multicenter prospective, randomized, open-label blinded end point trial demonstrated effectiveness in oral administration of cilostazol in preventing cerebral vasospasm with a low risk of severe adverse events following aSAH [64]. Niu et al.[65] conducted a systematic review and meta-analysis on the treatment of aSAH patients and found cilostazol significantly decreased the rate of symptomatic CVS ($p < 0.001$), severe CVS ($p = 0.007$), CVS-related cerebral infarcts ($p = 0.001$), and poor outcomes, defined as modified Rankin Scale score of at least 3 at follow-up ($p = 0.011$). Based on this meta-analysis, cilostazol appears to reduce CVS-related morbidity following aSAH without affecting its mortality.

Cilostazol alleviates CVS, but the specific mechanism is unclear. The effect is supported by Shimamura et al.'s study [66] in which cilostazol is used to prevent phenotypic transformation of smooth muscle cells (SMC) along with requisite experimental evidence.

To conquer CVS in its complexity, it is necessary to elucidate its general, underlying mechanism. Additionally, studies with longer follow-up and more detailed functional measurements are required to determine the effect of cilostazol on neurocognitive outcomes following aSAH.

g) *Endothelin-1 Antagonists: Clazosentan*

It is widely accepted that interaction between ET-1 and NO is critical for maintaining adequate cerebral vascular dilatation and sufficient cerebral blood flow during Asah[67]. Clazosentan is one of the most promising pharmacological agents employed for the prevention or reversal of CVS. Animal studies have demonstrated that clazosentan is a competitive endothelin-1 receptor antagonist[68]. It is reported that clazosentan prevents CVS and improves outcomes of aSAH in a dose-dependent manner[69].

Two meta-analyses of randomized controlled trials[70, 71] examined whether clazosentan treatment after aneurysmal SAH significantly reduced the incidence of DINDs and DCI and improved outcomes. Both showed that clazosentan treatment after aneurysmal SAH significantly reduced the incidence of the vasospasm-related DINDs and DCI. However, subsequently a randomized, double-blind, placebo-controlled study[72] claimed that clazosentan did not significantly decrease mortality/vasospasm-related morbidity and increase poor functional outcomes in patients with aneurysmal SAH undergoing surgical clipping.

As the treatment of CVS after aSAH, clazosentan is still controversial, and there is still a long way to go for its wide use in clinical practice. Further study is required to elucidate the dissociation between vasospasm-related morbidity and outcomes.

h) *Nitric Oxide (NO)*

NO is a key signaling molecule in the regulation of cerebral blood flow. Reduced NO in blood and cerebrospinal fluid is a possible mechanism underlying CVS. Hemoglobin released following aneurysmal rupture inhibits NO production by endothelial NO synthase and decreases NO concentration for smooth muscle cells, leading to vasoconstriction[73]. It has been shown that the presence of hemoglobin and its degradation products disrupt signaling between the vascular endothelium and the underlying smooth muscular layer[74]. It has been demonstrated that NO constitutes a potent endogenous vasodilator, which directly acts on vascular smooth cells, causing vascular relaxation [75]. In addition, NO also has neuroprotective function[76].

Earlier studies have demonstrated that decrease of cerebrospinal fluid NO metabolites is observed within 10 min after aSAH, which is associated with vasoconstriction[77]. This is thought to be secondary to destruction of nitric oxide synthase NOS function by haemoglobin. Decreased NO bioavailability is also caused by the reaction of cerebral NO and superoxide anions to produce peroxynitrite [78].

Despite the controversies about NO dysfunction after aSAH, animal evidence has indicated that increasing cerebral NO levels either directly using

© 2016 Global Journals Inc. (US)

inhaled NO or indirectly using NO donors has neuroprotective effects. More prospective randomized controlled experiments are required in the future, and more in-depth research on the clinical application of NO is necessary to provide a more reliable basis for its clinical application.

i) Heparin

Heparin is a pleiotropic drug, which has many effects on antagonizing molecular mechanisms of secondary brain injury after aSAH, including endothelin mediated vasoconstriction, the activity of free radicals and antifibrotic effects. A recent study has revealed that low-dose intravenous heparin infusion in patients with aSAH may reduce occurrences of symptomatic vasospasm and infarcts with high safety and efficacy [79]. An double-blind, randomized comparison of enoxaparin versus placebo has showed that enoxaparin may reduce CVS and ischemia following SAH (Hunt Hess grades I–III) [80]. However, more trials about dose and safety assessment of heparin after aSAH will be needed to reduce or prevent related complications and improve outcomes.

j) Fibrinolysis

The severity of CVS may be associated with the volume and distribution of the subarachnoid clots. Intraventricular fibrinolysis has been clinically tested to faster clearance of subarachnoid clots since the early 1990s. Intracisternal administration of low-dose rt-PA for the prevention of CVS after SAH has been demonstrated safe and effective [81]. Recently, a randomized, open-label phase II study on concomitant low-frequency head-motion therapy and intraventricular rt-PA has been administrated in patients after surgical or endovascular treatment for aSAH, with effective subarachnoid clot reduction, despite a poor effect on radiographic vasospasm, cerebral infarction, or neurological outcome [82]. Though clearance of subarachnoid clots to prevent CVS has been accepted, optimal administration and dosage of fibrinolysis still need to be established.

III. Results

At present, there are many CVS medications, including calcium channel blockers, phosphodiesterase inhibitors, endothelin antagonist-1, hormones, nitric oxide preparation, etc. Administration is also various, including oral, intra arterial injection, intravenous injection, intrathecal injection, etc. However, oral administration of nimodipine is still a valid approach for the treatment of CVS, which is also the only FDA-approved agent for treatment of vasospasm. During clinical practice, clinicians rarely use a single drug, and the combined use of two or more drugs is more common.

IV. Discussion

CVS is a potentially devastating complication that occurs in nearly half of patients who survive within the first 24h after aSAH from a ruptured cerebral aneurysm. Subsequent DCI and/or DINDs are contributed to death of these patients. Early prevention and/or treatment of CVS are very important. The pathogenesis of CVS is a complex process, which is still not very clear. Thus the treatment is relatively difficult. At present, drug treatment is still the main therapeutic choice to prevent or reverse CVS, especially oral administration of nimodipine. Although endovascular devices and treatment techniques are continuously developing, these minimally invasive procedures still carry treatment-specific risks. Transluminal balloon angioplasty is probably a more durable intervention, and posterior cerebral artery may also be amenable to angioplasty. Angioplasty should be considered a complementary choice to intraarterial vasodilator therapy; angioplasty should be reserved for proximal vessels and vasodilator therapy is more useful for distal or diffuse disease. Although these IA vasodilators available may increase vessel diameter, there is still lacking convincing evidence about improvement in clinical outcomes of the patients.

V. Conclusion

Vasospasm still represents a challenging problem after aSAH. Its pathogenesis is not clear, although there have been many researches on the treatment of CVS. There are abundant treatment schemes, but only oral nimodipine is proved to be effective. Several IA vasodilators are also available, but they merely increase the diameter of blood vessels without robust evidence of improving clinical outcomes of the patients. This discrepancy may be explained by the fact that vasospasm is not the sole factor responsible for poor functional outcomes. More in-depth study on the pathogenesis of CVS and targeted research of the effective treatments are required, so as to improve poor outcomes of the patients and reduce the related mortality and morbidity of CVS.

List of abbreviations

CVS	cerebral vasospasm
aSAH	aneurysmal subarachnoid hemorrhage
PHCV	posthemorrhagic cerebral vasospasm
DIND	delayed ischemic neurological deficit
SAH	subarachnoid hemorrhage
CCB	calcium channel blocker
IA	intra-arterial
IV	intravenous
IT	intrathecal injection
CBF	cerebral blood flow
TCD	transcranial Doppler
DCI	cerebral ischemia

© 2016 Global Journals Inc. (US)

CAS carotid angioplasty and stenting
HMG-CoA 3-hydroxy-3-methylglutaryl coenzyme A
EPO Erythropoietin; iNOS: nitric oxide synthase
eNOS endothelial nitric oxide synthase
TNFα tumor necrosis factorα
JNK c-JunN-terminal kinase
Trx thioredoxin
Ngb Neuroglobin
A2aAR A2a receptor
ERK1/2 extracellular signal-regulated kinases 1 and 2
cAMP cyclic adenosine monophosphate
NO Nitric Oxide

Competing interests

The authors declare that this work does not involve competing interests.

VI. Acknowledgments

We acknowledged the reviewers for making significant revision of the manuscript.

References Références Referencias

1. Bederson JB, Connolly EJ, Batjer HH, Dacey RG, Dion JE, Diringer MN, et al. Guidelines for the management of aneurysmal subarachnoid hemorrhage: A statement for healthcare professionals from a special writing group of the Stroke Council, American Heart Association. *Stroke*. 2009; 40: 994-1025.
2. Lovelock CE, Rinkel GJ, Rothwell PM. Time trends in outcome of subarachnoid hemorrhage: Population-based study and systematic review. *Neurology*. 2010; 74: 1494-1501.
3. Murayama Y, Malisch T, Guglielmi G, Mawad ME, Vinuela F, Duckwiler GR, et al. Incidence of cerebral vasospasm after endovascular treatment of acutely ruptured aneurysms: Report on 69 cases. *J Neurosurg*. 1997; 87: 830-835.
4. Yalamanchili K, Rosenwasser RH, Thomas JE, Liebman K, McMorrow C, Gannon P. Frequency of cerebral vasospasm in patients treated with endovascular occlusion of intracranial aneurysms. AJNR Am *J Neuroradiol*. 1998; 19: 553-558.
5. Charpentier C, Audibert G, Guillemin F, Civit T, Ducrocq X, Bracard S, et al. Multivariate analysis of predictors of cerebral vasospasm occurrence after aneurysmal subarachnoid hemorrhage. *Stroke*. 1999; 30: 1402-1408.
6. Keyrouz SG, Diringer MN. Clinical review: Prevention and therapy of vasospasm in subarachnoid hemorrhage. *Crit Care*. 2007; 11: 220.
7. Castanares-Zapatero D, Hantson P. Pharmacological treatment of delayed cerebral ischemia and vasospasm in subarachnoid hemorrhage. *ANNALS OF INTENSIVE CARE*. 2011;1.
8. Velat GJ, Kimball MM, Mocco JD, Hoh BL. Vasospasm after aneurysmal subarachnoid hemorrhage: Review of randomized controlled trials and meta-analyses in the literature. *World Neurosurg*. 2011; 76: 446-454.
9. Raya AK, Diringer MN. Treatment of subarachnoid hemorrhage. *Crit Care Clin*. 2014; 30: 719-733.
10. Rabinstein AA, Lanzino G, Wijdicks EF. Multidisciplinary management and emerging therapeutic strategies in aneurysmal subarachnoid haemorrhage. *Lancet Neurol*. 2010; 9: 504-519.
11. MacKenzie M, Gorman SK, Doucette S, Green R. Incidence of and factors associated with manipulation of nimodipine dosage in patients with aneurysmal subarachnoid hemorrhage. *Can J Hosp Pharm*. 2014; 67: 358-365.
12. Hänggi D, Perrin J, Eicker S, Beseoglu K, Etminan N, Kamp MA, et al. Local delivery of nimodipine by Prolonged-Release microparticles—feasibility, effectiveness and Dose-Finding in experimental subarachnoid hemorrhage. *PLoS ONE*. 2012; 7: e42597.
13. Ott S, Jedlicka S, Wolf S, Peter M, Pudenz C, Merker P, et al. Continuous selective intra-arterial application of nimodipine in refractory cerebral vasospasm due to aneurysmal subarachnoid hemorrhage. *Biomed Res Int*. 2014; 2014: 970741.
14. Kronvall E, Undren P, Romner B, Saveland H, Cronqvist M, Nilsson OG. Nimodipine in aneurysmal subarachnoid hemorrhage: A randomized study of intravenous or peroral administration. *J Neurosurg*. 2009; 110: 58-63.
15. Onal MB, Civelek E, Kircelli A, Solmaz I, Ugurel S, Narin F, et al. Comparison of nimodipine delivery routes in cerebral vasospasm after subarachnoid hemorrhage: An experimental study in rabbits. *Acta Neurochir Suppl*. 2011; 110: 23-28.
16. Wang F, Yin Y, Jia F, Jiang J. Effects of Topical Administration of Nimodipine on Cerebral Blood Flow following Subarachnoid Hemorrhage in Pigs. *Journal of Neurotrauma*. 2013; 30: 591-596.
17. Hoh BL, Ogilvy CS. Endovascular treatment of cerebral vasospasm: Transluminal balloon angioplasty, intra-arterial papaverine, and intra-arterial nicardipine. *Neurosurg Clin N Am*. 2005; 16: 501-516.
18. Huang R, Jiang F, Feng Z, Wang T. Nicardipine in the treatment of aneurysmal subarachnoid haemorrhage: A meta-analysis of published data. *Acta Neurologica Belgica*. 2013; 113: 3-6.
19. Jun P, Ko NU, English JD, Dowd CF, Halbach VV, Higashida RT, et al. Endovascular treatment of medically refractory cerebral vasospasm following aneurysmal subarachnoid hemorrhage. *AJNR Am J Neuroradiol*. 2010; 31: 1911-1916.
20. Stuart RM, Helbok R, Kurtz P, Schmidt M, Fernandez L, Lee K, et al. High-dose intra-arterial verapamil for the treatment of cerebral vasospasm after subarachnoid hemorrhage: Prolonged effects

