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Neurogenic Talipes Equinovarus

Endonasal Approach to the Skull Base

Highlights

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Surgical Cavity in Extended Endoscopic Endonasal Approach to the Skull Base and their Relationship with Cerebrospinal Fluidleak

By Marlon Ortiz Machín MD PhD, Omar López Arbolay MD PhD,
Carlos Vargas Gálvez MD & Ambiorix Ottenwalder Díaz MD

Abstract- Cerebrospinal fluid leak represents a fearsome complication after Extended Endoscopic Endonasal Approach to the skull base. A descriptive observational study was performed in 550 patients operated for skull base tumors through Extended Endoscopic Endonasal Approaches, between 2010 and 2021 at the Ameijeiras Hospital. Surgical cavity was classified according to relation with intracranial hydrodynamic system into: type 0 (no contact with the hydrodynamic system), type 1 (subarachnoid cavity), type 2 (cisternal cavity), and type 3 (ventricular cavity). A significant increase CSF leak incidence was determined in type 2 (10,8 %) and type 3 (18 %) cavity and it was associated to increment of hydrodynamic energy secondary to Bernoulli laws.

Keywords: extended endonasal endoscopic approach (EEEA), cerebrospinal fluid (CSF) leak, surgical cavity, bernoulli laws.

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Marlon Ortiz Machín MD PhD ^α, Omar López Arbolay MD PhD ^σ, Carlos Vargas Gálvez MD ^ρ
& Ambiorix Ottenwalder Díaz MD ^ω

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Keywords: extended endonasal endoscopic approach (EEEA), cerebrospinal fluid (CSF) leak, surgical cavity, bernoulli laws.

I. INTRODUCTION

Surgery of cranial base tumors has historically been one of the most complex and challenging disciplines in Neurosurgery. The difficult access and its intimate relationship with critical neurovascular structures make any surgical procedure a high-risk one.¹ Endoscopic approaches through natural corridors, Endoscopic Endonasal Approaches, allow minimizing the degree of cerebral invasiveness and improving tumor resection, with excellent results, visualization and dynamism.² With endoscopic approaches, there is evidence of a lower frequency of complications

compared to traditional transcranial approaches, however, the CSF leak increases and can trigger other cascading complications such as meningitis and hydrocephalus.³ In the following article, surgical cavity are classified depending on the contact with the intracranial hydrodynamic system and are related to the appearance of CSF fistula.

II. METHOD

A descriptive observational study was performed in 550 patients operated for skull base tumors through Extended Endoscopic Endonasal Approaches, between 2010 and 2021 at the Ameijeiras Hospital. Surgical cavities were classified in relation to the intracranial hydrodynamic system into: type 0 (no contact with the hydrodynamic system), type 1 (subarachnoid cavity), type 2 (cisternal cavity), and type 3 (ventricular cavity) (Table 1) (Figure1). The statistical analysis was performed using the IBM® SPSS® version 23.0 program. To determine the relationship between postoperative CSF leak and the type of surgical cavity, it was performed the Pearson's chi-square test, with statistical significance $p < 0.05$. In all cases, the same multilayer repair method was used at the cranial base, which included: fat, fascia lata, and Hadad-Basagasteguy nasoseptal flap.

Table 1: Type of surgical cavity according to relation to the intracranial hydrodynamic system

Surgical cavity	Description	Examples of tumors
Type 0	No contact with the hydrodynamic system	Adenomas with intracapsular dissection, chordomas of the clivus and malignant sinonasal tumors without intracranial invasion
Type 1	Subarachnoid (contact and subarachnoid dissection)	Adenomas with rupture of the arachnoid, meningiomas of the olfactory groove, small meningiomas of the sellar tubercle
Type 2	Cisternal (contact and cisternal dissection)	Adenomas with extracapsular dissection, large meningiomas of the sellar tubercle, cisternal craniopharyngiomas, clivus and petroclival meningiomas or cholesteatomas, chordomas with intracranial invasion
Type 3	Ventricular (contact and intraventricular dissection)	Craniopharyngiomas with ventricular invasion, giant adenomas with ventricular invasion, gliomas, and hypothalamic hamartomas

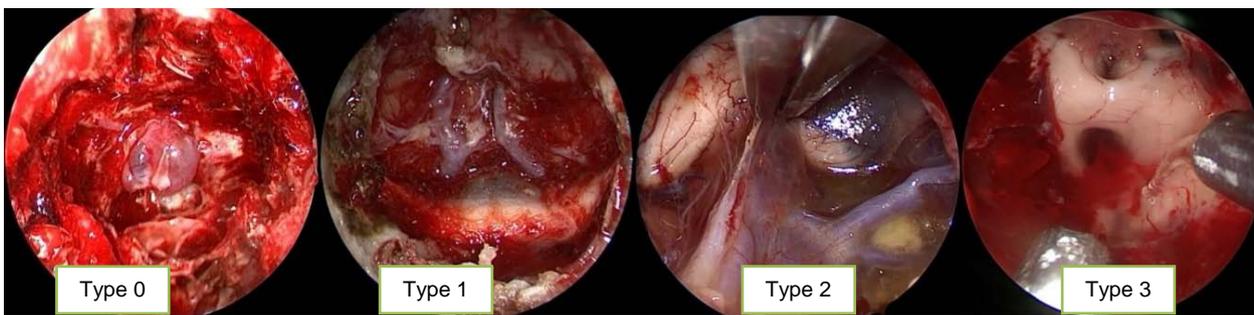


Fig. 1: Type of surgical cavity in relation to the intracranial hydrodynamic system. Type 0: no contact with the hydrodynamic system, Type 1: subarachnoid contact and dissection, Type 2: cisternal dissection, in this case in the interpeduncular cistern, Type 3: dissection inside the third ventricle.

III. RESULTS

Table 2 shows the distribution of patients with CSF leak according to the type of surgical cavity. It can be seen that in type 0 the incidence of fistula was 0.7%,

in type 1 it was 5%, while in type 2 it was 10.8% and in type 3 it was 18%. Figure 2 shows the increase in the CSF fistula as the type of surgical cavity increases.

Table 2: Distribution of patients with CSF leak according to the type of surgical cavity

CSF leak	Type of surgical cavity								Total		P
	Type0	%	Type1	%	Type2	%	Type3	%	N	%	
No	265	99,3 %	76	95 %	107	89,2%	68	82 %	516	93,8 %	0,000
Yes	2	0,7 %	4	5 %	13	10,8 %	15	18 %	34	6,2 %	
Total	267	100 %	80	100 %	120	100 %	83	100 %	550	100 %	

Source: Medical records

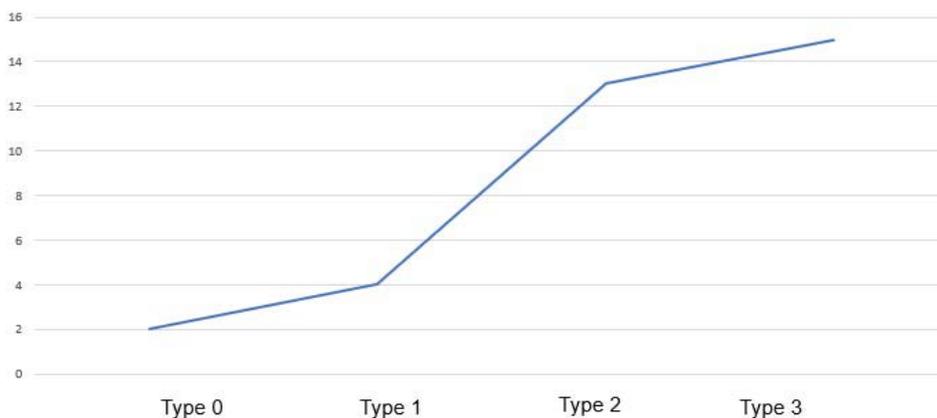


Fig. 2: Incidence of CSF fistula according to the type of surgical cavity

IV. DISCUSSION

The intracranial CSF circulation system is considered a hydrodynamic system. In physics and physiology, liquids do not flow through a pressure or velocity gradient, but through an energy gradient, which explains why sometimes the liquid flows against pressure and velocity gradients, which constitutes the Bernoulli Effect, where the pressure and velocity are part of that energy.^{4,5}

The CSF circulates from central hydrodynamic points of high energy, for example the cerebral ventricles, to points of lower energy such as the cisternal and subarachnoid spaces, until it is finally absorbed into the venous system through the arachnoid villi (point of very low energy).⁶

Intracranial tumors and especially cranial base tumors are approached by advanced surgical techniques such as Extended Endoscopic Endonasal

Approaches, achieving radical surgical exeresis in most cases. However, the resulting surgical cavity may contact or be part of some point of the intracranial hydrodynamic system therefore receives the influences of the hydrodynamic laws.^{1,2,6}

Table 2 and Figure 2 show a significant increase in the CSF leak index as the type of surgical cavity increases, showing a higher incidence in types 2 and 3.