© 2016 Global Journals Inc. (US)

on hemodynamic parameters and brain metabolism. *Neurosurgery*. 2011; 68: 337-345, 345.
21. Flexman AM, Ryerson CJ, Talke PO. Hemodynamic stability after intraarterial injection of verapamil for cerebral vasospasm. *Anesthesia & Analgesia*. 2012; 114: 1292-1296.
22. Mikeladze KG, Eliava S, Shekhtman OD, Lubnin A, Tabasaranskii TF, Iakovlev SB. Intra-arterial injection of verapamil in treatment of cerebral vasospasm in a patient with acute subarachnoid hemorrhage from an aneurysm: Case report. *Zh Vopr Neirokhir Im N N Burdenko*. 2013; 77: 57-60, 60.
23. Keuskamp J, Murali R, Chao KH. High-dose intraarterial verapamil in the treatment of cerebral vasospasm after aneurysmal subarachnoid hemorrhage. *J Neurosurg*. 2008; 108: 458-463.
24. Muroi C, Seule M, Mishima K, Keller E. Novel treatments for vasospasm after subarachnoid hemorrhage. *Current Opinion in Critical Care*. 2012; 18: 119-126.
25. Schirmer CM, Hoit DA, Malek AM. Iatrogenic vasospasm in carotid artery stent angioplasty with distal protection devices. *Neurosurg Focus*. 2008; 24: E12.
26. Liu J, Yao G, Zhou H, Jiang X, Xie P. Clinical investigation of fasudil for the prevention of cerebral vasospasm in extracranial carotid artery stenting. *Cell Biochemistry and Biophysics*. 2014; 68: 185-188.
27. Satoh S, Takayasu M, Kawasaki K, Ikegaki I, Hitomi A, Yano K, et al. Antivasospastic effects of hydroxyfasudil, a Rho-Kinase inhibitor, after subarachnoid hemorrhage. *Journal of Pharmacological Sciences*. 2012; 118: 92-98.
28. Naraoka M, Munakata A, Matsuda N, Shimamura N, Ohkuma H. Suppression of the Rho/Rho-kinase pathway and prevention of cerebral vasospasm by combination treatment with statin and fasudil after subarachnoid hemorrhage in rabbit. *Transl Stroke Res*. 2013; 4: 368-374.
29. Liu GJ, Wang ZJ, Wang YF, Xu LL, Wang XL, Liu Y, et al. Systematic assessment and meta-analysis of the efficacy and safety of fasudil in the treatment of cerebral vasospasm in patients with subarachnoid hemorrhage. *European Journal of Clinical Pharmacology*. 2012; 68: 131-139.
30. Taccone FS, Castanares-Zapatero D, Peres-Bota D, Vincent JL, Berre' J, Melot C. Cerebral autoregulation is influenced by carbon dioxide levels in patients with septic shock. *Neurocrit Care*. 2010; 12: 35-42.
31. van den Bergh WM, Dijkhuizen RM, Rinkel GJ. Potentials of magnesium treatment in subarachnoid haemorrhage. *Magnes Res*. 2004; 17: 301-313.
32. Ortega-Gutierrez S, Mayer SA. Is the magnesium era for aneurysmal subarachnoid hemorrhage over? *Curr Neurol Neurosci Rep*. 2010; 10: 420-422.
33. Diringer MN, Bleck TP, Claude HJR, Menon D, Shutter L, Vespa P, et al. Critical care management of patients following aneurysmal subarachnoid hemorrhage: Recommendations from the Neurocritical Care Society's Multidisciplinary Consensus Conference. *Neurocrit Care*. 2011; 15: 211-240.
34. van den Bergh WM, Algra A, van Kooten F, Dirven CM, van Gijn J, Vermeulen M, et al. Magnesium sulfate in aneurysmal subarachnoid hemorrhage: A randomized controlled trial. *Stroke*. 2005; 36: 1011-1015.
35. Golan E, Vasquez DN, Ferguson ND, Adhikari NKJ, Scales DC. Prophylactic magnesium for improving neurologic outcome after aneurysmal subarachnoid hemorrhage: Systematic review and meta-analysis. *Journal of Critical Care*. 2013; 28: 173-181.
36. Bradford CM, Finfer S, O'Connor A, Yarad E, Firth R, McCallister R, et al. A randomised controlled trial of induced hypermagnesaemia following aneurysmal subarachnoid haemorrhage. *Crit Care Resusc*. 2013; 15: 119-125.
37. Yamamoto T, Mori K, Esaki T, Nakao Y, Tokugawa J, Watanabe M. Preventive effect of continuous cisternal irrigation with magnesium sulfate solution on angiographic cerebral vasospasms associated with aneurismal subarachnoid hemorrhages: a randomized controlled trial. *J Neurosurg*. 2015; 31: 1-9.
38. Endo A, Kuroda M, Tanzawa K. Competitive inhibition of 3-hydroxy-3-methylglutaryl coenzyme a reductase by ML-236A and ML-236B fungal metabolites, having hypocholesterolemic activity. *FEBS Lett*. 1976; 72: 323-326.
39. Bautista C. Unresolved issues in the management of aneurysmal subarachnoid hemorrhage. *AACN Advanced Critical Care*. 2012; 23: 175-185.
40. Yamada M, Huang Z, Dalkara T, Endres M, Laufs U, Waeber C, et al. Endothelial nitric oxide synthase-dependent cerebral blood flow augmentation by L-arginine after chronic statin treatment. *J Cereb Blood Flow Metab*. 2000; 20: 709-717.
41. Vergouwen MD, de Haan RJ, Vermeulen M, Roos YB. Effect of statin treatment on vasospasm, delayed cerebral ischemia, and functional outcome in patients with aneurysmal subarachnoid hemorrhage: A systematic review and meta-analysis update. *Stroke*. 2010; 41: e47-e52.
42. Garg K, Sinha S, Kale SS, Chandra PS, Suri A, Singh MM, et al. Role of simvastatin in prevention of vasospasm and improving functional outcome after aneurysmal sub-arachnoid hemorrhage: A prospective, randomized, double-blind, placebo-controlled pilot trial. *Br J Neurosurg*. 2013; 27: 181-186.
43. Su SH, Xu W, Hai J, Wu YF, Yu F. Effects of statins-use for patients with aneurysmal subarachnoid

© 2016 Global Journals Inc. (US)

hemorrhage: a meta-analysis of randomized controlled trials. *Sci Rep*. 2014; 4: 4573.
44. Junhui Liu, Qianxue Chen. Effect of statins treatment for patients with aneurysmal subarachnoid hemorrhage: a systematic review and meta-analysis of observational studies and randomized controlled trials. *Int J Clin Exp Med*. 2015; 8(5): 7198–7208.
45. Kumral A, Ozer E, Yilmaz O, Akhisaroglu M, Gokmen N, Duman N, et al. Neuroprotective effect of erythropoietin on hypoxic-ischemic brain injury in neonatal rats. *Biol Neonate*. 2003; 83: 224-228.
46. Turner JD, Mammis A, Prestigiacomo CJ. Erythropoietin for the treatment of subarachnoid hemorrhage: A review. *World Neurosurg*. 2010; 73: 500-507.
47. Jerndal M, Forsberg K, Sena ES, Macleod MR, O'Collins VE, Linden T, et al. A systematic review and meta-analysis of erythropoietin in experimental stroke. *J Cereb Blood Flow Metab*. 2010; 30: 961-968.
48. Güresir E, Vasiliadis N, Konczalla J, Raab P, Hattingen E, Seifert V, et al. Erythropoietin prevents delayed hemodynamic dysfunction after subarachnoid hemorrhage in a randomized controlled experimental setting. *Journal of the Neurological Sciences*. 2013; 332: 128-135.
49. Ding D, Starke RM, Dumont AS, Owens GK, Hasan DM, Chalouhi N, et al. Therapeutic implications of estrogen for cerebral vasospasm and delayed cerebral ischemia induced by aneurysmal subarachnoid hemorrhage. *BioMed Research International*. 2014; 2014: 1-9.
50. Lin CL, Dumont AS, Wu SC, Wang CJ, Howng SL, Huang YF, et al. 17Beta-estradiol inhibits endothelin-1 production and attenuates cerebral vasospasm after experimental subarachnoid hemorrhage. *Exp Biol Med (Maywood)*. 2006; 231: 1054-1057.
51. Lin CL, Shih HC, Dumont AS, Kassell NF, Lieu AS, Su YF, et al. The effect of 17beta-estradiol in attenuating experimental subarachnoid hemorrhage-induced cerebral vasospasm. *J Neurosurg*. 2006; 104: 298-304.
52. Srivastava S, Weitzmann MN, Cenci S, Ross FP, Adler S, Pacifici R. Estrogen decreases TNF gene expression by blocking JNK activity and the resulting production of c-Jun and JunD. *J Clin Invest*. 1999; 104: 503-513.
53. Lee SY, Andoh T, Murphy DL, Chiueh CC. 17Beta-estradiol activates ICI 182,780-sensitive estrogen receptors and cyclic GMP-dependent thioredoxin expression for neuroprotection. *FASEB J*. 2003; 17: 947-948.
54. Burmester T, Weich B, Reinhardt S, Hankeln T. A vertebrate globin expressed in the brain. *Nature*. 2000; 407: 520-523.
55. De Marinis E, Acaz-Fonseca E, Arevalo MA, Ascenzi P, Fiocchetti M, Marino M, et al. 17Beta-Oestradiol anti-inflammatory effects in primary astrocytes require oestrogen receptor beta-mediated neuroglobin up-regulation. *J Neuroendocrinol*. 2013; 25: 260-270.
56. Lin CL, Dumont AS, Tsai YJ, Huang JH, Chang KP, Kwan AL, et al. 17Beta-estradiol activates adenosine A(2a) receptor after subarachnoid hemorrhage. *J Surg Res*. 2009; 157: 208-215.
57. Kao CH, Chang CZ, Su YF, Tsai YJ, Chang KP, Lin TK, et al. 17Beta-Estradiol attenuates secondary injury through activation of Akt signaling via estrogen receptor alpha in rat brain following subarachnoid hemorrhage. *J Surg Res*. 2013; 183: e23-e30.
58. Arakawa Y, Kikuta K, Hojo M, Goto Y, Ishii A, Yamagata S. Milrinone for the treatment of cerebral vasospasm after subarachnoid hemorrhage: Report of seven cases. *Neurosurgery*. 2001; 48: 723-728, 728-730.
59. Shankar JJ, Dos SM, Deus-Silva L, Lum C. Angiographic evaluation of the effect of intra-arterial milrinone therapy in patients with vasospasm from aneurysmal subarachnoid hemorrhage. *Neuroradiology*. 2011; 53: 123-128.
60. Anand S, Goel G, Gupta V. Continuous intra-arterial dilatation with nimodipine and milrinone for refractory cerebral vasospasm. *Journal of neurosurgical anesthesiology*. 2014; 26: 92.
61. Chowdhury FH, Haque MR. Severe hypotension, cardiac arrest, and death after intracisternal instillation of papaverine during anterior communicating artery aneurysm clipping. A case report. *Acta Neurochir (Wien)*. 2013; 155: 281-282.
62. Rahme R, Jimenez L, Pyne-Geithman GJ, Serrone J, Ringer AJ, Zuccarello M, et al. Endovascular management of posthemorrhagic cerebral vasospasm: Indications, technical nuances, and results. *Acta Neurochir Suppl*. 2013; 115: 107-112.
63. Deshaies EM, Boulos AS, Drazin D, Popp AJ. Evidence-based pharmacotherapy for cerebral vasospasm. *Neurological Research*. 2009; 31: 615-620.
64. Senbokuya N, Kinouchi H, Kanemaru K, Ohashi Y, Fukamachi A, Yagi S, et al. Effects of cilostazol on cerebral vasospasm after aneurysmal subarachnoid hemorrhage: a multicenter prospective, randomized, open-label blinded end point trial. *J Neurosurg*. 2013; 118: 121-30.
65. Niu PP, Yang G, Xing YQ, Guo ZN, Yang Y. Effect of cilostazol in patients with aneurysmal subarachnoid hemorrhage: A systematic review and meta-analysis. *J Neurol Sci*. 2014; 336: 146-151.
66. Shimamura N, Ohkuma H. Phenotypic transformation of smooth muscle in vasospasm

© 2016 Global Journals Inc. (US)

after aneurysmal subarachnoid hemorrhage. *Transl Stroke Res*. 2014; 5: 357-364.
67. Siasios I, Kapsalaki EZ, Fountas KN. Cerebral vasospasm pharmacological treatment: An update. *Neurology Research International*. 2013; 2013: 1-20.
68. Vatter H, Zimmermann M, Tesanovic V, Raabe A, Schilling L, Seifert V. Cerebrovascular characterization of clazosentan, the first nonpeptide endothelin receptor antagonist clinically effective for the treatment of cerebral vasospasm. Part I: Inhibitory effect on endothelin(A) receptor-mediated contraction. *J Neurosurg*. 2005; 102: 1101-1107.
69. Povlsen GK, Edvinsson L. MEK1/2 inhibitor U0126 but not endothelin receptor antagonist clazosentan reduces upregulation of cerebrovascular contractile receptors and delayed cerebral ischemia, and improves outcome after subarachnoid hemorrhage in rats. *J Cereb Blood Flow Metab*. 2015; 35: 329-37.
70. Wang X, Li YM, Li WQ, Huang CG, Lu YC, Hou LJ. Effect of clazosentan in patients with aneurysmal subarachnoid hemorrhage: a meta-analysis of randomized controlled trials. *PLoS One*. 2012; 7: e47778.
71. Shen J, Pan JW, Fan ZX, Xiong XX, Zhan RY. Dissociation of vasospasm-related morbidity and outcomes in patients with aneurysmal subarachnoid hemorrhage treated with clazosentan: A meta-analysis of randomized controlled trials. *J Neurosurg*. 2013; 119: 180-189.
72. Macdonald RL, Higashida RT, Keller E, Mayer SA, Molyneux A, Raabe A, et al. Randomised trial of clazosentan, an endothelin receptor antagonist, in patients with aneurysmal subarachnoid hemorrhage undergoing surgical clipping (CONSCIOUS-2). *Acta Neurochir Suppl*. 2013; 115: 27-31.
73. Kim H, Britton GL, Peng T, Holland CK, McPherson DD, Huang SL. Nitric oxide-loaded echogenic liposomes for treatment of vasospasm following subarachnoid hemorrhage. *Int J Nanomedicine*. 2014; 9: 155-16579.
74. Fathi AR, Bakhtian KD, Pluta RM. The role of nitric oxide donors in treating cerebral vasospasm after subarachnoid hemorrhage. *Acta Neurochir Suppl*. 2011; 110:93-97.
75. Clatterbuck RE, Gailloud P, Tierney T, Clatterbuck VM, Murphy KJ, Tamargo RJ. Controlled release of a nitric oxide donor for the prevention of delayed cerebral vasospasm following experimental subarachnoid hemorrhage in nonhuman primates. *J Neurosurg*. 2005; 103: 745-751.
76. Garry PS, Ezra M, Rowland MJ, Westbrook J, Pattinson KTS. The role of the nitric oxide pathway in brain injury and its treatment — From bench to bedside. *Experimental Neurology*. 2015; 263: 235-243.
77. Sehba FA, Schwartz AY, Chereshnev I, Bederson JB. Acute decrease in cerebral nitric oxide levels after subarachnoid hemorrhage. *J Cereb Blood Flow Metab*. 2000; 20: 604-611.
78. Radi R. Peroxynitrite, a stealthy biological oxidant. *J Biol Chem*. 2013; 288: 26464-26472.
79. Simard JM, Aldrich EF, Schreibman D, James RF, Polifka A, Beaty N. Low-dose intravenous heparin infusion in patients with aneurysmal subarachnoid hemorrhage: a preliminary assessment. *J Neurosurg*. 2013; 119: 1611-1619.
80. Wurm G, Tomancok B, Nussbaumer K, Adelwöhrer C, Holl K. Reduction of ischemic sequelae following spontaneous subarachnoid hemorrhage: a double-blind, randomizedcomparison of enoxaparin versus placebo. *Clin Neurol Neurosurq*. 2004; 106: 97-103.
81. Yamamoto T, Esaki T, Nakao Y, Mori K. Efficacy of low-dose tissue-plasminogen activator intracisternal administration for the prevention of cerebral vasospasm after subarachnoid hemorrhage. *World Neurosurg*. 2010; 73: 675–682.
82. Etminan N, Beseoglu K, Eicker SO, Turowski B, Steiger HJ, Hänggi D. Prospective, randomized, open-label phase II trial on concomitant intraventricular fibrinolysis and low-frequencyrotation after severe subarachnoid hemorrhage. *Stroke*. 2013; 44: 2162-2168.

© 2016 Global Journals Inc. (US)

Global Journal of Medical Research: a
Neurology and Nervous System
Volume 16 Issue 1 Version 1.0 Year 2016
Type: Double Blind Peer Reviewed International Research Journal
Publisher: Global Journals Inc. (USA)
Online ISSN: 2249-4618 & Print ISSN: 0975-5888

Evaluation of Neurobehavioural and Cognitive Changes Induced by Carbamazepine and/or Phenytoin in Wistar Rats

By H. Aliyu, J. O. Ayo, S. F. Ambali, A. U. Zezi, P. I. Kobo & C. Uchendu

Ahmadu Bello University, Zaria

Abstract- The study was to evaluate the neurobehavioural and cognitive changes in Wistar rats administered carbamazepine (CBZ), phenytoin (PHE) and their combination. Forty, apparently, healthy adult male Wistar rats weighing about 300 g were divided into four groups of 10 animals each. Group I rats were administered distilled water at 10 ml/kg. CBZ, 20 mg/kg, PHE 100 mg/kg and CBZ+PHE, 20 mg/kg and 100 mg/kg respectively were administered to groups II, III and IV, per os. The regimens were given once daily for eight weeks, the rats were monitored for neurobehavioural and cognitive changes. The results showed that administration of CBZ, CBZ+PHE and PHE decreased ($P < 0.05$) locomotion of the treated rats. Rearing decreased ($P < 0.05$) in rats treated with PHE. Cognition was not significantly affected by the treatments. In conclusion, chronic administration of CBZ, PHE and CBZ+PHE decreased locomotion, while PHE alone decreased rearing in Wistar rats.

Keywords: cognitive function, carbamazepine, phenytoin, locomotion, short-term memory, rearing.

GJMR-A Classification : NLMC Code: WM 170

EVALUATIONOFNEUROBEHAVIOURALANDCOGNITIVECHANGESINDUCEDBYCARBAMAZEPINEANDORPHENYTOININWISTARRATS

Strictly as per the compliance and regulations of:

Open Association of Research Society, USA
Research | Diversity | Ethics

© 2016. H. Aliyu, J. O. Ayo, S. F. Ambali, A. U. Zezi, P. I. Kobo & C. Uchendu. This is a research/review paper, distributed under the terms of the Creative Commons Attribution-Noncommercial 3.0 Unported License http://creativecommons.org/licenses/by-nc/3.0/), permitting all non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

Evaluation of Neurobehavioural and Cognitive Changes Induced by Carbamazepine and/or Phenytoin in Wistar Rats

H. Aliyu [α], J. O. Ayo [σ], S. F. Ambali [ρ], A. U. Zezi [ω], P. I. Kobo [¥] & C. Uchendu [§]

Abstract- The study was to evaluate the neurobehavioural and cognitive changes in Wistar rats administered carbamazepine (CBZ), phenytoin (PHE) and their combination. Forty, apparently, healthy adult male Wistar rats weighing about 300 g were divided into four groups of 10 animals each. Group I rats were administered distilled water at 10 ml/kg. CBZ, 20 mg/kg, PHE 100 mg/kg and CBZ+PHE, 20 mg/kg and 100 mg/kg respectively were administered to groups II, III and IV, *per os*. The regimens were given once daily for eight weeks, the rats were monitored for neurobehavioural and cognitive changes. The results showed that administration of CBZ, CBZ+PHE and PHE decreased ($P < 0.05$) locomotion of the treated rats. Rearing decreased ($P < 0.05$) in rats treated with PHE. Cognition was not significantly affected by the treatments. In conclusion, chronic administration of CBZ, PHE and CBZ+PHE decreased locomotion, while PHE alone decreased rearing in Wistar rats.

Keywords: cognitive function, carbamazepine, phenytoin, locomotion, short-term memory, rearing.

I. Introduction

Epilepsy is a disorder of the brain, characterized by an enduring predisposition to generate at least one seizure (Fisher *et al*., 2005). The term 'epilepsy' is usually restricted to those cases with a tendency for recurrent seizures (Nair, 2003). It has been reported that patients with epilepsy are at substantial risk of memory impairment, and results obtained from animal studies have demonstrated impaired hippocampal function as measured by spatial memory in rodents subjected to seizures (Zhou *et al*., 2007). Therefore, memory impairment is one of the neurobehavioural complications associated with epilepsy (Ali *et al*., 2003).

It was reported that rather than being overtly manifest, subtle changes in cognitive and psychomotor functions do occur commonly with long-term antiepileptic drug therapy, especially PHE sodium (Meador *et al*., 1991). However, recent findings indicate that rats with focal onset of spontaneous seizures respond to treatment following antiepileptic drug administration; but like humans, the responses to antiepileptic drugs can vary substantially between animals (Nissinen and Pitkanen, 2007). Polytherapy in epilepsy is a preferred treatment regimen in patients with intractable seizures (Macdonald and Meldrum, 1995). Rational polypharmacy of antiepileptic drugs is one of the treatment strategies for refractory epilepsy (Sun *et al*., 2002). Antiepileptic drugs, particularly those used in polytherapy, are the main causes of cognitive impairment in epileptic patients (Bernadi and Barros, 2004). However, the effects of some of the drug combinations on neurobehavioural and cognitive changes have not been elucidated. Carbamazepine (CBZ) is an anticonvulsant used to treat epilepsy and mood disorders (Almgrem *et al*., 2008). It is administered alone or in combination with other medications to treat certain types of seizures in patients with epilepsy (Porter and Meldrum, 2007). Its main function is reduction of sustained repetitive firing in neurones by blocking voltage-gated sodium channels (Mathew *et al*., 2011). It also potentiates gamma-aminobutyric acid (GABA) receptors (Granger *et al.,* 1995). Thus, CBZ exerts therapeutic effects via inhibition of brain neuronal activities. The drug is widely used in Nigeria for the treatment of seizure disorders and trigeminal and other neuralgias (Shannon and Love, 2004). Phenytoin sodium (PHE), a hydantoin anticonvulsant, is one of the classical antiepileptic drugs (Kšerk *et al*., 1998) and its systemic administration induces anticonvulsant effects in humans and experimental animals (Rykaczewska-Czerwińska, 2007). It is used widely in the treatment of generalized or partial seizures, except absence seizures (Vijay *et al*., 2009). It acts by blocking sodium channels and inhibits persistent sodium currents in neurones, thus inhibiting neuronal firing in the brain (Bryan and Waxman, 2005). It has also been shown to protect against axonal degeneration of spinal cord axons, and it improves neurological outcome of experimental allergic encephalomyelitis in mice (Luszcki, 2004). Unfortunately, none of the new antiepileptic drugs is superior in efficacy to the older drugs in terms of seizure remission (Shannon and Love, 2005).

Author α ¥ §: Department of veterinary pharmacology and Toxicology, Ahmadu Bello University, Zaria. e-mails: haliyu63@gmail.com, patriciabako@yahoo.com, uchech@yahoo.com
Author σ: Department of Veterinary Physiology, Ahmadu Bello University, Zaria. e-mail: ayojo94@yahoo.com
Author ρ: Department of Veterinary Physiology and Pharmacology, University of Ilorin, Ilorin. e-mail: fambali2001@yahoo.com
Author ω: Department of pharmacology and Therapeutics, Faculty of Pharmaceutical Sciences, Ahmadu Bello University, Zaria. e-mail: auzezi@yahoo.com

© 2016 Global Journals Inc. (US)

II. Objective

The objective of the present study was to evaluate the effects of long-term administration of a combination of CBZ and PHE on neurobehavioural and cognitive changes in Wistar rats.

III. Materials and Methods

a) Animals

For the present study, 40 adult male Albino rats weighing between 144 and 300 g were used for the experiment. The animals were obtained from the animal house of the Department of Veterinary Pharmacology and Toxicology, Ahmadu Bello University, Zaria and were housed in rat cages. The animals were given access to feed pellets made from growers' mash (Grand Cereals, Jos, Nigeria), maize bran and groundnut cake in the ratio 4:2:1, with wheat flour serving as binder, and water was provided *ad libitum.* The animals were allowed to acclimatize for a period of two weeks before the commencement of the experiment. The animals were divided at random into four groups of 10 animals each. Rats in groups II, III and IV were given CBZ (20 mg/kg), PHE (100 mg/kg) and CBZ+PHE (20 and 100 mg/kg separately), respectively. Rats in group I were given distilled water at 10 ml/kg and served as the untreated control. All treatments were administered orally by gavage once daily for a period of eight weeks. During this period, the rats were monitored for clinical and neurobehavioural signs.

b) Anticonvulsant drugs

The anticonvulsant drugs used in this study were CBZ tablets (Hovid Bhd, Malaysia) at 20 mg/kg (Rajesh *et al*., 1991) and PHE capsules (Biomedicine, Belgium) at 100 mg/kg (Vijay *et al*., 2009)

c) Evaluation of locomotor activity

The effect of the regimens on locomotor activity was evaluated weekly till the end of the experiment using the open-field apparatus (Zhu *et al*., 2001). The open-field apparatus was constructed using cardboard box (50 × 50 × 46 cm high) with clear Plexiglas on the floor. The floor of the box was divided into 25 equal squares. The locomotor activity was assessed by placing a rat in the box and allowing it to roam freely for 3 minutes to familiarize itself with the environment. The number of squares crossed with all the paws during the next 2 minutes was recorded. The arena was cleaned first with soapy water, followed by 90% alcohol solution to eliminate odours from the preceding animal.

d) Evaluation of rearing activity

Rearing activity was evaluated weekly till the end of the experiment, using the open-field apparatus (Zhu *et al*., 2001). Rearing was assessed by placing a rat in the box and allowing it to roam freely for 3 minutes to familiarize itself with environment. The number of times an animal stood on its hind limb trying to peep out of the box in the next 2 minutes was recorded. Soapy water followed by 90% alcohol solution was used to clean the arena.

e) Assessment of learning

This experiment was performed 48 hours prior to the termination of the study. It was done using the step-down inhibitory avoidance learning task as (Zhu *et al*., 2001). The apparatus used was made of 40 × 25 × 25cm acrylic chamber, consisting of a floor made of parallel 2 mm calibre stainless steel bars spaced 1 cm apart. An electric shock was administered through the floor bars. A 25cm high, 8cm by 25cm wooden platform was placed at the extreme end of the chamber. Each animal was placed gently on the platform; upon stepping down, the rat received a single 80 volts foot-shock. If the animal did not return to the platform, the foot-shock was repeated every 5 seconds. A rat was considered to have learned the avoidance task if it remained on the platform for more than 2 minutes. The number of foot-shocks applied before the animal learned the avoidance task was recorded as an index of learning acquisition.

f) Assessment of short-term memory

Memory was also assessed using the step-down inhibitory avoidance task (Zhu *et al*., 2001). The apparatus used was the same as that described for learning. Briefly, individual rats were again placed gently on the platform 24 hours after performing the learning task. The time during which the animal remained on the platform was recorded as an index of memory retention. Staying of the rat on the platform for 2 minutes was counted as maximum memory retention (ceiling response).

The research was carried out according to the Ahmadu Bello University Animal Research Committee and in accordance with the National Institutes of Health Guide for Care and Use of Laboratory Animals (Publication number 85-23), revised 1985, also according to the Guidelines for the use of animals in Neuroscience Research, 1992.

g) Statistical analysis

Values obtained were calculated as mean ± SEM and analysed using one-way analysis of variance (ANOVA).The differences between the variant means were separated using Tukey's post-hoc test. GraphPad prism version 4.0 for windows from GraphPad Software, San Diego, Carlifonia, USA (www.graphpad.com) was used for the analysis. Values of $P < 0.05$ were considered significant.

IV. Results

a) Effect of treatments on locomotion in Wistar rat

There were significant ($P < 0.05$) decreases in the number of squares crossed by rats in the CBZ and

© 2016 Global Journals Inc. (US)

CBZ+PHE groups. The number of squares crossed by rats in the PHE group decreased significantly ($P < 0.01$), when compared to that of the control group, and no significant ($P > 0.05$) change in the number of squares crossed by rats was obtained when the treatment groups were compared (Figure 1).

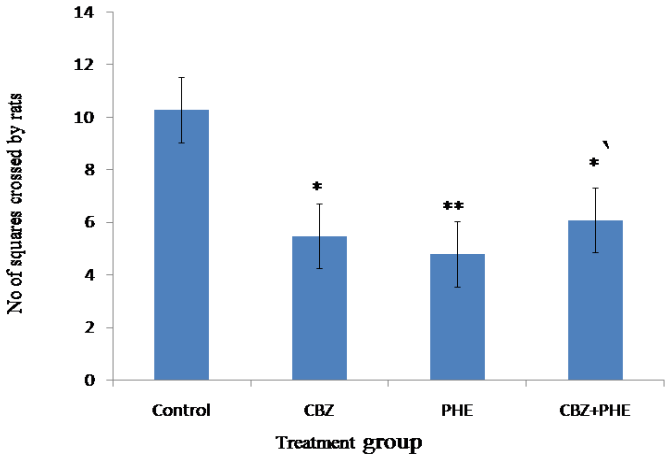


Figure 1 : Effect of repeated administrations of carbamazepine (CBZ) and/or phenytoin (PHE) on locomotion in Wistar rats (n = 10)

**(P < 0.05), **(P < 0.01)*

b) Effect of treatments on rearing activity in Wistar rats

There was a significant ($P < 0.05$) decrease in rearing in the PHE group when compared to the control group. There was no significant ($P > 0.05$) change in the CBZ and CBZ+PHE groups when compared to control. Likewise rearing did not change when the treatment groups were compared. (Figure 2).

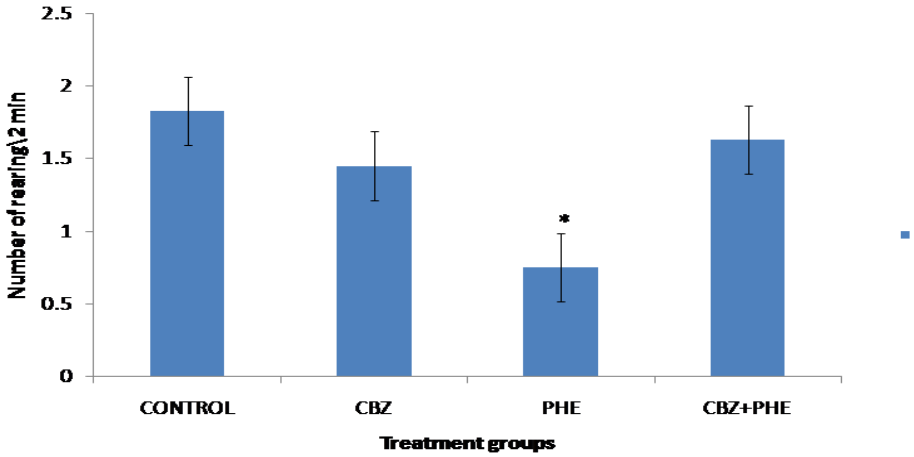


Figure 2 : Effect of repeated administrations of carbamazepine (CBZ) and/or phenytoin (PHE) on rearing activity in Wistar rats (n = 10)

**(P < 0.05)*

c) Effect of treatments on learning ability in Wistar rats

There was no significant ($P > 0.05$) change in the number of foot-shocks when the drug-treated groups were compared to the control group. Similarly, there was no significant ($P > 0.05$) change in the number of foot-shocks applied in between the treatment groups (Figure 3).