Before analyzing this behavior, it is important to consider some concepts:

Surgical cavity: after a systematic review we did not find a precise concept, therefore, we define it as the anatomical space resulting from the surgical approach once the tumor exeresis has been performed.

Hydrodynamic pressure: It is the force exerted by the fluid in motion on the walls of the cavity. This movement is defined by a vector field of velocities corresponding to the particles of the fluid and a scalar field of pressures, corresponding to the different points of the fluid in the cavity.^{6,7}

Flow rate or output: It is the amount of liquid that flows in a given time by a part of the hydrodynamic system, for example, the amount of liquid that flows through the surgical cavity in 1 second.⁶

How do the laws of hydrodynamics influence surgical cavity?

First, if the surgical site is high-energy (the ventricular system), the hydrodynamic effect can overcome the resistance of the repair barrier, impede healing, and cause a CSF leak.

Second, the pressure of the CSF in motion increases in the surgical cavity above the pressure of the corresponding hydrodynamic point, that is, the pressure in the type 3 or ventricular surgical bed is going to be higher than the pressure in the Monroe hole, this effect occurs because this surgical space will constitute a widening of the hydrodynamic system.⁶⁻⁸

If we take an Extended Endoscopic Endonasal Approach to the Tubercle and Sphenoid Plane in the excision of a suprasellar tumor that reaches the third ventricle (Example: Craniopharyngioma) as an example, the surgical cavity that is created is type 3 (ventricular). That is, a cavity is created wide in ventricular contact that will suffer an increase in pressure higher than other normal ventricular points, for example, the hole of Monroe.^{6,7,9,10}

For this demonstration, the law of fluid continuity must be applied; the amount of liquid that flows through Monroe's foramen in a given time is the same as that which will flow through the surgical cavity, that is:

$$\text{Monro flow} = \text{Surgical cavity flow}$$

As the areas of the Monroe foramen and the surgical cavity are different; to establish that equality

then the liquid experiences an increase or decrease in flow velocity. For example, it increases its speed at the level of Monroe's foramen and decreases at the level of the surgical cavity.

If we apply Bernoulli's theorem, which deals with the law of conservation of energy, then the sum of the kinetic, potential and pressure energies of a moving liquid at a given point is equal to that of any other point and mathematically is expressed:

$$P_1 + KE_1 + GPE_1 = P_2 + KE_2 + GPE_2$$

If we take into account that the Potential Energy is similar in a patient lying down at rest with a slight flexion of the head of 15 degrees, at point 1 (Monro's hole) and Point 2 (surgical cavity), then:

$$P_1 + KE_1 + GPE_1 = P_2 + KE_2 + GPE_2$$

$P_1 + KE_1 = P_2 + KE_2$, so using the formula for kinetic energy:

$P_1 + \frac{1}{2} \text{Density} \times V_1^2 = P_2 + \frac{1}{2} \text{Density} \times V_2^2$, since it is the same fluid, the density is the same.

$P_1 + \text{Density} \times V_1^2 = P_2 + \frac{1}{2} \text{Density} \times V_2^2$, then this equality depends on the variables pressure and speed of the liquid.

We had previously defined that the velocity of the liquid in the surgical cavity was lower than in the Monroe Foramen, then: according to the laws of hydrodynamics to maintain equality in this Bernoulli equation, the pressure of the liquid in the surgical cavity is greater than the fluid pressure in the Monroe foramen. These equations can be applied to both ventricular, cisternal and subarachnoid points.^{6,7,11}

This hydrodynamic increase in CSF pressure in the surgical cavity explains the higher frequency of CSF fistula appearance as the type of surgical cavity increases.

V. CONCLUSIONS

According to the obtained results, it is essential to define the type of surgical cavity resulting from tumor exeresis and predict consequent hydrodynamic effects. The skull base repair strategy should have a broader concept that includes a multilayer repair barrier as a point of high resistance, as well as a decrease in hydrodynamic pressure in the surgical cavity through different methods: transient continuous spinal drainage (in Type 2) as well as permanent or temporary ventricular drainage (in Type 3). This would favor total healing and a decrease in the incidence of CSF leak.

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A Retrospective Study on the Complications of Ilizarov Technique in the Treatment of Neurogenic Talipes Equinovarus

By Xinjiang Lin, Shouping Chen & Shengke Xie

Abstract- In order to discuss the postoperative complications of Ilizarov technique in the treatment of neurogenic talipes equinovarus, we conducted a retrospective study on the postoperative complications of neurogenic talipes equinovarus patients treated with Ilizarov technique from January 2013 to December 2020. 182 patients (228 feet), 134 males (171 feet) and 48 females (57 feet). The age ranged from 4 to 70 ($\bar{x}23.6 \pm 13.9$) years old. There were 44 cases of sequelae of cerebral palsy (24.2%), 112 cases of sequelae of poliomyelitis (61.5%), 18 cases of congenital horseshoe foot (9.9%), and 8 cases of traumatic horseshoe foot (4.4%). The postoperative curative effect was evaluated, and the types of complications and their correlation with age were statistically analyzed. According to ICFSG score, the excellent and good rate of this group was 89.04%.

Keywords: *Ilizarov technology; Horseshoe varus foot; complications; tissue displacement syndrome; Retrospective study.*

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A RETROSPECTIVE STUDY ON THE COMPLICATIONS OF ILIZAROV TECHNIQUE IN THE TREATMENT OF NEUROGENIC TALIPES EQUINOVARUS

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Keywords: *Ilizarov technology; Horseshoe varus foot; complications; tissue displacement syndrome; Retrospective study.*

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I. INTRODUCTION

Neurogenic talipes equinovarus is a disease with the highest prevalence and the greatest harm among the modern disabled people. It is one of the common orthopedic malformations, and also a disease with the longest treatment cycle, greater difficulty and poor patient satisfaction. The main pathological change is due to the dislocation of calcaneus, talus and scaphoid, which leads to imbalance of muscle force and local tendon contracture. It is a three-dimensional deformity caused by complex pathological changes of soft tissue and bone and joint, mainly manifested as foot drop, high arch, varus, adduction and other foot and ankle deformities. Due to the relative lack of subcutaneous soft tissue and poor blood supply in the ankle, traditional surgery is easy to cause skin ischemic necrosis, postoperative secondary infection, soft tissue scar contracture and other complications, and the recurrence rate is as high as about 20% [1]. In order to reduce the complications of correction of neurogenic talipes equinovarus and reduce the recurrence rate after operation, we applied Ilizarov technology for treatment. Ilizarov technology is to install a special external fixator in the ankle, and gradually correct the deformity of horseshoe foot through slow tissue drafting. The clinical application of many scholars has proved that [2~3], not only the deformity correction is satisfactory, but also the shape and function of the foot can be preserved to the maximum extent, and at the same time, serious complications can be avoided and reduced. It is a safe and reliable method for the correction of neurogenic clubfoot. Due to the different treatment methods and various methods, it is necessary to carry out personalized force line analysis, osteotomy plane and angle design, neuromyoelectric test and analysis, determine tendon transposition, repair of nerve, blood vessel and skin tissues, and long-term, systematic and comprehensive rehabilitation training after surgery according to the patient's different age, sex, occupation, deformity, etc. Therefore, orthopedic physicians need to have comprehensive knowledge of basic medicine and clinical medicine. However, at present, there are not many orthopedic doctors who have received standardized training in China, and the amount of orthopedic operations is large, with many

therapeutic effects and postoperative complications. Therefore, this paper conducts a retrospective clinical study on the treatment effect and postoperative complications of 182 patients with complete data from 262 patients with neurogenic talipes equinovarus treated with Ilizarov technology in our hospital from January 2013 to December 2020.