© 2016 Global Journals Inc. (US)

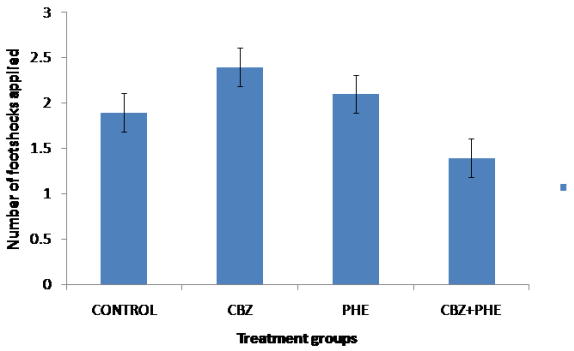


Figure 3 : Effect of repeated administrations of carbamazepine (CBZ) and/or phenytoin (PHE) on learning ability in Wistar rats (n = 10)

Values are not significantly different (P > 0.05)

d) Effect of treatments on short-term memory in Wistar rats

There was no significant (P > 0.05) change in the duration of stay on the platform when the treatment groups were respectively compared to the control group. The changes observed were insignificant (P > 0.05) between the treatment groups (Figure 4).

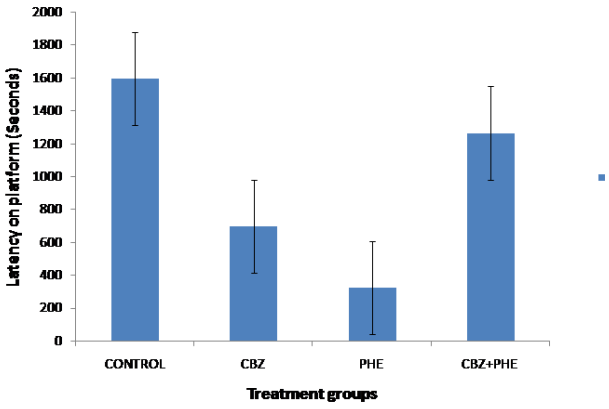


Figure 4 : Effect of repeated administrations of carbamazepine (CBZ) and/or phenytoin (PHE) on short-term memory in Wistar rats (n = 10)

Values are not significantly different (P > 0.05)

V. Discussion

The decrease in locomotion recorded in the CBZ group agreed with the findings of (Luszcki, 2004), who reported a decrease in ambulatory activity and total distance covered in mice administered with CBZ. Nowakowska *et al.* (2011) also attributed the decrease in locomotor activity in the CBZ monotherapy in rats to the sedative effects of the drug, and suggested that this may be related to the induction of microsomal enzymes of the P_{450} cytochrome.

The decrease in locomotion (Fig. 1) observed with the polytherapy group agrees with the findings of Luszcki (2004) who reported that combining two sodium-channel blockers may result in a considerable reduction in locomotor activity of the animals tested; which, apparently, induced the potentiation rather than the summation of hypolocomotor effects produced by the combination of the antiepileptic drugs.

Rearing

Rearing reflects adaptive strategy of animals to explore their environment and also responses to environmental novelty and emotional states, such as stress levels in rodents (Ambali, 2009). Rearing responses observed upon repeated exposure to the same environment are strongly influenced by inter-individual differences in habituation and this could be influenced by a variety of pharmacologic and toxicologic agents (Ambali, 2009).

The decrease in rearing activity (Fig. 2) in the PHE-treated group agreed with the findings of Thakur *et al*. (2011), which attributed the decrease to the central nervous system depressant effect of the drug. This

© 2016 Global Journals Inc. (US)

finding may also be caused by the inhibition of calcium-induced secretory processes, including hormones and neurotransmitters released as a result of decrease in calcium permeability, with inhibition of calcium influx across the membrane (Porter and Meldrum, 2007). Kšerk *et al*. (1998) reported that PHE modulates the direct activation of the motor system by stimulating the sensorimotor cortex in the adult, but not immature, rats.

VI. Conclusion

Chronic administration of CBZ and CBZ+PHE decreased locomotion but PHE alone decreased rearing in Wistar rats. Patients taking these drugs should therefore be adequate monitoring while taking their medications and if the aforementioned signs are noticed should be placed on alternative medications.

VII. Acknowledgement

I appreciate the efforts of Prof SF Ambali who designed the work, Prof and Dr. JO Ayo and AU Zezi who went through the manuscript and made appropriate corrections and contributions for a better write-up. Drs. PI Kobo and C Uchendu who assisted with the laboratory work. Thank you all.

References Références Referencias

1. Ali A, Pillai KK, and Pal SN. Effect of folic acid and lamotrigine therapy in some rodent models of epilepsy and behaviour. Journal Pharmarcy and Pharmacology, 2003. 3:387-91.
2. Almgrem M, Nyengaard JR, Persson B. and Lavebralt, C. Carbamazepine protects against neuronal hyperplasia and abnormal gene expression in the megencephaly mouse. Neurobiology Diseases, 2008. 32:364-76.
3. Ambali, SF. Ameliorative effect of vitamins C /or E on neurotoxic, haematological and biochemical changes induced by chronic chlorpyrifos in Wistar rats. Doctor of Philosophy Dissertation. Ahmadu Bello University, Zaria. 2009. 355pp.
4. Bernardi RB and Barros HMT Carbamazepine enhances discriminative memory in a rat model of epilepsy. Epilepsia, 2004. *15*:1443-7.
5. Bryan CH and Waxman SG. Neuroprotection by sodium channel blockade with phenytoin in an experimental model of glaucoma. Investigative Ophthalmology and Visual Science, 2005. 46(11): 4164-4169.
6. Fisher RS, VanEmde Boas W, Blume W, Elger G, Genlon P, Lee P and Engel J. Jr. Epileptic seizure and epilepsy: definitions proposed by the International League against Epilepsy and the International Bureau for Epilepsy. Epilepsia, 2005. 4:470-2.
7. Granger P, Biton B, and Faure C. Modulation of GABA type A receptors by the antiepileptic drugs carbamazepine and phenytoin. Molecular Pharmacology, 1995. 47:1189-6.
8. Kšerk P, Haugvicovă P and Mareš P. Age-dependent phenytoin effects on cortical stimulation in rats. Physiology Research, 1998. 47:143-9.
9. Luszcki JJ. Effect of lamotrigine alone or in combination with conventional antiepileptic drugs on locomotor activity in mice. Indian Journal of Pharmacology, 2004. 5:306-1.
10. Macdonald RL, and Meldrum BS. Principles of antiepileptic drug action. Eds.: Mattson, RH and Meldrum, BS In: Antiepileptic Drugs. 4th Ed., Raven Press, New York. 1995. P. 61-78.
11. Meador KJ, Loring D, Allen ME, Zamrini EY, Moore EE. and Abney OL. Comparative cognitive effects of carbamazepine and phenytoin in healthy adults. Neurology, 1991. 41: 1537-40.
12. Mathew J, Gangadharam G, Karuvilla KP and Paulose CS. Behavioural deficit and decreased GABA receptor functional regulation in the hippocampus of epileptic rats: effects of *Bacopa monnieri*. Neurochemical Research, 2011. 36(1): 7-16.
13. Nair DR. 2003. Epilepsy. Cleveland Clinic Foundation. http://wwww.clvelandclinicmeded.com/medicalpubs/diseasemanagement/neuroly/epileptic-syndrome. Access date February 28, 2008.
14. Nissinen J and Pitkanen A. Effect of antiepileptic drugs on spontaneous seizures in epileptic rats. Epilepsy Research, 2007. 2:181-91.
15. Nowakowska E, Kus K, Polanski A, Burda K, Nowakoska A. and Sadowski C. Concomittant use of carbamazepine and olanzepine and the defect on some behavioural functions in rats. Pharmacology and Reproduction, 2011. 63: 372-80.
16. Porter RJ and Meldrum BS. Antiseizure drugs. Ed.: Katzung, BG *In*: Basic and Clinical Pharmacology, 10th Ed., New York, McGraw-Hill. 2007. PP. 374-394
17. Rajesh KR, Surendra R, and Thangam J. Effect of valproic acid and carbamazepine on learning and memory in rats. Indian Journal of Pharmacology, 1991. 30: 185-8.
18. Rykaczewska-Czerwińska M. Antinociceptive effect of phenytoin in rats. Pharmacology Reports, 2007. 59(1): 144-149.
19. Shannon HE and Love PL. Effects of antiepileptic drugs on working memoras assessed by spatial alteration performance in rats. Epilepsy and Behaviour, 2004. 5(6): 857-865.
20. Shannon HE and Love PL. Effects of antiepileptic drugs on attention as assessed by five-choice serial reaction time task in rats. Epilepsy and Behaviour, 2005. 7(4): 620-628.
21. Sun M, Van Rijn CM, Liu Y and Wang M. Combination of carbamazepine and valproate in different dose proportions in maximal electroshock

© 2016 Global Journals Inc. (US)

seizure model in mice. Epilepsy Research, 2002. 1-2: 5-11.
22. Thakur S, Saraswathy GR and Maheswari E. Effect of vitamin C supplementation on phenytoin-induced behavioural abnormalities and regional lipid peroxidation in rats. International Journal of Pharmacology Technology, 2011. 2: 2248-69.
23. Vijay P, Yeshwanth R and Bairy KL. (2009). Effect of phenytoin sodium on biochemical parameters of reproductive function in male albino Wistar rats. Available at: www.j-pbs.org/pdf/221/JPBS081001.pdf, Accessed on 8/2/2010.
24. Zhou JL, Shatskikh TN, Liu Y and Wang M. Impaired single cell firing and long-term potentiation parallels memory impairement following recurrent seizures. European Journal of Neuroscience, 2007. 12: 3667-77.
25. Zhu H, Robin W, Rockhold RW, Baker RC, Kramer R E and Ho IK. Effects of single or repeated dermal exposure to methyl parathion on behaviour and blood cholinesterase in rats. Journal of Biomedical Sciences, 2001. 8: 467-74.

© 2016 Global Journals Inc. (US)

Global Journal of Medical Research: a
Neurology and Nervous System
Volume 16 Issue 1 Version 1.0 Year 2016
Type: Double Blind Peer Reviewed International Research Journal
Publisher: Global Journals Inc. (USA)
Online ISSN: 2249-4618 & Print ISSN: 0975-5888

Epilespy and Enuresis of Teenagers and Young Adults: Attitudes, Practices and Knowledge in Togo

By Kokou Mensah Guinhouya, Nyinevi Anayo, Léhleng Agba, Mofou Belo & Agnon Ayeola Koffi Balogou

Université de Lomé

Abstract- *Introduction:* Enuresis is a public health issue, especially in the tropical areas and sometimes leads to dehumanizing and humiliating practices. Various etiologies can explain the occurrence of enuresis of teenagers and adults, especially epilepsy.

Materials and Methods: We have carried out a prospective study on enuresis and epilepsy in Togo. After the phase of recruiting enuresis and epilepsy patients at CHU- SO, an investigation phase followed in three main cultural areas in Togo and focused on three groups of people: the custodians of collective knowledge, the general population (120) and the medical staff (225). Open-ended questions were about the knowledge and the behaviors in case of enuresis as the only symptom of epilepsy.

Results: Enuresis is not considered like a manifestation of epilepsy in most subjects interviewed. This poor knowledge epilepsy seems to explain the relative tolerance in patients with enuresis within the society. But some attitudes and practices in the case of enuresis reveal risks of "social death" just like in non-treated epileptic subjects. On the other hand, adult subjects with enuresis revealed attitudes and practices that are conducive to care for the patients with enuresis and epilepsy.

Keywords: *enuresis, epilepsy, attitudes, practices, togo.*

GJMR-A Classification : *NLMC Code: WL 385, WS 322*



Strictly as per the compliance and regulations of:



© 2016. Kokou Mensah Guinhouya, Nyinevi Anayo, Léhleng Agba, Mofou Belo & Agnon Ayeola Koffi Balogou. This is a research/ review paper, distributed under the terms of the Creative Commons Attribution-Noncommercial 3.0 Unported License http://creativecommons.org/licenses/by-nc/3.0/), permitting all non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

Epilespy and Enuresis of Teenagers and Young Adults: Attitudes, Practices and Knowledge in Togo

Kokou Mensah Guinhouya [α], Nyinevi Anayo [σ], Léhleng Agba [ρ], Mofou Belo [ω] & Agnon Ayeola Koffi Balogou [¥]

Abstract- Introduction: Enuresis is a public health issue, especially in the tropical areas and sometimes leads to dehumanizing and humiliating practices. Various etiologies can explain the occurrence of enuresis of teenagers and adults, especially epilepsy.

Materials and Methods: We have carried out a prospective study on enuresis and epilepsy in Togo. After the phase of recruiting enuresis and epilepsy patients at CHU- SO, an investigation phase followed in three main cultural areas in Togo and focused on three groups of people: the custodians of collective knowledge, the general population (120) and the medical staff (225). Open-ended questions were about the knowledge and the behaviors in case of enuresis as the only symptom of epilepsy.

Results: Enuresis is not considered like a manifestation of epilepsy in most subjects interviewed. This poor knowledge epilepsy seems to explain the relative tolerance in patients with enuresis within the society. But some attitudes and practices in the case of enuresis reveal risks of "social death" just like in non-treated epileptic subjects. On the other hand, adult subjects with enuresis revealed attitudes and practices that are conducive to care for the patients with enuresis and epilepsy.

Conclusion: Once the attitudes and practices of the patients with enuresis and epilepsy are known, better strategies can be developed for a better care for these patients in order to rescue them from "social death".

Keywords: enuresis, epilepsy, attitudes, practices, togo.

I. Introduction

Enuresis (E) is the uncontrolled micturition during sleep. The International Children's Continence Society defines enuresis as an intermittent urinary incontinence or a sullying of the bed during sleep by a person under 5 [1]. This terminology is applicable only after bladder control acquisition or after 5 years, and is one of the most frequent pediatric disease [1]. Enuresis is a public health issue, especially in the tropical areas and sometimes leads to dehumanizing and humiliating practices. Various etiologies can explain the occurrence of enuresis of teenagers and adults, especially epilepsy. Actually, apart from headaches, epilepsy is the most frequent neurological pathology seen in the world. [2]. The World Health Organization believes that the number of epileptic subjects all over the world is about 50 million and that 80% of that number is found in the tropical latitudes [3]. Epilepsy is also a major public health issue considering its medical, social, cultural and economic consequences both for the epileptic patients and for the society. Epilepsy, just like any other disease, including enuresis, cannot be separated from its own social and cultural context. Each community, each society has its own peculiar vision about it and which is not without repercussion the care provided [4]. Il seemed interesting for us to study one of the unknown symptoms of the Epilepsy of the teenager and the young adult in Black Africa, namely enuresis. For us, knowing this vision seems to be a fact that cannot be overlooked if we want to put up a policy of information, sensitization and education adapted to social and cultural realities regarding epilepsy in Togo.

Author α σ ρ ω: Division of Neurology at CHU Sylvanus OLYMPIO; BP 57; 30284, Lomé- Togo. e-mail: herve_guinhouya@yahoo.fr
Author ¥: Division of Neurology at CHU du Campus.

II. Materials and Methods

Our study is carried out at the Clinic of Neurology, CHU Sylvanus OLYMPIO (CHU-SO), Lomé, Togo. It is a prospective crosscutting study carried out in two steps.

The first phase is carried out at the Clinic of Neurology, CHU-SO in patients with enuresis from January 1 to December 31, 2014. All the patients involved in our study have been recruited from January 1 to December 31. Each one of the patients involved has been monitored for three years. Patients that have consulted a practitioner for enuresis during that period of the study and whose electroencephalogram revealed epilepsy were included to our study. All the patients involved in our study have been checked in the division of urology, CHO-SO in order to eliminate any uroorganic affection. The patients that don't meet the inclusion criteria were excluded.

The second phase included collecting answers to a questionnaire from all the patients involved in the study, from their families and the medical staff of CHU-SO. Les various questionnaires used were inspired by the WHO standardized and validated protocols. They were translated into the local language when the need arises and tested before the survey. The surveys were

© 2016 Global Journals Inc. (US)

carried out the same team trained by a neurologist, a general practitioner from the same region with the patient, a psychologist and a medicine student from the same region with the patient. Finally, the surveys in general took into consideration three groups of people: the custodians of the family knowledge, the patients and the general population, as well as the medical staff. All the surveys complied with ethics and were validated by the National Health Commission. The Togolese League against Epilepsy provided a funding of 500 euros to pay all those involved in the phase of the survey with the custodians of collective knowledge in the interior of Togo.

Togo is a West African country with a population of about 6,500,000 inhabitants in 2010. CHU-SO is the first national health care center of reference in Togo with 1050 workers. These workers include 320 Medical Doctors, 105 Advanced Health Technicians, 93 midwives, 150 nurses and 382 nurse's aids. All the categories of the population go there to consult on a regular basis. Togo is featured by a subdivision in five economic regions (Savannah, Kara, Central, Plateau and Maritime Regions) and an ethnic map made up of three major cultural areas (Para Gourma, Kabyè and Adja Ewe).

For the survey with the medical staff at CHU-SO, the questionnaires were about the definition, the curability, the diagnosis and the place of enuresis in epilepsy. Over a total of 300 questionnaires distributed to the medical staff of CHU-SO, 252 have been exploited (42 Medical Doctors, 54 Advanced Health Technicians, 48 midwives, 58 nurses and 50 nurse's aids).

The participants in these study were drawn at random.

The survey with the patients and their families was preceded by the identification of the seniors of the family or the village of origin of the family. These "custodians of collective knowledge", called the tradition and culture keepers included well-known and famous healers in their respective regions, elders, notables and traditional chiefs,… They were 90 in number and were identified four months before the surveys stated thanks to the cooperation of the parents. The data collection technique was the oral questioning with an interview guide. The answers were recorded in writing and on tape recorder. The survey with the custodians of collective knowledge focused on enuresis as a symptom of epilepsy: knowing and ignoring that enuresis is the manifestation of epilepsy; attitudes and practices in case of enuresis during epilepsy: therapeutic baths, therapeutic rituals, initiation rituals, contagiousness. The questions were open-ended; a content analysis was done for the answers to the questions. We used the chi2 correlation and validation test of Mandel Haenszel for the qualitative comparisons. The links between the variables were considered as statistically significant at the probability threshold of $p \leq 0.05$.

III. Results

During the period of our study, 104 patients were checked for enuresis. 15 patients had a normal electroencephalogram, 12 patients had an organic and/or urologic etiology that could explain the enuresis. Finally, 10 patients were lost. 67 patients that complied with our inclusion criteria were monitored till the end of the study. Our results will therefore focus on these 67 patients. We dealt with 21 female patients and 46 male patients i.e. a sex-ratio of 2.19. The mean age of the patients was 15.15±6.9 years with extremes of 10 years and 36 years. 18 (26.86%) patients were between 10 and 12 years old. 44 (65.68%) patients consulted for enuresis, followed by 15 (22.38%) cases of epilepsy associated with convulsive attacks and by 8 (11.94%) cases of enuresis with fainting. According to the period of occurrence of the enuresis, 48 (71.64%) patients had nighttime enuresis, 12 (17.91%) had daytime and nighttime enuresis and 2 (2.98%) had a daytime enuresis. In 5 (7.47%) patients, the type of enuresis has not been specified. Finally, 57 (85%) patients had a secondary enuresis.

Attitudes, Practices and Knowledge

Table 1 : The answers of the medical staff

	Medical Doctors (N= 42)	Nurses (N= 58)	Midwives (N= 48)	Nurse's Aids (N= 50)	Advanced Technicians (N= 54)
Enuresis as unique symptom of epilepsy	10 (23.80%)	12 (20.68%)	8 (16.66%)	2 (4%)	9 (16.66%)
Right definition of epilepsy	12 (28.57%)	4 (6.89%)	5 (10.41%)	3 (6%)	10 (18.51%)
Right answers on curability of associated with epilepsy	20 (47.61%)	18 (31.03%)	22 (45.83%)	10 (20%)	16 (29.62%)

© 2016 Global Journals Inc. (US)

Table 2 : The answers of the custodians of collective knowledge

	Adja Ewe (N= 30)	Kabyè Tem (N= 30)	Para Gourma (N= 30)
Enuresis as unique symptom of epilepsy: right answer	5 (20%)	5 (20%)	3 (10%)
Ritual baths: naked in pond with toads	30 (100%)	25 (83.33%)	30 (100%)
Ritual practices: carry the wet mat (with urine) around the area or the village and be shouted at	30 (100%)	30 (100%)	30 (100%)
Right answer on contagiousness	30 (100%)	30 (100%)	30 (100%)
Right answer on curability	30 (100%)	30 (100%)	30 (100%)

In general, enuresis is not known as a manifestation of epilepsy, this explains the fact that the patients with enuresis and epilepsy are not systematically excluded like the other epileptic patients in our country, which usually leads to a "social death" of the subject affected. In fact, this ignorance about enuresis as a possible symptom of epilepsy gives room to patients with enuresis to speak in meetings, to share the meat from hunting, to do his daily business without assistance and to participate in initiation ceremonies. Even if the "secret" seems to be usually well kept by the family cell, the patient with enuresis just like any other epileptic patient also undergoes "social death" as testified by the low number of wedding or the high number of divorce in these patients. Actually, enuresis is seen in the teenager and in the young adult in general as a shameful and dirty disease, mentioning that name alone can be horrible. It is therefore hidden from anybody who is not from the family circle. Very often, the subjects of our study had a "peculiar medical" background. This includes ritual baths in a pond or with water already used by toads for bathing, or carry the wet mat (with urine) around the area or the village and be shouted at. These humiliating and dehumanizing practices usually leave psychological aftereffects.

IV. Discussion

This study carried out in the division of neurology at CHU-SO, is somehow biased and this should be underlined. Because of the recruitment done in neurology, the study had a selection bias. Some patients with enuresis have been taken care of in other divisions at CHU-SO. Furthermore, some patients were excluded from our study due to the fact that the para clinical check-up was not done since this check-up is fully at the expenses of the patient. Nevertheless, despite the challenges relating to this type of study in the context of a developing country, where majority of the population is illiterate and where one has to do with questioning, it seems like the studies that are appropriate for this matter are the prospective ones. Johnson in the USA [5], who worked in a very different context, also thinks that prospective study even if it is controlled, is the better method to assess health care institutions.

Majority of the patients in our study was men with a sex-ratio of 2.19. This male predominance can be explained by social and cultural realities and believes [6]. It is in fact clear that the desire to marry is so strong that men with enuresis, after any traditional care attempt has failed, end up coming to consult, while women in the tropics where the society is style dominated by men, prefer to "hide" instead of confessing that they are suffering from this "dirty" and shameful affection [7].

The analysis of the perception of enuresis as a unique manifestation of epilepsy is very low both within the medical body, as well as within the population in general. This can be explained by the fact that enuresis a very frequent pediatric disease [8] which persistence in the adult is not considered as secondary to a pathology but a continuity of the pediatric disease. But primary enuresis only reveals epilepsy in exceptional cases [8]. Secondary enuresis can be the unique symptom that brings to mind epilepsy with nighttime convulsive attacks, mostly in adults. But is possible have favorable and unfavorable elements from the answers of our study. The favorable elements are represented by the curability of enuresis and its non-contagiousness unanimously acknowledged by all the groups that participated in the survey. This will facilitate the introduction of a modern treatment after an etiologic research. The most important unfavorable element lies in the ignorance of enuresis as a symptom epilepsy in the majority of the subjects interviewed. In the medical staff, 23.80% of the Medical Doctors interviewed recognized enuresis as a symptom of epilepsy. This worrisome situation translates without any doubt, the need for a total review of training curricula.

A special attention should be paid to chronical diseases. Unlike the other epileptics, who, according to Apetse and al [9], seem to have a special status in the community, the patient with enuresis, because of the ignorance of its possible etiologies, doesn't seem to suffer from social rejection. But very curious ritual baths are performed in order to get rid of this affection. All these rituals, according to the sociologist Kpegba [10], are in connection with water and purification. Actually, bathing with water infested by toads i.e. polluted water, should be appropriate to remove enuresis which is seen as pollution. With the aversion and the shame witnessed

© 2016 Global Journals Inc. (US)

by the patient with enuresis, a better bladder check-up should be done by the patient for him to avoid enuresis. The same topics seem to be found in a practice which consist of moving in the street with the bed or the polluted mat (with urines). Shame, loss of self-esteem generated could only have one goal which is making the patient with enuresis react for a permanent bladder check-up. All these dehumanizing practices that cause the patient with enuresis "disclose him/herself" for "help" from the community will finally produce the opposite effect in patients with enuresis and epilepsy since these practices will not heal epilepsy. Due to the fact that enuresis is persistent in the subjects that "disclosed" themselves to the community will end up leading to impossibility to marry, set up a family, which is "social death".

V. Conclusion

As the attitudes and practices of the patients with enuresis and epilepsy are known, better strategies can be developed for a better care for these patients in order to rescue them from "social death". This possible positive evolution can only be effective with the improvement of the level education and the establishment of a programme of health education and primary health care.

Conflict of interests: no

References Bibliograhiques

1. Nevéus T, von Gontard A, Hoebeke P, Hjälmås K, Bauer S, Bower W, Jørgensen TM, Rittig S, Walle JV, Yeung CK, et al. The standardization of terminology of lower urinary tract function in children and adolescents: report from the Standardisation Committee of the International Children's Continence Society. J Urol 2006; 176: 314-24.
2. De Toffol B, Autret A. Epilepsie. In: Serratrice G, Autret A (éds.). Neurologie. Paris: Ellipses; 1996.
3. OMS. Campagne mondiale contre l'epilepsie. Faire sortir l'epilepsie de l'ombre en Afrique. Geneve: OMS, 2000.
4. Pilard M, Brosset C, Junod A. Les représentations sociales et culturelles de l'épilepsie. Med Afr Noire 1992; 39: 652-7.
5. Johnson WG. The costs of epilepsy and cost-based evaluations of anticonvulsants. Pharmacoeconomics. 1997; 12: 446–59.
6. OMS. L'épilepsie: conséquences sociales et aspects économiques. Genève: OMS; 2001.
7. Guinhouya KM, Aboki A, Kombaté D, Kumako V, Apétsé K, Mofou B, Agnon A Balogou, Kodjo E Grunitzky. Déficits de traitement et épilepsie dans six unités de soins périphériques du Togo de 2007 à 2009.
8. Minki Baek, Kwanjin Park, Hahn-Ey Lee, Ju Hyung Kang, Hong Jin Suh, Ji Hong Kim, Sang Don Lee, Ki Soo Pai, Sang Won Han, Yong Hoon Park, Kyung Do Kim. A Nationwide Epidemiological Study of Nocturnal Enuresis in Korean Adolescents and Adults: Population Based Cross Sectional Study. J Korean Med Sci 2013; 28: 1065-1070.
9. Kossivi Apetse, Komi Assogba, Mofou Belo, Damelan Kombate, Vinyo Kumako, Kokou M. Guinhouya, Kokou Kevi, Koffi A.A. Balogou, Éric K. Grunitzky. Perception de l'épilepsie de l'enfant et de l'adulte par la population et le personnel soignant au Togo. Cahiers Santé vol. 20, n° 2,avril-mai-juin 2010.
10. Kpegba K.A. Des pratiques et des rituels au Togo. Lomé: Harmattan, 2006.

© 2016 Global Journals Inc. (US)

Global Journals Inc. (US) Guidelines Handbook 2016

www.GlobalJournals.org

FELLOWS

FELLOW OF ASSOCIATION OF RESEARCH SOCIETY IN MEDICAL (FARSM)

Global Journals Incorporate (USA) is accredited by Open Association of Research Society (OARS), U.S.A and in turn, awards "FARSM" title to individuals.The 'FARSM' title is accorded to a selected professional after the approval of the Editor-in-Chief/Editorial Board Members/Dean.



- The "FARSM" is a dignified title which is accorded to a person's name viz. Dr. John E. Hall,Ph.D., FARSS or William Walldroff, M.S., FARSM.

FARSM accrediting is an honor. It authenticates your research activities. After recognition as FARSM, you can add 'FARSM' title with your name as you use this recognition as additional suffix to your status. This will definitely enhance and add more value and repute to your name. You may use it on your professional Counseling Materials such as CV, Resume, and Visiting Card etc.

The following benefits can be availed by you only for next three years from the date of certification:

FARSM designated members are entitled to avail a 40% discount while publishing their research papers (of a single author) with Global Journals Incorporation (USA), if the same is accepted by Editorial Board/Peer Reviewers. If you are a main author or co-author in case of multiple authors, you will be entitled to avail discount of 10%.

Once FARSM title is accorded, the Fellow is authorized to organize a symposium/seminar/conference on behalf of Global Journal Incorporation (USA). The Fellow can also participate in conference/seminar/symposium organized by another institution as representative of Global Journal. In both the cases, it is mandatory for him to discuss with us and obtain our consent.





You may join as member of the Editorial Board of Global Journals Incorporation (USA) after successful completion of three years as Fellow and as Peer Reviewer. In addition, it is also desirable that you should organize seminar/symposium/conference at least once.

We shall provide you intimation regarding launching of e-version of journal of your stream time to time.This may be utilized in your library for the enrichment of knowledge of your students as well as it can also be helpful for the concerned faculty members.

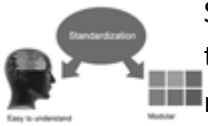


© Copyright by Global Journals Inc.(US) | Guidelines Handbook

The FARSM can go through standards of OARS. You can also play vital role if you have any suggestions so that proper amendment can take place to improve the same for the benefit of entire research community.



As FARSM, you will be given a renowned, secure and free professional email addres with 100 GB of space e.g. johnhall@globaljournals.org. This will include Webmail, Spam Assassin, Email Forwarders,Auto-Responders, Email Delivery Route tracing, etc.



The FARSM will be eligible for a free application of standardization of their researches. Standardization of research will be subject to acceptability within stipulated norms as the next step after publishing in a journal. We shall depute a team of specialized research professionals who will render their services for elevating your researches to next higher level, which is worldwide open standardization.



The FARSM member can apply for grading and certification of standards of their educational and Institutional Degrees to Open Association of Research, Society U.S.A. Once you are designated as FARSM, you may send us a scanned copy of all of you credentials. OARS will verify, grade and certify them. This will be based on your academic records, quality of research papers published by you, and some more criteria. After certification of all your credentials by OARS, they will be published on your Fellow Profile link on website https://associationofresearch.org which will be helpful to upgrade the dignity.