II. PROPOSED METHOD

a) Inclusion criteria

- 1) Foot deformity secondary to nervous system diseases, such as cerebral palsy, poliomyelitis sequela, congenital horseshoe foot, etc;
- 2) Type III (severe) or above according to Dimeglio classification method;
- 3) No severe osteoporosis;
- 4) Patients with complete clinical data and follow-up ≥ 3 times.

b) Exclusion criteria

- 1) Soft clubfoot;
- 2) Plantar flexion deformity is less than 40° and there is no complaint of discomfort;

- 3) Patients with incomplete clinical data and follow-up less than 3 times.

c) General data

182 patients (228 feet) in this group. Among them, 136 were unilateral and 46 bilateral. 134 males (171 feet) and 48 females (57 feet). The age ranged from 4 to 70 (\bar{x} 23.64 \pm 13.96) years, 12 cases were ≤ 7 years old (6.6%), 52 cases were 8-17 years old (28.6%), 72 cases were 18-30 years old (39.6%), 44 cases were 31-59 years old (24.2%), and 2 cases were ≥ 60 years old (1.1%). Figure 1. Classification of diseases: 44 cases (24.2%) of sequelae of cerebral palsy, 112 cases (61.5%) of sequelae of poliomyelitis, 18 cases (9.9%) of congenital clubfoot, and 8 cases (4.4%) of traumatic clubfoot. Figure 2. Hospitalization time: 7~271 days (\bar{x} 83.19 \pm 43.8 days), return visits after discharge: 3~6 times (\bar{x} 3.4 \pm 0.63 times)

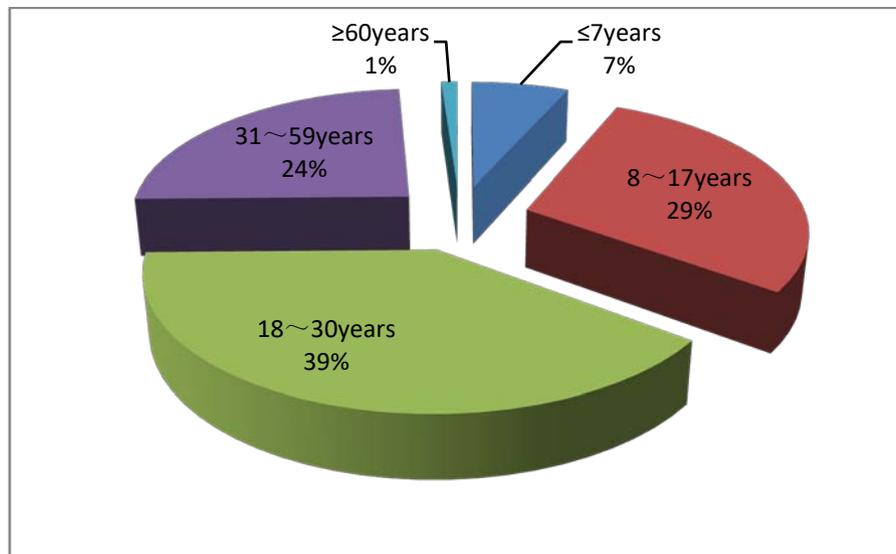


Figure 1: Age group (%)

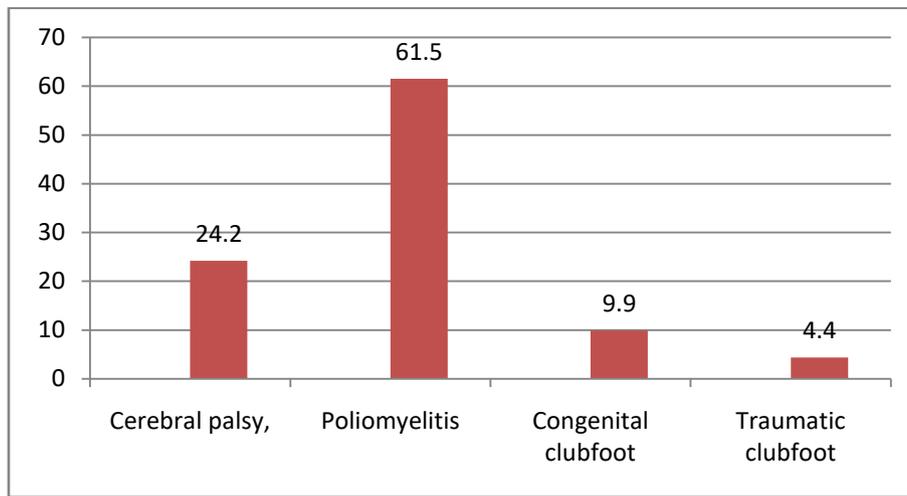


Figure 2: Disease classification (%)

d) *Treatment method*

According to the degree of bone deformity of the patient's foot, muscle strength, age, the degree of cooperation of the patient and his family, the ability of the doctor to master this technology and other factors, a personalized surgical plan is formulated. First, according to the degree of deformity of the patient's foot, the posterior medial soft tissue release, Achilles tendon lengthening, external transfer of tibial anterior muscle, osteotomy of the three joints of the foot, internal rotation osteotomy under the tibial tubercle and other soft tissue release, muscle force balance, osteotomy correction and joint fusion were selected, and then the Ilizarov external fixator was used for correction.

e) *Data collection and sorting*

During the hospitalization, the responsible physician (with 5-10 years of clinical experience) is responsible for tabulating, statistical analysis and sorting out the clinical symptoms, signs and relevant examinations of patients after using the Ilizarov external fixator. After the patient leaves the hospital, the responsible physician and the customer service department personnel will conduct telephone or on-site follow-up to the patient and his family members 1 month, 3 months, 6 months, 1 year or 2 years after the patient leaves the hospital. The responsible physician focuses on understanding the patient's disease, guiding the later rehabilitation, prevention and treatment of complications, frame adjustment, frame removal, reexamination, etc. The customer service department staff mainly understand the patient's recent situation, physical recovery, and the evaluation and suggestions on the hospital's work.

f) *Statistical methods*

All data were analyzed by SPSS 20.0 software. The measurement data are expressed as mean \pm standard deviation ($\bar{x} \pm S$). Take the percentage of 5 groups of data of the same variable, calculate the 99%

confidence interval and the correlation between the variables. The P value of the detection level is less than 0.05 on both sides, which is considered to be statistically significant.

III. RESULTS AND ANALYSIS

a) *Evaluation method and efficacy*

According to the ICFSG scoring standard, the patients were scored according to the 2-year follow-up after surgery. 228 feet, ICFSG score: excellent 136 feet, good 67 feet, fair 11 feet, poor 8 feet, the excellent and good rate is 89.04%.

b) *Postoperative complications and analysis*

The time of using Ilizarov external frame for this group of cases was 36~381 days ($\bar{x}86.3 \pm 56.5$). The patients were followed up for 1 month, 3 months, 6 months, 1 year or 2 years after discharge. The follow-up time ranged from 1 to 24 months, with an average of 16.2 months. Among them, 65 people (77 feet) had 16 kinds of complications, the incidence was 33.77%. It is significantly higher than 22.5% reported in the data [4]. We think it is related to different statistical caliber. English literature records the frequency of various complications during limb lengthening of Ilizarov, which may reach 100% [5,6].

i. *Early complications*

In this group, 147 patients (178 feet) had pain, swelling, numbness and other symptoms after operation, accounting for 78.07%. It lasted for 2~12 ($\bar{x} 5.85 \pm 2.41$) weeks, 13 feet had needle infection, 17 feet had loose connecting rods, 5 feet had broken needles, 3 feet had nerve injury and 2 feet had skin necrosis. Needle infection is a common complication in the process of Ilizarov external fixation device orthopedics, with an incidence of 21%~42% [7,8,9,10]. The incidence of cases in this group is low (5.7%). The main causes are thermal burns to tissues during operation, skin and muscle injuries caused by long-term traction, exposed



needle mouth pollution, and skin diseases of a few patients themselves. The causes of this group of cases were prevented in advance, such as using a protective sleeve when threading the needle during the operation, paying attention to the direction and strength of the steel needle and the condition of skin displacement, ensuring the skin is clean, and timely dealing with early infection. Therefore, the needle infection rate is far lower than that reported in the literature. In this group, one patient suffered from allergic dermatitis with infection and finally osteomyelitis due to untimely treatment of early needle infection. The loose connecting rod is mainly due to the loose screw fixation or more patient activities, especially in the rehabilitation training of patients with spastic cerebral palsy. In order to relieve local tension pain, individual patients adjust the screw by themselves. Two cases of common peroneal nerve injury and one case of posterior tibial nerve injury were caused by intraoperative traction. After the application of neurotrophic drugs, rehabilitation physiotherapy and other treatments, they all recovered completely. Two patients suffered from skin necrosis within 1 cm around the anterior medial tibial needle path due to skin heat injury, and recovered after dressing change. 5. The needle breaks at the edge of the fixed screw. Pull out the broken end and fix the broken pin again with the connecting piece, which does not affect the fixing effect.

ii. *Late complications*

The application of Ilizarov technology has created unique technical advantages for limb orthopedics, but there may be a variety of complications

in the application of Ilizarov technology, including needle infection, osteomyelitis, footswelling, toe flexion deformity, metatarsophalangeal joint subluxation, foot stiffness and even recurrence [11,12,13]. It is difficult to treat adult neurogenic talipes equinovarus, especially in patients with long course and severe deformity. Although there are many methods of surgical treatment, it is difficult to correct all malformations in one operation [14]. Repeated soft tissue release and osteotomy orthopaedic surgery are more likely to cause stiffness, small and pain of the foot and ankle [15,16]. Beaty JH. Freedman JA et al. [12,13,] believed that ankle and subtalar joint stiffness, arthritis, pain and residual deformity existed for a long time. In this group, 1.8% of the patients had limited knee movement, 2.6% had ankle arthritis and 1.3% had subtalar joint stiffness, which was lower than that reported in the literature. The deformity of toe flexion contracture was 5.7%. After orthopedic surgery, a kind of instinctive anti fall reflex causes the toe to flex and contract for a long time when the foot touches the ground, resulting in toe flexion contracture deformity. Parmanand Gupta et al. [17] believed that toe flexion contracture deformity is a complication that is difficult to treat, and once it occurs, it will not be able to participate in sports competitions as a professional athlete. In this group, 43 patients (49 feet) had limb pain, swelling, numbness and other symptoms more than 3 months after surgery, which we call "tissue displacement syndrome", accounting for 21.49%. The incidence of complications in different age groups is shown in Table 1.

Table 1: Postoperative complications at different ages

complication	≤7 year	8~17 year	18~30 year	31~59 year	≥60 year	Total (%)
Pain (>3 months)	1	2	12	9	1	25 (10.96)
Swelling (> 3 months)	1	2	10	9	1	23 (10.09%)
Numbness (> March)	1	5	16	12	1	35 (15.35%)
Needle infection	1	1	5	6	0	13 (5.7%)
Broken needle	0	0	2	3	0	5 (2.2%)
Loose connecting rod	1	2	6	8	0	17 (7.5%)
osteomyelitis	0	0	1	0	0	1 (0.4%)
Restricted knee movement	0	0	2	2	0	4 (1.8%)
Nonunion of bone	0	0	1	1	0	2 (0.9%)
Skin necrosis	0	1	0	1	0	2 (0.9%)
Nerve injury	0	0	1	1	0	3 (1.3%)
Ankle dislocation	0	0	2	1	0	3 (1.3%)
Toe flexion deformity	1	3	5	4	0	13 (5.7%)
recrudescence	0	1	1	1	0	3 (1.3%)
Ankle arthritis	0	0	3	3	0	6 (2.6%)
Subtalar joint stiffness	0	0	2	1	0	3 (1.3%)

iii. *Tissue displacement syndrome*

The clinical characteristics of equinovarus foot are mainly ankle plantar flexion, heel varus and forefoot adduction [18]. During the surgical correction, tendon transposition, such as Achilles tendon extension and tibial anterior tendon insertion, should be done. A few

patients need to do rectangular shortening osteotomy of the lateral column of the calcaneus, then use a steel needle to cross the calcaneus and metatarsal, connect the half ring and fix it on the calcaneus and foot back, and then slowly pull it for 2 to 3 months, so that the forefoot and midfoot gradually rotate outward and turn

outward, so as to restore the normal appearance of the foot. During the whole operation and slow tissue traction process, the tissue has been displaced, local microvessels have been damaged, and circulation obstacles have occurred, leading to local swelling; Pain caused by tissue injury, hemorrhage, edema, and inflammatory stimulation; Tissue compression, nerve damage, numbness. This series of pathophysiological reactions is called "tissue displacement syndrome". The similar reaction in the earlier stage is "tissue displacement reaction". If the angle of the external frame is adjusted properly or the speed of frame adjustment is slowed down, drug treatment, physical therapy and other comprehensive treatments are carried out, and the symptoms still have no significant change and affect the normal walking function after more than 3 months, it is called "tissue displacement syndrome". The severity of the syndrome is related to surgical trauma, displacement angle, traction time, speed, patient age, and body regeneration and repair ability. In this group, most of the patients with "tissue displacement syndrome" occurred in adults over 18 years old, and

there was a significant positive correlation with age ($P < 0.05-0.01$). Among the 43 patients with "tissue displacement syndrome" in this group, 26 (60.47%) were followed up 1 year after discharge, and 12 (27.91%) were followed up 2 years after discharge. The symptoms such as swelling and pain of the patients' limbs basically disappeared, and some patients felt a little numbness locally, but the walking function of the limbs was not affected. Five patients were not followed up. The symptoms of patients with "tissue displacement syndrome" persist, but the prognosis is good.

c) *Correlation between complications and age*

The correlation test was conducted between the first 6 complications with high incidence rate and different age variables. Among them, pain, swelling and numbness (tissue displacement syndrome) were positively correlated with age ($P < 0.05-0.01$). There was no correlation between needle infection, loose connecting rod and toe flexion deformity and age ($P > 0.05$). Table 2.

Table 2: Correlation between major complications and different age variables

age (year)	pain	swelling	numbness	needle infection	Loose connecting rod	toe flexion deformity
≤7	0.83	0.83	0.83	8.3	8.3	8.3
8~17	3.85	3.85	9.62	1.9	3.8	5.8
18~30	16.67	13.89	22.22	6.9	8.7	6.9
31~59	20.45	20.45	27.27	13.6	18.2	9.1
≥60岁	50.00	50.00	50.00	0	0	0
r	0.93	0.926	0.976	-0.144	0.51	-0.585
p	<0.05	<0.05	<0.01	>0.05	>0.05	>0.05

d) *Prevention measures*

The distraction osteogenesis theory of Ilizarov technology has proved that the external fixator is beneficial to the shape recovery of various bone tissues, the adjustment and maintenance of limb length during the slow traction process, so that the correction of talipes equinovarus deformity can obtain satisfactory results for clinicians and patients [18, 19]. However, due to the wide variety of configurations of external fixation devices, wide surgical indications, and long learning curve of postoperative management process and doctors, errors are inevitable in the treatment process, and problems in any link, such as needle threading and installation of external fixators, needle bag, postoperative management and guidance of patients' functional training, and the time to remove external fixators, may occur large and small complications [4]. However, through our efforts, most of these complications can be avoided. Paley [20] divided the problems arising from the application of Ilizarov technology into three categories: one is called problems, which can be solved without surgery; The second type is called obstacle, which needs to be solved by reoperation, but will not leave sequela; The

three types are called complications, which will still leave morphological abnormalities or dysfunction after treatment. According to the Paley classification, there are 6 kinds of "problems" in this group, of which 3 are "tissue displacement syndrome"; 6 "obstacles"; There were 4 kinds of "complications", 25 feet, accounting for 10.96%.

Orthopedic surgery (including peripheral nerve surgery) is recommended by the bone and joint professional committee of the Chinese Rehabilitation Medical Association, the China Brain Palsy Multidisciplinary Cooperation Alliance, and the surgical treatment experts of spastic cerebral palsy by consensus as the second stage surgery of spastic cerebral palsy, an important supplement to SPR surgery, and is not recommended to take corrective surgery first. It is suggested that rehabilitation training is an important guarantee for postoperative functional improvement. Advocate the concept of "three points operation, seven points training" [21]. Therefore, the key to the successful treatment of neurogenic clubfoot is to objectively predict the surgical effect, fully communicate with patients, reduce patients' expectations, improve patients' compliance, strengthen the sense of

responsibility of medical personnel, scientifically, rigorously and strictly control the surgical indications, reduce complications, strengthen long-term and standardized rehabilitation training for patients after surgery, and cooperate with doctors and patients.

IV. CONCLUSION

In this group, 182 patients (228 feet) with neurogenic clubfoot were treated with Ilizarov external fixator, and the excellent and good rate was 89.04%. There were 16 kinds of complications, accounting for 33.77%. In the early stage, pain, swelling, numbness and other "tissue displacement reactions" were the main symptoms (78.07%). In the later stage, "tissue displacement syndrome" occurred (21.49%), but the prognosis was good. Among them, 88.37% of the patients had basically recovered from follow-up data within two years. The loose connecting rod accounted for 7.5%, toe flexion deformity and needle infection accounted for 5.7% respectively. The main complications increased with age, and there was a significant positive correlation between complications and age ($P < 0.05$). However, through our efforts, most of these complications can be avoided. Therefore, in the process of applying Ilizarov technology to correct neurogenic talipes equinovarus, we should strengthen the sense of responsibility of medical personnel and improve their professional skills. Scientific, rigorous and strict control of surgical indications. Do a good job of communication between doctors and patients before surgery to improve patients' compliance with treatment. Personalized installation and adjustment of the external frame, strengthening long-term postoperative rehabilitation training, and other factors are the key to reduce complications and successfully treat neurogenic clubfoot.