The FARSM members can avail the benefits of free research podcasting in Global Research Radio with their research documents. After publishing the work, (including published elsewhere worldwide with proper authorization) you can upload your research paper with your recorded voice or you can utilize chargeable services of our professional RJs to record your paper in their voice on request.



The FARSM member also entitled to get the benefits of free research podcasting of their research documents through video clips. We can also streamline your conference videos and display your slides/ online slides and online research video clips at reasonable charges, on request.

© Copyright by Global Journals Inc.(US)| Guidelines Handbook



The FARSM is eligible to earn from sales proceeds of his/her researches/reference/review Books or literature, while publishing with Global Journals. The FARSS can decide whether he/she would like to publish his/her research in a closed manner. In this case, whenever readers purchase that individual research paper for reading, maximum 60% of its profit earned as royalty by Global Journals, will be credited to his/her bank account. The entire entitled amount will be credited to his/her bank account exceeding limit of minimum fixed balance. There is no minimum time limit for collection. The FARSM member can decide its price and we can help in making the right decision.



The FARSM member is eligible to join as a paid peer reviewer at Global Journals Incorporation (USA) and can get remuneration of 15% of author fees, taken from the author of a respective paper. After reviewing 5 or more papers you can request to transfer the amount to your bank account.

MEMBER OF ASSOCIATION OF RESEARCH SOCIETY IN MEDICAL (MARSM)

The ' MARSM ' title is accorded to a selected professional after the approval of the Editor-in-Chief / Editorial Board Members/Dean.



The "MARSM" is a dignified ornament which is accorded to a person's name viz. Dr. John E. Hall, Ph.D., MARSM or William Walldroff, M.S., MARSM.

MARSM accrediting is an honor. It authenticates your research activities. Afterbecoming MARSM,you can add 'MARSM' title with your name as you use this recognition as additional suffix to your status. This will definitely enhance and add more value and repute to your name. You may use it on your professional Counseling Materials such as CV, Resume, Visiting Card and Name Plate etc.

The following benefitscan be availed by you only for next three years from the date of certification.



MARSM designated members are entitled to avail a 25% discount while publishing their research papers (of a single author) in Global Journals Inc., if the same is accepted by our Editorial Board and Peer Reviewers. If you are a main author or co-author of a group of authors, you will get discount of 10%.

As MARSM, you willbe given a renowned, secure and free professional email address with 30 GB of space e.g. johnhall@globaljournals.org. This will include Webmail, Spam Assassin, Email Forwarders,Auto-Responders, Email Delivery Route tracing, etc.



© Copyright by Global Journals Inc.(US) | Guidelines Handbook



We shall provide you intimation regarding launching of e-version of journal of your stream time to time.This may be utilized in your library for the enrichment of knowledge of your students as well as it can also be helpful for the concerned faculty members.

The MARSM member can apply for approval, grading and certification of standards of their educational and Institutional Degrees to Open Association of Research, Society U.S.A.





Once you are designated as MARSM, you may send us a scanned copy of all of your credentials. OARS will verify, grade and certify them. This will be based on your academic records, quality of research papers published by you, and some more criteria.

It is mandatory to read all terms and conditions carefully.

© Copyright by Global Journals Inc.(US)| Guidelines Handbook

AUXILIARY MEMBERSHIPS

Institutional Fellow of Open Association of Research Society (USA) - OARS (USA)

Global Journals Incorporation (USA) is accredited by Open Association of Research Society, U.S.A (OARS) and in turn, affiliates research institutions as "Institutional Fellow of Open Association of Research Society" (IFOARS).



The "FARSC" is a dignified title which is accorded to a person's name viz. Dr. John E. Hall, Ph.D., FARSC or William Walldroff, M.S., FARSC.

The IFOARS institution is entitled to form a Board comprised of one Chairperson and three to five board members preferably from different streams. The Board will be recognized as "Institutional Board of Open Association of Research Society"-(IBOARS).

The Institute will be entitled to following benefits:

The IBOARS can initially review research papers of their institute and recommend them to publish with respective journal of Global Journals. It can also review the papers of other institutions after obtaining our consent. The second review will be done by peer reviewer of Global Journals Incorporation (USA) The Board is at liberty to appoint a peer reviewer with the approval of chairperson after consulting us.

The author fees of such paper may be waived off up to 40%.

The Global Journals Incorporation (USA) at its discretion can also refer double blind peer reviewed paper at their end to the board for the verification and to get recommendation for final stage of acceptance of publication.





The IBOARS can organize symposium/seminar/conference in their country on behalf of Global Journals Incorporation (USA)-OARS (USA). The terms and conditions can be discussed separately.

The Board can also play vital role by exploring and giving valuable suggestions regarding the Standards of "Open Association of Research Society, U.S.A (OARS)" so that proper amendment can take place for the benefit of entire research community. We shall provide details of particular standard only on receipt of request from the Board.



The board members can also join us as Individual Fellow with 40% discount on total fees applicable to Individual Fellow. They will be entitled to avail all the benefits as declared. Please visit Individual Fellow-sub menu of GlobalJournals.org to have more relevant details.

© Copyright by Global Journals Inc.(US) | Guidelines Handbook

We shall provide you intimation regarding launching of e-version of journal of your stream time to time. This may be utilized in your library for the enrichment of knowledge of your students as well as it can also be helpful for the concerned faculty members.



After nomination of your institution as "Institutional Fellow" and constantly functioning successfully for one year, we can consider giving recognition to your institute to function as Regional/Zonal office on our behalf.
The board can also take up the additional allied activities for betterment after our consultation.

The following entitlements are applicable to individual Fellows:



Open Association of Research Society, U.S.A (OARS) By-laws states that an individual Fellow may use the designations as applicable, or the corresponding initials. The Credentials of individual Fellow and Associate designations signify that the individual has gained knowledge of the fundamental concepts. One is magnanimous and proficient in an expertise course covering the professional code of conduct, and follows recognized standards of practice.

Open Association of Research Society (US)/ Global Journals Incorporation (USA), as described in Corporate Statements, are educational, research publishing and professional membership organizations. Achieving our individual Fellow or Associate status is based mainly on meeting stated educational research requirements.



Disbursement of 40% Royalty earned through Global Journals : Researcher = 50%, Peer Reviewer = 37.50%, Institution = 12.50% E.g. Out of 40%, the 20% benefit should be passed on to researcher, 15 % benefit towards remuneration should be given to a reviewer and remaining 5% is to be retained by the institution.

We shall provide print version of 12 issues of any three journals [as per your requirement] out of our 38 journals worth $ 2376 USD.

Other:

The individual Fellow and Associate designations accredited by Open Association of Research Society (US) credentials signify guarantees following achievements:

- The professional accredited with Fellow honor, is entitled to various benefits viz. name, fame, honor, regular flow of income, secured bright future, social status etc.

© Copyright by Global Journals Inc.(US)| Guidelines Handbook

- In addition to above, if one is single author, then entitled to 40% discount on publishing research paper and can get 10%discount if one is co-author or main author among group of authors.
- The Fellow can organize symposium/seminar/conference on behalf of Global Journals Incorporation (USA) and he/she can also attend the same organized by other institutes on behalf of Global Journals.
- The Fellow can become member of Editorial Board Member after completing 3yrs.
- The Fellow can earn 60% of sales proceeds from the sale of reference/review books/literature/publishing of research paper.
- Fellow can also join as paid peer reviewer and earn 15% remuneration of author charges and can also get an opportunity to join as member of the Editorial Board of Global Journals Incorporation (USA)
- • This individual has learned the basic methods of applying those concepts and techniques to common challenging situations. This individual has further demonstrated an in–depth understanding of the application of suitable techniques to a particular area of research practice.

Note :

"

- In future, if the board feels the necessity to change any board member, the same can be done with the consent of the chairperson along with anyone board member without our approval.
- In case, the chairperson needs to be replaced then consent of 2/3rd board members are required and they are also required to jointly pass the resolution copy of which should be sent to us. In such case, it will be compulsory to obtain our approval before replacement.
- In case of "Difference of Opinion [if any]" among the Board members, our decision will be final and binding to everyone.

"

Process of submission of Research Paper

The Area or field of specialization may or may not be of any category as mentioned in 'Scope of Journal' menu of the GlobalJournals.org website. There are 37 Research Journal categorized with Six parental Journals GJCST, GJMR, GJRE, GJMBR, GJSFR, GJHSS. For Authors should prefer the mentioned categories. There are three widely used systems UDC, DDC and LCC. The details are available as 'Knowledge Abstract' at Home page. The major advantage of this coding is that, the research work will be exposed to and shared with all over the world as we are being abstracted and indexed worldwide.

The paper should be in proper format. The format can be downloaded from first page of 'Author Guideline' Menu. The Author is expected to follow the general rules as mentioned in this menu. The paper should be written in MS-Word Format (*.DOC,*.DOCX).

The Author can submit the paper either online or offline. The authors should prefer online submission.Online Submission: There are three ways to submit your paper:

(A) (I) First, register yourself using top right corner of Home page then Login. If you are already registered, then login using your username and password.

(II) Choose corresponding Journal.

(III) Click 'Submit Manuscript'. Fill required information and Upload the paper.

(B) If you are using Internet Explorer, then Direct Submission through Homepage is also available.

(C) If these two are not conveninet , and then email the paper directly to dean@globaljournals.org.

Offline Submission: Author can send the typed form of paper by Post. However, online submission should be preferred.

© Copyright by Global Journals Inc.(US)| Guidelines Handbook

Preferred Author Guidelines

MANUSCRIPT STYLE INSTRUCTION (Must be strictly followed)

Page Size: 8.27" X 11'"

- Left Margin: 0.65
- Right Margin: 0.65
- Top Margin: 0.75
- Bottom Margin: 0.75
- Font type of all text should be Swis 721 Lt BT.
- Paper Title should be of Font Size 24 with one Column section.
- Author Name in Font Size of 11 with one column as of Title.
- Abstract Font size of 9 Bold, "Abstract" word in Italic Bold.
- Main Text: Font size 10 with justified two columns section
- Two Column with Equal Column with of 3.38 and Gaping of .2
- First Character must be three lines Drop capped.
- Paragraph before Spacing of 1 pt and After of 0 pt.
- Line Spacing of 1 pt
- Large Images must be in One Column
- Numbering of First Main Headings (Heading 1) must be in Roman Letters, Capital Letter, and Font Size of 10.
- Numbering of Second Main Headings (Heading 2) must be in Alphabets, Italic, and Font Size of 10.

You can use your own standard format also.
Author Guidelines:

1. General,

2. Ethical Guidelines,

3. Submission of Manuscripts,

4. Manuscript's Category,

5. Structure and Format of Manuscript,

6. After Acceptance.

1. GENERAL

Before submitting your research paper, one is advised to go through the details as mentioned in following heads. It will be beneficial, while peer reviewer justify your paper for publication.

Scope

The Global Journals Inc. (US) welcome the submission of original paper, review paper, survey article relevant to the all the streams of Philosophy and knowledge. The Global Journals Inc. (US) is parental platform for Global Journal of Computer Science and Technology, Researches in Engineering, Medical Research, Science Frontier Research, Human Social Science, Management, and Business organization. The choice of specific field can be done otherwise as following in Abstracting and Indexing Page on this Website. As the all Global

Journals Inc. (US) are being abstracted and indexed (in process) by most of the reputed organizations. Topics of only narrow interest will not be accepted unless they have wider potential or consequences.

2. ETHICAL GUIDELINES

Authors should follow the ethical guidelines as mentioned below for publication of research paper and research activities.

Papers are accepted on strict understanding that the material in whole or in part has not been, nor is being, considered for publication elsewhere. If the paper once accepted by Global Journals Inc. (US) and Editorial Board, will become the copyright of the Global Journals Inc. (US).

Authorship: The authors and coauthors should have active contribution to conception design, analysis and interpretation of findings. They should critically review the contents and drafting of the paper. All should approve the final version of the paper before submission

The Global Journals Inc. (US) follows the definition of authorship set up by the Global Academy of Research and Development. According to the Global Academy of R&D authorship, criteria must be based on:

1) Substantial contributions to conception and acquisition of data, analysis and interpretation of the findings.

2) Drafting the paper and revising it critically regarding important academic content.

3) Final approval of the version of the paper to be published.

All authors should have been credited according to their appropriate contribution in research activity and preparing paper. Contributors who do not match the criteria as authors may be mentioned under Acknowledgement.

Acknowledgements: Contributors to the research other than authors credited should be mentioned under acknowledgement. The specifications of the source of funding for the research if appropriate can be included. Suppliers of resources may be mentioned along with address.

Appeal of Decision: The Editorial Board's decision on publication of the paper is final and cannot be appealed elsewhere.

Permissions: It is the author's responsibility to have prior permission if all or parts of earlier published illustrations are used in this paper.

Please mention proper reference and appropriate acknowledgements wherever expected.

If all or parts of previously published illustrations are used, permission must be taken from the copyright holder concerned. It is the author's responsibility to take these in writing.

Approval for reproduction/modification of any information (including figures and tables) published elsewhere must be obtained by the authors/copyright holders before submission of the manuscript. Contributors (Authors) are responsible for any copyright fee involved.

3. SUBMISSION OF MANUSCRIPTS

Manuscripts should be uploaded via this online submission page. The online submission is most efficient method for submission of papers, as it enables rapid distribution of manuscripts and consequently speeds up the review procedure. It also enables authors to know the status of their own manuscripts by emailing us. Complete instructions for submitting a paper is available below.

Manuscript submission is a systematic procedure and little preparation is required beyond having all parts of your manuscript in a given format and a computer with an Internet connection and a Web browser. Full help and instructions are provided on-screen. As an author, you will be prompted for login and manuscript details as Field of Paper and then to upload your manuscript file(s) according to the instructions.



To avoid postal delays, all transaction is preferred by e-mail. A finished manuscript submission is confirmed by e-mail immediately and your paper enters the editorial process with no postal delays. When a conclusion is made about the publication of your paper by our Editorial Board, revisions can be submitted online with the same procedure, with an occasion to view and respond to all comments.

Complete support for both authors and co-author is provided.

4. MANUSCRIPT'S CATEGORY

Based on potential and nature, the manuscript can be categorized under the following heads:

Original research paper: Such papers are reports of high-level significant original research work.

Review papers: These are concise, significant but helpful and decisive topics for young researchers.

Research articles: These are handled with small investigation and applications

Research letters: The letters are small and concise comments on previously published matters.

5.STRUCTURE AND FORMAT OF MANUSCRIPT

The recommended size of original research paper is less than seven thousand words, review papers fewer than seven thousands words also.Preparation of research paper or how to write research paper, are major hurdle, while writing manuscript. The research articles and research letters should be fewer than three thousand words, the structure original research paper; sometime review paper should be as follows:

Papers: These are reports of significant research (typically less than 7000 words equivalent, including tables, figures, references), and comprise:

(a)Title should be relevant and commensurate with the theme of the paper.

(b) A brief Summary, "Abstract" (less than 150 words) containing the major results and conclusions.

(c) Up to ten keywords, that precisely identifies the paper's subject, purpose, and focus.

(d) An Introduction, giving necessary background excluding subheadings; objectives must be clearly declared.