Data Availability

The data used to support the study are included in the paper.

Conflicts of Interest

The authors declare that there are no conflicts of interest.

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Mexican Screening Test for Olfactory Dysfunction using Essential Oils

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Abstract- Introduction: Olfaction is important for us to relate to the environment. Approximately 25% of the population over 40 years of age has an olfactory disorder. Olfactory alterations have a negative impact on quality of life, affecting self-esteem, generating depression, social isolation, and even altering eating habits. There are multiple etiologies: post-viral, traumatic, metabolic, secondary to medication, smoking and alcoholism, neurodegenerative diseases, among others. The tests available to screen for hyposmia include pens and books that give off scents, are expensive, difficult to access, require trained personnel to apply them and have been standardized in populations culturally different from the Mexican population, which makes it difficult to detect patients.

Objectives: To create, standardize and validate a screening test for olfactory alterations based on essential oils for the Mexican population.

Keywords: *olfactory disorders, olfactory loss, screening, diagnosis.*

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Mexican Screening Test for Olfactory Dysfunction using Essential Oils

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Abstract- Introduction: Olfaction is important for us to relate to the environment. Approximately 25% of the population over 40 years of age has an olfactory disorder. Olfactory alterations have a negative impact on quality of life, affecting self-esteem, generating depression, social isolation, and even altering eating habits. There are multiple etiologies: post-viral, traumatic, metabolic, secondary to medication, smoking and alcoholism, neurodegenerative diseases, among others. The tests available to screen for hyposmia include pens and books that give off scents, are expensive, difficult to access, require trained personnel to apply them and have been standardized in populations culturally different from the Mexican population, which makes it difficult to detect patients.

Objectives: To create, standardize and validate a screening test for olfactory alterations based on essential oils for the Mexican population.

Methods: A smell test was created with the aromas: lemon, cinnamon, chocolate, coffee and mint, and it was standardized in a previous work, with the application of 630 tests. Subsequently, the results of application were compared with the results obtained by applying the University of Pennsylvania Smell Identification Test and the identification part of the Sniffin Sticks test.

Results: The test obtained a sensitivity of 0.93, specificity of 0.77, negative predictive value of 0.9 and positive of 0.77, data compared with the Gold Standard test, demonstrating its non-inferiority.

Conclusion: The screening test with essential oils is a valid, reliable, affordable, fast and easy to apply test to detect olfactory alterations in the Mexican population.

Keywords: olfactory disorders, olfactory loss, screening, diagnosis.

1. INTRODUCTION

The ability to smell allows us to enjoy food, relate to others and even protect ourselves from danger. Moreover, because of its connections with the limbic system, it allows us to evoke intense emotions and memories¹.

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Olfactory disorders are classified into qualitative problems (dysosmias, i.e., altered olfactory perception) and quantitative problems (where the intensity of olfactory perception is affected and includes hyposmia and anosmia)².

Of people over 40 years of age, 25% have some olfactory disorder, which increases with age, reaching a prevalence of 40-62% in people over 80 years of age^{3,4}. The causes of these conditions are: nasosinusal alterations, post-infectious olfactory dysfunction, presbyosmia, post-traumatic, secondary to medication, chronic smoking and alcoholism, neurodegenerative diseases, metabolic and genetic diseases^{5,6}.

The presence of olfactory alterations has an impact on the quality of life of sufferers, generating depression, social isolation, feelings of vulnerability, self-esteem problems and causing insecurity, since up to 60% of those affected report difficulty in noticing a gas leak or the presence of smoke. Eating habits, personal hygiene and sexual performance are affected^{7,8,9}.

Olfactory impairment is a predictor of mortality, since subjects > 60 years of age with anosmia are 3 times more likely to die at 5 years than normosmic patients¹⁰.

Existing tests for screening for hyposmia are variable, including pens such as the Sniffin Sticks (SS) test^{11,12}, booklets such as the University of Pennsylvania Smell Identification Test (UPSIT) or disks that give off scents^{13,14}. They are expensive, not very accessible in Mexico and require training to perform them. These tests have been standardized in populations culturally very different from the Mexican population, so the type of aromas^{15,16,17} their familiarity and therefore their identification are different in Mexico. This makes it difficult to detect patients and to know the prevalence of hyposmia in our population.

So far no studies have been conducted on the usefulness of using commercial essential oils in the detection of hyposmia, which are readily available, inexpensive, and easy and quick to use.

In Mexico there is no standardized test for the screening of olfactory alterations, so this work proposes the development and validation of a test of essential oils for this purpose.

II. MATERIALS AND METHODS

A descriptive study was carried out, in which two groups were created, one with subjective hyposmia of different etiologies and another age and gender matched control group made up of healthy people who denied symptomatic hyposmia.

The patients were recruited at the National Rehabilitation Institute-LGII within the period June 2021-March 2022.

The case group included subjects older than 18 years with hyposmia caused by nasal conditions: attic septal deviation, acute sinusitis, chronic sinusitis with and without polyps, nasal tumors, upper airway infections including COVID 19 corroborated by PCR, Parkinson's disease.

All subjects underwent nasal endoscopy to corroborate the presence of nasal conditions. Subjects with active smoking and those with a history of nose and sinus surgery were excluded.

The following scales were applied to each case with olfactory alterations: Sinonasal Outcome 22 (SNOT 22)^{19,20,21} and Questionnaire of Olfactory Disorders-Negative Statements (QOD NS),^{22,23} and an endoscopic scale was used to evaluate the state of the olfactory cleft: The olfactory cleft endoscopy scale (OCES).²⁴

To evaluate the olfactory function, the University of Pennsylvania Smell Identification Test (UPSIT) and the Sniffin Sticks test, the identification subset with 16 aromas, were applied. In this same consultation, the test with essential oils was applied to each participant. The order of the olfactory evaluation was as follows: UPSIT, essential oil test, Sniffin Sticks.

Between each test a 5-minute break was taken to prevent olfactory memory from influencing the results and to allow for mental relaxation of the participants.

In a previous investigation, this test of commercial essential oils was standardized²⁵. This test consists briefly in the use of 5 aromas: lemon, chocolate, cinnamon, coffee, mint and a control with no odor (Image 1).

The interpretation of this test will be only if the patient correctly or incorrectly identified each aroma, therefore it fluctuates between 0-5, if the subject obtains 0=anosmia, 1,2,3= hyposmia and 4,5 points= normosmia (Image 2). (Image 2).

The statistical package Prisma was used. Statistical significance was considered with a $p < 0.05$.

For olfactory function, each participant obtained three scores derived from the tests used: number of essential oils correctly identified, score on the University of Pennsylvania Smell Identification Test and score on the Sniffin Sticks test and also obtained an olfactory diagnosis from each test: Normosmia, hyposmia or anosmia.

Fisher's exact test was used to compare the numbers of anosmic, hyposmic and normosmic

subjects with scores of 0- 5 correctly identified oils, these results were compared with the UPSIT and Sniffin Sticks scores.

Sensitivity and specificity of test results were determined by performing 2 x 2 contingency tables.

III. RESULTS

A total of 33 subjects were analyzed, 17 in the case group and 16 in the control group. The case group consisted of 7 women and 10 men, the age range was 18-82 years with a mean age of 41 years. The control group consisted of 7 women and 9 men, the age range was 18-81 years with a mean age of 46 years.

Regarding the cause of hyposmia in the case group, 2 had no identifiable cause, 5 were due to COVID 19, 3 due to nasosinus conditions, 4 due to Parkinson's disease and 3 due to cranioencephalic trauma.

The presence of nasal alterations, tumors or infectious diseases was ruled out in all the controls by nasal endoscopy. The mean score on the endoscopic evaluation scale of the olfactory sulcus "OCES", in the cases, was 1.1 points in the right nostril and 1.2 in the left nostril.

Regarding quality of life, in the group of cases, the range of scores was 8-33 points, with a mean of 25, which in percentage of affection of 1-100 translates into 14%-57.8%.

For the Sniffin Sticks test the scores were 1 - 15 in the case group and for the controls 11- 15.

In the UPSIT test the score in the case group was 9-29 and in the controls from 25 to 40. With this test in the group of cases all had some degree of hyposmia and in the group of controls 4 had mild microsmia, 2 with moderate and 1 with severe, the subjects with mild and moderate microsmia had no alterations in the other two tests and the one with severe hyposmia was normal in the Sniffin Sticks test and with hyposmia in the essential oils test.

For the essential oils test, a score of 4 and 5 points was taken as normal, hyposmia 1-3 and anosmia 0. An additional point was added to be taken into account in the final score; for each aroma, the intensity with which each aroma was perceived was questioned and if the subject did not perceive an aroma or if 3 of the aromas were perceived with slight intensity, one point was subtracted from the total number of correctly identified aromas (this variant was called modified oils test in the analysis).

Table 1 shows the olfactory results obtained with the different tests, sensitivity, specificity, positive and negative predictive value and confidence interval calculated with Fisher's test.

IV. DISCUSSION

The screening test for olfactory disorders with essential oils proved to be an option with acceptable

sensitivity and specificity. Figures ranging from 0.88-0.93 and 0.41- 0.77 respectively.

In 2018 in Barcelona Campabadal et al. determined the sensitivity and specificity of the UPSIT test Spanish version in a population with Parkinson's disease: 97 subjects, and healthy controls: 65 and determined that the sensitivity was 81.4% and specificity 100% with a cut-off point ≤ 25 points.²⁶

Hummel and his team in 1997 created the Sniffin Sticks test, applied it to a group of 104 healthy subjects (52 women, 52 men, mean age 49.5 years, range 18-84 years) and compared it to an established measure of olfactory performance; the Connecticut Clinical Chemosensory Research Center Test, CCCRC²⁷. The use of the different subsets separately has been found to have a sensitivity and specificity of 84%.²⁸

Sorokowska et al. in 2019 conducted a multicenter study in Germany with 333 subjects with olfactory disturbances of different etiologies, aged 12-88 years. In whom they evaluated the clinical utility of employing a test created by the researchers "Q-Sticks test", a test composed of the aromas of clove, coffee and roses. Their test obtained a sensitivity of 91.8% and a specificity of 92%.²⁹

A retrospective study was carried out in Germany in 2016 with 613 subjects with an age range of 18-96 years, they included subjects with olfactory disturbances (464) of different etiologies and controls (149), to whom they applied the Sniffin Sticks olfactory identification subset containing 16 scents. All participants underwent nasal endoscopy and medical history. They created a score for each aroma based on the following division: % of subjects with normosmia who correctly identified it between % of subjects with identifiable cause of hyposmia who correctly identified it and called it "odor specificity score", then using a calculated ABC analysis which is a classification method used in economics, which allows identifying items that have an important impact on an overall value they selected 3 aromas. Cinnamon, fish and banana were correctly identified by the largest number of normosmic subjects, with this battery of tests they obtained a sensitivity of 80.4%, specificity of 84.3% and a negative predictive value of 91.3%.³⁰

It is important to mention that, during the analysis of the test results, we noticed the differences between the tests at the time of interpreting their results, i.e., the UPSIT test graduates the level of hyposmia into mild microsmia, moderate or severe hyposmia, while the Sniffin Sticks and the essential oils test only identifies normosmia, hyposmia or anosmia. Because of these differences, subjects who obtained normosmia in the last two tests, but mild microsmia in the UPSIT test were considered to have normosmia, thus obtaining different figures for sensitivity, specificity, negative predictive value and positive predictive value.

In addition, when taking into account the intensity of aroma perception in the oil test; "modified oil test" increased all the parameters analyzed.

The essential oil screening test we propose is an effective method, easily accessible, cost-effective and quick to apply. With respect to its sensitivity and specificity, it is very similar to that shown by other tests, thus determining its non-inferiority.

The great limitation of this study is the low number of samples; however, due to the favorable behavior of the data, it can be inferred that by increasing the number of subjects, similar results will be obtained.

V. CONCLUSION

This is a first step in the detection of olfactory disorders in Mexico; however, future research is needed to extend the level of diagnosis, in order to obtain a test with which to follow up patients or even determine the efficacy of certain treatments.

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Ophthalmological and Psychological Sequelae in Children Investigated in the Retinopathy of Prematurity Program between 2002 and 2010

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Resumen- La retinopatía del prematuro es una enfermedad vasoproliferativa de origen multifactorial cuyo principal factor de riesgo es la inmadurez vascular dejando secuelas visuales y neurocognitivas.

Objetivo: Caracterizar la evolución oftalmológica y psicológica de los pacientes diagnosticados con algún grado de ROP del año 2002 al 2010.

Metodología: Se realizó un estudio de investigación-desarrollo, descriptivo y de corte transversal en el Hospital Clínico Quirúrgico Universitario “Arnaldo Milián Castro” de la Ciudad de Santa Clara en el período comprendido desde septiembre del 2002 hasta septiembre del 2010.

Palabras claves: retinopatía del prematuro, secuelas oftalmológicas, secuelas psicológicas.

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OPHTHALMOLOGICAL AND PSYCHOLOGICAL SEQUELAE IN CHILDREN INVESTIGATED IN THE RETINOPATHY OF PREMATURITY PROGRAM BETWEEN 2002 AND 2010

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Ophthalmological and Psychological Sequelae in Children Investigated in the Retinopathy of Prematurity Program between 2002 and 2010

“Secuelas Oftalmológicas y Psicológicas En Los Niños Pesquisados En El Programa De Retinopatía De La Prematuridad Entre Los Años 2002 y 2010”

Dra. Zoila Fariñas Falcón ^α, Dra. Dailenys Peña Mollineda ^σ, Lic. Gladys Diosdada Membrides Pérez ^ρ & Lic. Yipsi Ruiz Vega ^ω

Resumen- La retinopatía del prematuro es una enfermedad vasoproliferativa de origen multifactorial cuyo principal factor de riesgo es la inmadurez vascular dejando secuelas visuales y neurocognitivas.

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Resultados: Predominaron los niños que nacieron desde las 30 hasta las 31,6 semanas, con un peso de 1 250gr hasta 1 499 gr, el factor de riesgo más frecuente fue la oxigenoterapia, y predominó la ROP 1, lo que concuerda con las secuelas oftalmológicas y psicológica encontradas, los más frecuentes fueron los trastornos en la organicidad.

Conclusiones: Los niños que presentaron estadíos avanzados de la enfermedad fueron los de mayores secuelas en la esfera visual y psicológica.

Palabras claves: retinopatía del prematuro, secuelas oftalmológicas, secuelas psicológicas.

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I. INTRODUCCIÓN

La retinopatía del prematuro (ROP, siglas en inglés) es una enfermedad vasoproliferativa de origen multifactorial. ⁽¹⁻³⁾

Los primeros indicios datan de 1940 cuando el Dr. Steward reconoce la patología ⁽⁴⁾. En países industrializados se describen dos epidemias de la misma, la tercera es la que se vive actualmente en países en vías de desarrollo, particularmente en América Latina ⁽⁵⁻⁷⁾.

El principal factor de riesgo es la inmadurez vascular, niños prematuros especialmente con menos de 1 500g de peso al nacer y/o menores de 30 semanas de gestación ⁽⁸⁾, cuanto menores son el peso y la edad gestacional mayor es la incidencia ⁽⁹⁻¹²⁾. También se han asociado otros como la fluctuación en la oxigenación temprana (hiperoxia e hipoxia) ⁽¹³⁻¹⁵⁾ que aunado al desequilibrio de los factores de crecimiento, llevarán a la neoformación de vasos ⁽¹⁶⁻¹⁷⁾, la apnea, acidosis metabólica, sepsis, transfusiones sanguíneas, la hemorragia intraventricular, ventilación mecánica, la persistencia del ducto arterioso ^(5, 18, 19), de gran importancia pues es el origen de más de la mitad de las condiciones patológicas del recién nacido ⁽²⁰⁾, las drogas y la genética. ⁽⁵⁾ Los estudios futuros que hagan uso de la genómica podrían ser útiles para la identificación de factores genéticos relevantes. ⁽²¹⁾

Los niños con ROP tienen múltiples alteraciones oftalmológicas como errores refractivos altos, catarata y glaucoma, numerosas secuelas en el segmento posterior, hasta la ceguera por desprendimiento de la retina ^(22,23).