(e) Resources and techniques with sufficient complete experimental details (wherever possible by reference) to permit repetition; sources of information must be given and numerical methods must be specified by reference, unless non-standard.

(f) Results should be presented concisely, by well-designed tables and/or figures; the same data may not be used in both; suitable statistical data should be given. All data must be obtained with attention to numerical detail in the planning stage. As reproduced design has been recognized to be important to experiments for a considerable time, the Editor has decided that any paper that appears not to have adequate numerical treatments of the data will be returned un-refereed;

(g) Discussion should cover the implications and consequences, not just recapitulating the results; conclusions should be summarizing.

(h) Brief Acknowledgements.

(i) References in the proper form.

Authors should very cautiously consider the preparation of papers to ensure that they communicate efficiently. Papers are much more likely to be accepted, if they are cautiously designed and laid out, contain few or no errors, are summarizing, and be conventional to the approach and instructions. They will in addition, be published with much less delays than those that require much technical and editorial correction.

The Editorial Board reserves the right to make literary corrections and to make suggestions to improve briefness.

It is vital, that authors take care in submitting a manuscript that is written in simple language and adheres to published guidelines.

Format

Language: The language of publication is UK English. Authors, for whom English is a second language, must have their manuscript efficiently edited by an English-speaking person before submission to make sure that, the English is of high excellence. It is preferable, that manuscripts should be professionally edited.

Standard Usage, Abbreviations, and Units: Spelling and hyphenation should be conventional to The Concise Oxford English Dictionary. Statistics and measurements should at all times be given in figures, e.g. 16 min, except for when the number begins a sentence. When the number does not refer to a unit of measurement it should be spelt in full unless, it is 160 or greater.

Abbreviations supposed to be used carefully. The abbreviated name or expression is supposed to be cited in full at first usage, followed by the conventional abbreviation in parentheses.

Metric SI units are supposed to generally be used excluding where they conflict with current practice or are confusing. For illustration, 1.4 l rather than 1.4 × 10-3 m3, or 4 mm somewhat than 4 × 10-3 m. Chemical formula and solutions must identify the form used, e.g. anhydrous or hydrated, and the concentration must be in clearly defined units. Common species names should be followed by underlines at the first mention. For following use the generic name should be constricted to a single letter, if it is clear.

Structure

All manuscripts submitted to Global Journals Inc. (US), ought to include:

Title: The title page must carry an instructive title that reflects the content, a running title (less than 45 characters together with spaces), names of the authors and co-authors, and the place(s) wherever the work was carried out. The full postal address in addition with the e-mail address of related author must be given. Up to eleven keywords or very brief phrases have to be given to help data retrieval, mining and indexing.

Abstract, used in Original Papers and Reviews:

Optimizing Abstract for Search Engines

Many researchers searching for information online will use search engines such as Google, Yahoo or similar. By optimizing your paper for search engines, you will amplify the chance of someone finding it. This in turn will make it more likely to be viewed and/or cited in a further work. Global Journals Inc. (US) have compiled these guidelines to facilitate you to maximize the web-friendliness of the most public part of your paper.

Key Words

A major linchpin in research work for the writing research paper is the keyword search, which one will employ to find both library and Internet resources.

One must be persistent and creative in using keywords. An effective keyword search requires a strategy and planning a list of possible keywords and phrases to try.

Search engines for most searches, use Boolean searching, which is somewhat different from Internet searches. The Boolean search uses "operators," words (and, or, not, and near) that enable you to expand or narrow your affords. Tips for research paper while preparing research paper are very helpful guideline of research paper.

Choice of key words is first tool of tips to write research paper. Research paper writing is an art.A few tips for deciding as strategically as possible about keyword search:

- One should start brainstorming lists of possible keywords before even begin searching. Think about the most important concepts related to research work. Ask, "What words would a source have to include to be truly valuable in research paper?" Then consider synonyms for the important words.
- It may take the discovery of only one relevant paper to let steer in the right keyword direction because in most databases, the keywords under which a research paper is abstracted are listed with the paper.
- One should avoid outdated words.

Keywords are the key that opens a door to research work sources. Keyword searching is an art in which researcher's skills are bound to improve with experience and time.

Numerical Methods: Numerical methods used should be clear and, where appropriate, supported by references.

Acknowledgements: Please make these as concise as possible.

References

References follow the Harvard scheme of referencing. References in the text should cite the authors' names followed by the time of their publication, unless there are three or more authors when simply the first author's name is quoted followed by et al. unpublished work has to only be cited where necessary, and only in the text. Copies of references in press in other journals have to be supplied with submitted typescripts. It is necessary that all citations and references be carefully checked before submission, as mistakes or omissions will cause delays.

References to information on the World Wide Web can be given, but only if the information is available without charge to readers on an official site. Wikipedia and Similar websites are not allowed where anyone can change the information. Authors will be asked to make available electronic copies of the cited information for inclusion on the Global Journals Inc. (US) homepage at the judgment of the Editorial Board.

The Editorial Board and Global Journals Inc. (US) recommend that, citation of online-published papers and other material should be done via a DOI (digital object identifier). If an author cites anything, which does not have a DOI, they run the risk of the cited material not being noticeable.

The Editorial Board and Global Journals Inc. (US) recommend the use of a tool such as Reference Manager for reference management and formatting.

Tables, Figures and Figure Legends

Tables: Tables should be few in number, cautiously designed, uncrowned, and include only essential data. Each must have an Arabic number, e.g. Table 4, a self-explanatory caption and be on a separate sheet. Vertical lines should not be used.

Figures: Figures are supposed to be submitted as separate files. Always take in a citation in the text for each figure using Arabic numbers, e.g. Fig. 4. Artwork must be submitted online in electronic form by e-mailing them.

Preparation of Electronic Figures for Publication

Even though low quality images are sufficient for review purposes, print publication requires high quality images to prevent the final product being blurred or fuzzy. Submit (or e-mail) EPS (line art) or TIFF (halftone/photographs) files only. MS PowerPoint and Word Graphics are unsuitable for printed pictures. Do not use pixel-oriented software. Scans (TIFF only) should have a resolution of at least 350 dpi (halftone) or 700 to 1100 dpi (line drawings) in relation to the imitation size. Please give the data for figures in black and white or submit a Color Work Agreement Form. EPS files must be saved with fonts embedded (and with a TIFF preview, if possible).

For scanned images, the scanning resolution (at final image size) ought to be as follows to ensure good reproduction: line art: >650 dpi; halftones (including gel photographs) : >350 dpi; figures containing both halftone and line images: >650 dpi.

Color Charges: It is the rule of the Global Journals Inc. (US) for authors to pay the full cost for the reproduction of their color artwork. Hence, please note that, if there is color artwork in your manuscript when it is accepted for publication, we would require you to complete and return a color work agreement form before your paper can be published.

Figure Legends: Self-explanatory legends of all figures should be incorporated separately under the heading 'Legends to Figures'. In the full-text online edition of the journal, figure legends may possibly be truncated in abbreviated links to the full screen version. Therefore, the first 100 characters of any legend should notify the reader, about the key aspects of the figure.

6. AFTER ACCEPTANCE

Upon approval of a paper for publication, the manuscript will be forwarded to the dean, who is responsible for the publication of the Global Journals Inc. (US).

6.1 Proof Corrections

The corresponding author will receive an e-mail alert containing a link to a website or will be attached. A working e-mail address must therefore be provided for the related author.

Acrobat Reader will be required in order to read this file. This software can be downloaded

(Free of charge) from the following website:

www.adobe.com/products/acrobat/readstep2.html. This will facilitate the file to be opened, read on screen, and printed out in order for any corrections to be added. Further instructions will be sent with the proof.

Proofs must be returned to the dean at dean@globaljournals.org within three days of receipt.

As changes to proofs are costly, we inquire that you only correct typesetting errors. All illustrations are retained by the publisher. Please note that the authors are responsible for all statements made in their work, including changes made by the copy editor.

6.2 Early View of Global Journals Inc. (US) (Publication Prior to Print)

The Global Journals Inc. (US) are enclosed by our publishing's Early View service. Early View articles are complete full-text articles sent in advance of their publication. Early View articles are absolute and final. They have been completely reviewed, revised and edited for publication, and the authors' final corrections have been incorporated. Because they are in final form, no changes can be made after sending them. The nature of Early View articles means that they do not yet have volume, issue or page numbers, so Early View articles cannot be cited in the conventional way.

6.3 Author Services

Online production tracking is available for your article through Author Services. Author Services enables authors to track their article - once it has been accepted - through the production process to publication online and in print. Authors can check the status of their articles online and choose to receive automated e-mails at key stages of production. The authors will receive an e-mail with a unique link that enables them to register and have their article automatically added to the system. Please ensure that a complete e-mail address is provided when submitting the manuscript.

6.4 Author Material Archive Policy

Please note that if not specifically requested, publisher will dispose off hardcopy & electronic information submitted, after the two months of publication. If you require the return of any information submitted, please inform the Editorial Board or dean as soon as possible.

6.5 Offprint and Extra Copies

A PDF offprint of the online-published article will be provided free of charge to the related author, and may be distributed according to the Publisher's terms and conditions. Additional paper offprint may be ordered by emailing us at: editor@globaljournals.org .



Before start writing a good quality Computer Science Research Paper, let us first understand what is Computer Science Research Paper? So, Computer Science Research Paper is the paper which is written by professionals or scientists who are associated to Computer Science and Information Technology, or doing research study in these areas. If you are novel to this field then you can consult about this field from your supervisor or guide.

TECHNIQUES FOR WRITING A GOOD QUALITY RESEARCH PAPER:

1. Choosing the topic: In most cases, the topic is searched by the interest of author but it can be also suggested by the guides. You can have several topics and then you can judge that in which topic or subject you are finding yourself most comfortable. This can be done by asking several questions to yourself, like Will I be able to carry our search in this area? Will I find all necessary recourses to accomplish the search? Will I be able to find all information in this field area? If the answer of these types of questions will be "Yes" then you can choose that topic. In most of the cases, you may have to conduct the surveys and have to visit several places because this field is related to Computer Science and Information Technology. Also, you may have to do a lot of work to find all rise and falls regarding the various data of that subject. Sometimes, detailed information plays a vital role, instead of short information.

2. Evaluators are human: First thing to remember that evaluators are also human being. They are not only meant for rejecting a paper. They are here to evaluate your paper. So, present your Best.

3. Think Like Evaluators: If you are in a confusion or getting demotivated that your paper will be accepted by evaluators or not, then think and try to evaluate your paper like an Evaluator. Try to understand that what an evaluator wants in your research paper and automatically you will have your answer.

4. Make blueprints of paper: The outline is the plan or framework that will help you to arrange your thoughts. It will make your paper logical. But remember that all points of your outline must be related to the topic you have chosen.

5. Ask your Guides: If you are having any difficulty in your research, then do not hesitate to share your difficulty to your guide (if you have any). They will surely help you out and resolve your doubts. If you can't clarify what exactly you require for your work then ask the supervisor to help you with the alternative. He might also provide you the list of essential readings.

6. Use of computer is recommended: As you are doing research in the field of Computer Science, then this point is quite obvious.

7. Use right software: Always use good quality software packages. If you are not capable to judge good software then you can lose quality of your paper unknowingly. There are various software programs available to help you, which you can get through Internet.

8. Use the Internet for help: An excellent start for your paper can be by using the Google. It is an excellent search engine, where you can have your doubts resolved. You may also read some answers for the frequent question how to write my research paper or find model research paper. From the internet library you can download books. If you have all required books make important reading selecting and analyzing the specified information. Then put together research paper sketch out.

9. Use and get big pictures: Always use encyclopedias, Wikipedia to get pictures so that you can go into the depth.

10. Bookmarks are useful: When you read any book or magazine, you generally use bookmarks, right! It is a good habit, which helps to not to lose your continuity. You should always use bookmarks while searching on Internet also, which will make your search easier.

11. Revise what you wrote: When you write anything, always read it, summarize it and then finalize it.

12. Make all efforts: Make all efforts to mention what you are going to write in your paper. That means always have a good start. Try to mention everything in introduction, that what is the need of a particular research paper. Polish your work by good skill of writing and always give an evaluator, what he wants.

13. Have backups: When you are going to do any important thing like making research paper, you should always have backup copies of it either in your computer or in paper. This will help you to not to lose any of your important.

14. Produce good diagrams of your own: Always try to include good charts or diagrams in your paper to improve quality. Using several and unnecessary diagrams will degrade the quality of your paper by creating "hotchpotch." So always, try to make and include those diagrams, which are made by your own to improve readability and understandability of your paper.

15. Use of direct quotes: When you do research relevant to literature, history or current affairs then use of quotes become essential but if study is relevant to science then use of quotes is not preferable.

16. Use proper verb tense: Use proper verb tenses in your paper. Use past tense, to present those events that happened. Use present tense to indicate events that are going on. Use future tense to indicate future happening events. Use of improper and wrong tenses will confuse the evaluator. Avoid the sentences that are incomplete.

17. Never use online paper: If you are getting any paper on Internet, then never use it as your research paper because it might be possible that evaluator has already seen it or maybe it is outdated version.

18. Pick a good study spot: To do your research studies always try to pick a spot, which is quiet. Every spot is not for studies. Spot that suits you choose it and proceed further.

19. Know what you know: Always try to know, what you know by making objectives. Else, you will be confused and cannot achieve your target.

20. Use good quality grammar: Always use a good quality grammar and use words that will throw positive impact on evaluator. Use of good quality grammar does not mean to use tough words, that for each word the evaluator has to go through dictionary. Do not start sentence with a conjunction. Do not fragment sentences. Eliminate one-word sentences. Ignore passive voice. Do not ever use a big word when a diminutive one would suffice. Verbs have to be in agreement with their subjects. Prepositions are not expressions to finish sentences with. It is incorrect to ever divide an infinitive. Avoid clichés like the disease. Also, always shun irritating alliteration. Use language that is simple and straight forward. put together a neat summary.

21. Arrangement of information: Each section of the main body should start with an opening sentence and there should be a changeover at the end of the section. Give only valid and powerful arguments to your topic. You may also maintain your arguments with records.

22. Never start in last minute: Always start at right time and give enough time to research work. Leaving everything to the last minute will degrade your paper and spoil your work.

23. Multitasking in research is not good: Doing several things at the same time proves bad habit in case of research activity. Research is an area, where everything has a particular time slot. Divide your research work in parts and do particular part in particular time slot.

24. Never copy others' work: Never copy others' work and give it your name because if evaluator has seen it anywhere you will be in trouble.

25. Take proper rest and food: No matter how many hours you spend for your research activity, if you are not taking care of your health then all your efforts will be in vain. For a quality research, study is must, and this can be done by taking proper rest and food.

26. Go for seminars: Attend seminars if the topic is relevant to your research area. Utilize all your resources.



© Copyright by Global Journals Inc.(US)| Guidelines Handbook

27. Refresh your mind after intervals: Try to give rest to your mind by listening to soft music or by sleeping in intervals. This will also improve your memory.

28. Make colleagues: Always try to make colleagues. No matter how sharper or intelligent you are, if you make colleagues you can have several ideas, which will be helpful for your research.

29. Think technically: Always think technically. If anything happens, then search its reasons, its benefits, and demerits.

30. Think and then print: When you will go to print your paper, notice that tables are not be split, headings are not detached from their descriptions, and page sequence is maintained.