Muchos niños pretérminos tienen problemas con la atención, la memoria, el procesamiento complejo del lenguaje, el razonamiento no verbal, las habilidades viso-perceptuales, funciones ejecutivas, la relación personal y social y en la calidad de la lecto-escritura, lo que ocasiona, muchas veces, trastornos específicos del aprendizaje, básicamente dificultades para aprender la lectura y la escritura (dislexia y disgrafía) que interfieren

en el aprendizaje, la conducta y su rendimiento escolar.⁽²⁴⁾ Cada bebé es distinto a los demás y algunos pueden tener riesgo de alteraciones psicológicas⁽²⁵⁾ porque los gestos y las conductas sociales requieren de retroalimentación visual, por tanto, su falta parcial o total pone al niño en situación de riesgo.⁽²⁶⁾ Los déficits que se produzcan a partir de estos trastornos van a afectar los ámbitos personal, social y académico, y la capacidad funcional del individuo por el resto de su vida.^(27,28)

En Cuba, el perfeccionamiento del Programa Materno Infantil, ha hecho posible que cada vez sobrevivan más niños con pesos inferiores a los 1 250 gramos, aumentando la morbilidad de la ROP,⁽²⁹⁾ que es la primera causa de ceguera infantil: 16 de cada 100 niños pesquizados cada año desarrollan la enfermedad y se alcanza una tasa de sobre vida del 91%. La implementación del protocolo de investigación nacional y el desarrollo científico tecnológico alcanzado en las terapias de cuidados intensivos neonatales del país permiten que se logre este resultado.⁽⁵⁾

La prevención y la pesquisa de la ceguera por ROP es un programa internacional que se implementa en Cuba a finales del año 2002. Villa Clara es pionera en este programa de intervención para el seguimiento y el control de los pacientes afectados,⁽²⁹⁾ pues un número significativo que desarrollan ROP tendrá resultados visuales (14,5%) y estructurales (9,1%) desfavorables, haya o no recibido tratamiento, por tanto, el esmero en el seguimiento debe ser grande.⁽³⁰⁾

Motivado por esto y no habiendo estudios preliminares sobre la morbilidad en este grupo de pacientes pesquizados en la provincia, se decide hacer una investigación para saber cuáles son las secuelas oftalmológicas y psicológicas en los pacientes que nacieron de partos prematuros y que fueron pesquizados en el Programa de retinopatía de la prematuridad en el Hospital Materno “Mariana Grajales” de Villa Clara en el período comprendido del año 2002 al 2010.

II. MÉTODO

Se realizó un estudio de investigación-desarrollo, descriptivo y de corte transversal. La población estuvo constituida por los 45 pacientes pesquizados en el Programa de retinopatía de la prematuridad desde el año 2002 y hasta el año 2010,

que se encuentran en las edades escolares de 7 a 17 años y que presentaron algún estadio de ROP. La muestra quedó conformada por los 30 pacientes con los que se pudo contactar y acudieron a la consulta tanto de Oftalmología como de Psicología en los años 2018-2020.

a) Métodos de obtención de la información

Previo consentimiento informado de los padres de cada niño se les realizó una entrevista personal y se confeccionó una historia clínica para lo que fueron interrogados sobre aspectos relacionados con los antecedentes perinatales, se registró el estado del aparato visual que se evaluó mediante la realización del examen oftalmológico en el Hospital Clínico Quirúrgico Universitario “Arnaldo Milián Castro”. Se derivaron hacia la Consulta de Psicología del Hospital Pediátrico “José Luis Miranda” para evaluar las alteraciones psicológicas de estos pacientes mediante la realización de varias pruebas psicométricas.

b) Variables

Peso al nacer:
Edad gestacional:
Factores de riesgo al nacer:
Estadio clínico de ROP:
Edad en el momento del estudio:
Examen oftalmológico en el momento del estudio:
Agudeza visual
Examen refractivo
Fondo de ojo por oftalmoscopia binocular indirecta
Alteraciones psicológicas:

c) Procesamiento de la información

Las variables fueron tipificadas y los datos vertidos en bases de datos en Excel del paquete Microsoft Office 10 e importadas al programa estadístico SPSS 15 para su estudio. Se realizó análisis estadístico utilizando medidas de resumen para variables, determinándose frecuencias absolutas, porcentajes, media, mediana, valor mínimo y máximo. Las variables categóricas se analizaron con la prueba no paramétrica de independencia Chi cuadrado (X^2) y la prueba exacta de Fisher. Para una confiabilidad del 95% si $p < \alpha$ (0,05) se rechaza H_0 . Los resultados fueron interpretados mediante tablas y figuras.

III. RESULTADOS

Tabla 1: Distribución de los pacientes según el sexo y el grupo de edad en el momento del estudio.

Grupo de edad	Sexo				Total	%
	Masculino	%	Femenino	%		
De 7 a 11	5	16,67	5	16,67	10	33,33
De 12 a 17	9	30	11	36,67	20	66,67
Total	14	46,67	16	53,33	30	100

Fuente: historia clínica

La población estuvo constituida por 30 pacientes, el 53,33% corresponde al sexo femenino. El grupo de edad que con mayor frecuencia fue el comprendido entre los 12 y los 17 años (66,67%). El promedio de edad fue de 12,6 años, con desviación estándar de 3,03 años.

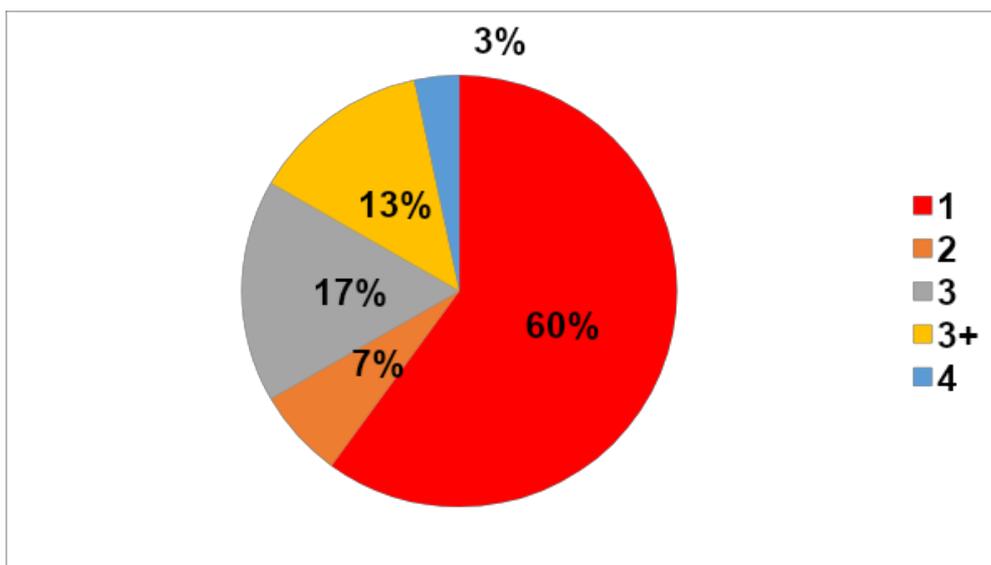
Tabla 2: Distribución de los niños según el peso al nacer y la edad gestacional.

Peso al nacer	Edad gestacional en semanas								Total	%
	Menos de 30	%	De 30 a 31,6	%	De 32 a 34,6	%	De 35 a 36,6	%		
Menos de 1 000	1	3,33	0	0	0	0	1	3,33	2	6,67
De 1 000 a 1 249	5	16,67	0	0	2	6,67	0	0	7	23,33
De 1 250 a 1 499	0	0	7	23,33	2	6,67	1	3,33	10	33,33
De 1 500 a 1 699	0	0	2	6,67	0	0	1	3,33	3	10
De 1 700 y más	0	0	1	3,33	3	10	4	13,33	8	26,67
Total	6	20	10	33,33	7	23,33	7	23,33	30	100

Estadístico exacto de Fisher: 25,399 p: 0,00

Fuente: historia clínica

El 33,33% del total de la muestra nació con un peso entre 1 250gr y 1 499gr, de igual forma el 33,33% nació entre las 30 semanas y las 31,6 semanas de gestación. Hubo asociación significativa entre el peso al nacer y la edad gestacional ($p < 0,05$).



Fuente: historia clínica

Gráfico 1: Distribución de la población según el estadio clínico de ROP

El 60% de los pacientes se clasificaron en el estadio 1 de ROP. Solo el 13% evolucionó a estadio 3+ y hubo solamente 1 paciente en estadio 4 (3,33%); no hubo pacientes clasificados en el estadio 5.