31. Adding unnecessary information: Do not add unnecessary information, like, I have used MS Excel to draw graph. Do not add irrelevant and inappropriate material. These all will create superfluous. Foreign terminology and phrases are not apropos. One should NEVER take a broad view. Analogy in script is like feathers on a snake. Not at all use a large word when a very small one would be sufficient. Use words properly, regardless of how others use them. Remove quotations. Puns are for kids, not grunt readers. Amplification is a billion times of inferior quality than sarcasm.

32. Never oversimplify everything: To add material in your research paper, never go for oversimplification. This will definitely irritate the evaluator. Be more or less specific. Also too, by no means, ever use rhythmic redundancies. Contractions aren't essential and shouldn't be there used. Comparisons are as terrible as clichés. Give up ampersands and abbreviations, and so on. Remove commas, that are, not necessary. Parenthetical words however should be together with this in commas. Understatement is all the time the complete best way to put onward earth-shaking thoughts. Give a detailed literary review.

33. Report concluded results: Use concluded results. From raw data, filter the results and then conclude your studies based on measurements and observations taken. Significant figures and appropriate number of decimal places should be used. Parenthetical remarks are prohibitive. Proofread carefully at final stage. In the end give outline to your arguments. Spot out perspectives of further study of this subject. Justify your conclusion by at the bottom of them with sufficient justifications and examples.

34. After conclusion: Once you have concluded your research, the next most important step is to present your findings. Presentation is extremely important as it is the definite medium though which your research is going to be in print to the rest of the crowd. Care should be taken to categorize your thoughts well and present them in a logical and neat manner. A good quality research paper format is essential because it serves to highlight your research paper and bring to light all necessary aspects in your research.

Informal Guidelines of Research Paper Writing

Key points to remember:

- Submit all work in its final form.
- Write your paper in the form, which is presented in the guidelines using the template.
- Please note the criterion for grading the final paper by peer-reviewers.

Final Points:

A purpose of organizing a research paper is to let people to interpret your effort selectively. The journal requires the following sections, submitted in the order listed, each section to start on a new page.

The introduction will be compiled from reference matter and will reflect the design processes or outline of basis that direct you to make study. As you will carry out the process of study, the method and process section will be constructed as like that. The result segment will show related statistics in nearly sequential order and will direct the reviewers next to the similar intellectual paths throughout the data that you took to carry out your study. The discussion section will provide understanding of the data and projections as to the implication of the results. The use of good quality references all through the paper will give the effort trustworthiness by representing an alertness of prior workings.

Writing a research paper is not an easy job no matter how trouble-free the actual research or concept. Practice, excellent preparation, and controlled record keeping are the only means to make straightforward the progression.

General style:

Specific editorial column necessities for compliance of a manuscript will always take over from directions in these general guidelines.

To make a paper clear

· Adhere to recommended page limits

Mistakes to evade

- Insertion a title at the foot of a page with the subsequent text on the next page
- Separating a table/chart or figure - impound each figure/table to a single page
- Submitting a manuscript with pages out of sequence

In every sections of your document

· Use standard writing style including articles ("a", "the," etc.)

· Keep on paying attention on the research topic of the paper

· Use paragraphs to split each significant point (excluding for the abstract)

· Align the primary line of each section

· Present your points in sound order

· Use present tense to report well accepted

· Use past tense to describe specific results

· Shun familiar wording, don't address the reviewer directly, and don't use slang, slang language, or superlatives

· Shun use of extra pictures - include only those figures essential to presenting results

Title Page:

Choose a revealing title. It should be short. It should not have non-standard acronyms or abbreviations. It should not exceed two printed lines. It should include the name(s) and address (es) of all authors.



© Copyright by Global Journals Inc.(US)| Guidelines Handbook

Abstract:

The summary should be two hundred words or less. It should briefly and clearly explain the key findings reported in the manuscript--must have precise statistics. It should not have abnormal acronyms or abbreviations. It should be logical in itself. Shun citing references at this point.

An abstract is a brief distinct paragraph summary of finished work or work in development. In a minute or less a reviewer can be taught the foundation behind the study, common approach to the problem, relevant results, and significant conclusions or new questions.

Write your summary when your paper is completed because how can you write the summary of anything which is not yet written? Wealth of terminology is very essential in abstract. Yet, use comprehensive sentences and do not let go readability for briefness. You can maintain it succinct by phrasing sentences so that they provide more than lone rationale. The author can at this moment go straight to shortening the outcome. Sum up the study, with the subsequent elements in any summary. Try to maintain the initial two items to no more than one ruling each.

- Reason of the study - theory, overall issue, purpose
- Fundamental goal
- To the point depiction of the research
- Consequences, including definite statistics - if the consequences are quantitative in nature, account quantitative data; results of any numerical analysis should be reported
- Significant conclusions or questions that track from the research(es)

Approach:

- Single section, and succinct
- As a outline of job done, it is always written in past tense
- A conceptual should situate on its own, and not submit to any other part of the paper such as a form or table
- Center on shortening results - bound background information to a verdict or two, if completely necessary
- What you account in an conceptual must be regular with what you reported in the manuscript
- Exact spelling, clearness of sentences and phrases, and appropriate reporting of quantities (proper units, important statistics) are just as significant in an abstract as they are anywhere else

Introduction:

The **Introduction** should "introduce" the manuscript. The reviewer should be presented with sufficient background information to be capable to comprehend and calculate the purpose of your study without having to submit to other works. The basis for the study should be offered. Give most important references but shun difficult to make a comprehensive appraisal of the topic. In the introduction, describe the problem visibly. If the problem is not acknowledged in a logical, reasonable way, the reviewer will have no attention in your result. Speak in common terms about techniques used to explain the problem, if needed, but do not present any particulars about the protocols here. Following approach can create a valuable beginning:

- Explain the value (significance) of the study
- Shield the model - why did you employ this particular system or method? What is its compensation? You strength remark on its appropriateness from a abstract point of vision as well as point out sensible reasons for using it.
- Present a justification. Status your particular theory (es) or aim(s), and describe the logic that led you to choose them.
- Very for a short time explain the tentative propose and how it skilled the declared objectives.

Approach:

- Use past tense except for when referring to recognized facts. After all, the manuscript will be submitted after the entire job is done.
- Sort out your thoughts; manufacture one key point with every section. If you make the four points listed above, you will need a least of four paragraphs.

- Present surroundings information only as desirable in order hold up a situation. The reviewer does not desire to read the whole thing you know about a topic.
- Shape the theory/purpose specifically - do not take a broad view.
- As always, give awareness to spelling, simplicity and correctness of sentences and phrases.

Procedures (Methods and Materials):

This part is supposed to be the easiest to carve if you have good skills. A sound written Procedures segment allows a capable scientist to replacement your results. Present precise information about your supplies. The suppliers and clarity of reagents can be helpful bits of information. Present methods in sequential order but linked methodologies can be grouped as a segment. Be concise when relating the protocols. Attempt for the least amount of information that would permit another capable scientist to spare your outcome but be cautious that vital information is integrated. The use of subheadings is suggested and ought to be synchronized with the results section. When a technique is used that has been well described in another object, mention the specific item describing a way but draw the basic principle while stating the situation. The purpose is to text all particular resources and broad procedures, so that another person may use some or all of the methods in one more study or referee the scientific value of your work. It is not to be a step by step report of the whole thing you did, nor is a methods section a set of orders.

Materials:

- Explain materials individually only if the study is so complex that it saves liberty this way.
- Embrace particular materials, and any tools or provisions that are not frequently found in laboratories.
- Do not take in frequently found.
- If use of a definite type of tools.
- Materials may be reported in a part section or else they may be recognized along with your measures.

Methods:

- Report the method (not particulars of each process that engaged the same methodology)
- Describe the method entirely
- To be succinct, present methods under headings dedicated to specific dealings or groups of measures
- Simplify - details how procedures were completed not how they were exclusively performed on a particular day.
- If well known procedures were used, account the procedure by name, possibly with reference, and that's all.

Approach:

- It is embarrassed or not possible to use vigorous voice when documenting methods with no using first person, which would focus the reviewer's interest on the researcher rather than the job. As a result when script up the methods most authors use third person passive voice.
- Use standard style in this and in every other part of the paper - avoid familiar lists, and use full sentences.

What to keep away from

- Resources and methods are not a set of information.
- Skip all descriptive information and surroundings - save it for the argument.
- Leave out information that is immaterial to a third party.

Results:

The principle of a results segment is to present and demonstrate your conclusion. Create this part a entirely objective details of the outcome, and save all understanding for the discussion.

The page length of this segment is set by the sum and types of data to be reported. Carry on to be to the point, by means of statistics and tables, if suitable, to present consequences most efficiently.You must obviously differentiate material that would usually be incorporated in a study editorial from any unprocessed data or additional appendix matter that would not be available. In fact, such matter should not be submitted at all except requested by the instructor.



© Copyright by Global Journals Inc.(US)| Guidelines Handbook

Content

- Sum up your conclusion in text and demonstrate them, if suitable, with figures and tables.
- In manuscript, explain each of your consequences, point the reader to remarks that are most appropriate.
- Present a background, such as by describing the question that was addressed by creation an exacting study.
- Explain results of control experiments and comprise remarks that are not accessible in a prescribed figure or table, if appropriate.
- Examine your data, then prepare the analyzed (transformed) data in the form of a figure (graph), table, or in manuscript form.

What to stay away from

- Do not discuss or infer your outcome, report surroundings information, or try to explain anything.
- Not at all, take in raw data or intermediate calculations in a research manuscript.
- Do not present the similar data more than once.
- Manuscript should complement any figures or tables, not duplicate the identical information.
- Never confuse figures with tables - there is a difference.

Approach

- As forever, use past tense when you submit to your results, and put the whole thing in a reasonable order.
- Put figures and tables, appropriately numbered, in order at the end of the report
- If you desire, you may place your figures and tables properly within the text of your results part.

Figures and tables

- If you put figures and tables at the end of the details, make certain that they are visibly distinguished from any attach appendix materials, such as raw facts
- Despite of position, each figure must be numbered one after the other and complete with subtitle
- In spite of position, each table must be titled, numbered one after the other and complete with heading
- All figure and table must be adequately complete that it could situate on its own, divide from text

Discussion:

The Discussion is expected the trickiest segment to write and describe. A lot of papers submitted for journal are discarded based on problems with the Discussion. There is no head of state for how long a argument should be. Position your understanding of the outcome visibly to lead the reviewer through your conclusions, and then finish the paper with a summing up of the implication of the study. The purpose here is to offer an understanding of your results and hold up for all of your conclusions, using facts from your research and generally accepted information, if suitable. The implication of result should be visibly described. Infer your data in the conversation in suitable depth. This means that when you clarify an observable fact you must explain mechanisms that may account for the observation. If your results vary from your prospect, make clear why that may have happened. If your results agree, then explain the theory that the proof supported. It is never suitable to just state that the data approved with prospect, and let it drop at that.

- Make a decision if each premise is supported, discarded, or if you cannot make a conclusion with assurance. Do not just dismiss a study or part of a study as "uncertain."
- Research papers are not acknowledged if the work is imperfect. Draw what conclusions you can based upon the results that you have, and take care of the study as a finished work
- You may propose future guidelines, such as how the experiment might be personalized to accomplish a new idea.
- Give details all of your remarks as much as possible, focus on mechanisms.
- Make a decision if the tentative design sufficiently addressed the theory, and whether or not it was correctly restricted.
- Try to present substitute explanations if sensible alternatives be present.
- One research will not counter an overall question, so maintain the large picture in mind, where do you go next? The best studies unlock new avenues of study. What questions remain?
- Recommendations for detailed papers will offer supplementary suggestions.

Approach:

- When you refer to information, differentiate data generated by your own studies from available information
- Submit to work done by specific persons (including you) in past tense.
- Submit to generally acknowledged facts and main beliefs in present tense.

Please carefully note down following rules and regulation before submitting your Research Paper to Global Journals Inc. (US):

Segment Draft and Final Research Paper: You have to strictly follow the template of research paper. If it is not done your paper may get rejected.

- The **major constraint** is that you must independently make all content, tables, graphs, and facts that are offered in the paper. You must write each part of the paper wholly on your own. The Peer-reviewers need to identify your own perceptive of the concepts in your own terms. NEVER extract straight from any foundation, and never rephrase someone else's analysis.

- Do not give permission to anyone else to "PROOFREAD" your manuscript.

- Methods to avoid Plagiarism is applied by us on every paper, if found guilty, you will be blacklisted by all of our collaborated research groups, your institution will be informed for this and strict legal actions will be taken immediately.)
- To guard yourself and others from possible illegal use please do not permit anyone right to use to your paper and files.



© Copyright by Global Journals Inc.(US)| Guidelines Handbook

Criterion for Grading a Research Paper (Compilation) by Global Journals Inc. (US)

Please note that following table is only a Grading of "Paper Compilation" and not on "Performed/Stated Research" whose grading solely depends on Individual Assigned Peer Reviewer and Editorial Board Member. These can be available only on request and after decision of Paper. This report will be the property of Global Journals Inc. (US).

Topics	Grades		
	A-B	**C-D**	**E-F**
Abstract	Clear and concise with appropriate content, Correct format. 200 words or below	Unclear summary and no specific data, Incorrect form Above 200 words	No specific data with ambiguous information Above 250 words
Introduction	Containing all background details with clear goal and appropriate details, flow specification, no grammar and spelling mistake, well organized sentence and paragraph, reference cited	Unclear and confusing data, appropriate format, grammar and spelling errors with unorganized matter	Out of place depth and content, hazy format
Methods and Procedures	Clear and to the point with well arranged paragraph, precision and accuracy of facts and figures, well organized subheads	Difficult to comprehend with embarrassed text, too much explanation but completed	Incorrect and unorganized structure with hazy meaning
Result	Well organized, Clear and specific, Correct units with precision, correct data, well structuring of paragraph, no grammar and spelling mistake	Complete and embarrassed text, difficult to comprehend	Irregular format with wrong facts and figures
Discussion	Well organized, meaningful specification, sound conclusion, logical and concise explanation, highly structured paragraph reference cited	Wordy, unclear conclusion, spurious	Conclusion is not cited, unorganized, difficult to comprehend
References	Complete and correct format, well organized	Beside the point, Incomplete	Wrong format and structuring

INDEX

A

Aneurysms · 20
Antiseizure · 6

C

Callosum · 1, 2
Carbamazepine · 6, 31, 33, 34, 35, 36, 37
Carbamazepinum · 1
Clazosentan · 25, 30
Coagulopathy · 1
Collodion · 6

E

Epileptogenic · 7, 8

F

Felbamate · 6, 9

H

Heterothopia · 1
Hydroxyfasudil · 22, 28
Hypsarrhythmia · 6

L

Lamotrigine · 6, 36
Levetiracetamum · 3

N

Neurocysticercosis · 8
Neuroprotective · 21, 23, 24, 25
Nimodipine · 21, 27

O

Oxcarbazepinum · 1

P

Phenitoinum · 1

S

Subarachnoid · 20, 27
Subcortical · 1, 3





Global Journal of Medical Research

Visit us on the Web at www.GlobalJournals.org | www.MedicalResearchJournal.org
or email us at helpdesk@globaljournals.org

ISSN 9755896



© Global Journals