Tabla 3: Frecuencia de los factores de riesgo al nacer

Factores de riesgo al nacer	Frecuencia	%
Gemelaridad	8	26,67
Síndrome de disfunción respiratoria	5	16,67
Transfusión	6	20,00
Oxigenoterapia	26	86,67

Ventilación artificial	4	13,33
Infecciones	10	33,33
Íctero	4	13,33
Otros	3	10

Fuente: historia clínica

Todos los pacientes presentaron factores de riesgo al nacer, la oxigenoterapia fue el más representativo (86,67%). Se encontraron otros factores de riesgo al nacer pero no resultaron frecuentes.

Tabla 4: Afectación de la agudeza visual según el estadio clínico de ROP

Afectación visual	Estadio clínico de ROP										Total	%
	1	%	2	%	3	%	3+	%	4	%		
Normal	9	30,00	1	3,33	1	3,33	0	0,00	0	0,00	11	36,67
Ligera	7	23,33	0	0,00	1	3,33	1	3,33	0	0,00	9	30,00
Moderada	1	3,33	1	3,33	1	3,33	1	3,33	0	0,00	4	13,33
Severa	1	3,33	0	0,00	2	6,67	2	6,67	1	3,33	6	20,00
Total	18	60,00	2	6,67	5	16,67	4	13,33	1	3,33	30	100,00

Estadístico exacto de Fisher= 16,249 P=0,042

Fuente: historia clínica

En el 36,67% de los pacientes la agudeza visual fue normal, de ellos 9 clasificados en estadio 1 de ROP, del 30% de los pacientes con afectación visual ligera 7 estaban clasificados en estadio 1 de ROP y solo el 20% tuvo afectación visual severa. La afectación visual estuvo significativamente asociada al estadio clínico de ROP ($p < 0,05$).

Tabla 5: Refracción acorde al estadio clínico de ROP

Refracción	Estadio clínico de ROP										Total	%
	1	%	2	%	3	%	3+	%	4	%		
Astigmatismo hipermetrópico	12	40,00	2	6,67	1	3,33	1	3,33	0	0,00	16	53,33
Astigmatismo miópico	3	10,00	0	0,00	3	10,00	2	6,67	1	3,33	9	30,00
Ambliopía	1	3,33	0	0,00	0	0,00	0	0,00	0	0,00	1	3,33
Anisometropía	2	6,67	0	0,00	1	3,33	1	3,33	0	0,00	4	13,33
Total	18	60,00	2	6,67	5	16,67	4	13,33	1	3,33	30	100,00

Estadístico exacto de Fisher 18,539 $p = 0,277$

Fuente: historia clínica

El 53,33% tiene astigmatismo hipermetrópico, de ellos 12 en el estadio 1 de ROP, con astigmatismo miopico se diagnosticó el 30% de los pacientes y solo el 3,3% tuvo ambliopía. No se observó asociación significativa entre la refracción y el estadio de ROP ($p > 0,05$).

Tabla 6: Hallazgos en el fondo de ojo por oftalmoscopia binocular indirecta según el estadio clínico de ROP

Hallazgos en el fondo de ojo	Estadíos de ROP					Total	%	Estadístico exacto de Fisher	P
	1	2	3	3+	4				
Palidez del disco	1	1	3	2	0	7	23,33	10,051	0,014
Ectopia macular	0	0	3	2	1	6	20,00	15,200	0,001
Ectopia papilar	0	0	1	2	0	3	10,00	8,917	0,039
Retinopatía miópica	3	0	0	0	0	3	10,00	2,311	1,000
Lesiones de crioterapia	0	0	4	0	1	5	16,67	17,882	0,002
Lesiones de láser	0	1	1	4	0	6	20,00	13,723	0,002
Ninguno	15	0	0	0	0	15	50,00		
Otros	0	0	0	1	1	2	6,67	6,493	0,110

Fuente: historia clínica

El 50% de los pacientes no presentó lesiones en el fondo de ojo. El 23,33% tuvo palidez del disco y el 20% ectopia macular, en ambos la frecuencia fue mayor en la ROP 3, la retinopatía miópica se presentó en el

10% de los casos, todos en estadio 1. Como secuelas de los tratamientos se observaron lesiones por la crioterapia y láser; En todos los hallazgos se observó una relación significativa con el grado ROP.

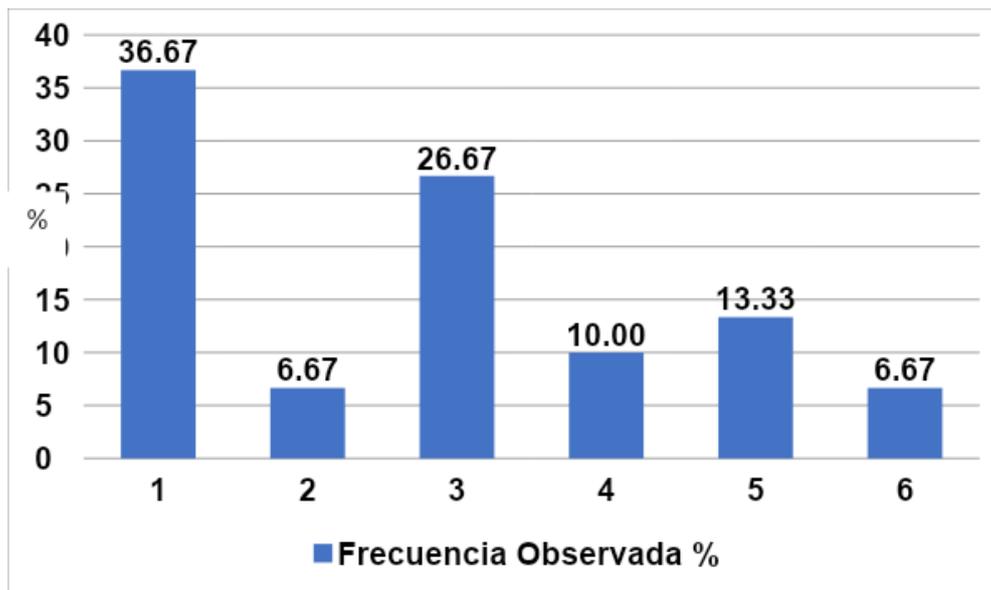


Gráfico 2: Distribución de la cantidad de alteraciones psicológicas encontradas

Las alteraciones más observadas fueron los trastornos en la organicidad (76,67%), los trastornos de memoria y atención 56,67% la mayoría con ROP 1 (13); El trastorno en la autoestima fue el menos frecuente, presente en el 10% de los pacientes. La asociación entre estos trastornos y el estadio clínico de ROP fue estadísticamente significativo solo para los trastornos en la autoestima y de personalidad ($p < 0,05$).

IV. DISCUSIÓN

La población en estudio estuvo constituida por 30 pacientes, predominó el sexo femenino, con el 53,33%, aunque la diferencia entre ambos sexos no fue significativa. Esto no coincide con M.A. De la Fuente-Torres⁽²²⁾ ni con la Dra. Luvia Curbelo Quiñones⁽⁹⁾ porque en sus estudios fue más frecuente el sexo masculino, lo que puede estar en asociación con la estadística que se presentó en esos años en cada región respecto a los nacimientos de cada sexo, algo que ocurre de forma aleatoria sin guardar relación con algo en específico. A la luz de los conocimientos actuales no se demuestra influencia del sexo en el desarrollo de la ROP.

Dentro de los factores que incrementan el riesgo para desarrollar ROP se encuentran indudablemente la edad gestacional y el peso al nacer. En este estudio el peso al nacer más representativo, con el 33,33%, fue el de 1 250gr a 1 499gr. Este resultado es similar al que obtiene Heladia García⁽³⁰⁾ en su estudio en el que los recién nacidos analizados se encuentran más frecuentemente con peso ≤ 1 250g y

≤ 1 500g. Otro trabajo que avala esto es el de la Dra. Luvia Curbelo Quiñones⁽⁹⁾ donde el mayor por ciento está entre los de 1 000 y 1 500g al nacer. La Dra. Berta Beauge Valeriano⁽⁶⁾ tampoco difiere totalmente porque el grupo en segundo lugar en frecuencia fue el de 1 700gr y más.

El 33,33% de los pacientes nacieron de 30 a 31,6 semanas de gestación. Este resultado estuvo en concordancia con varios estudios como el de Roberto Chaskel⁽²⁷⁾ que evidencia una mayor frecuencia en los menores de 32 semanas, así como en el de M.A. De la Fuente-Torres⁽²²⁾ con mayor prevalencia de ROP en los prematuros moderados entre 32 y 33 semanas, edades gestacionales muy semejantes a las informadas por otros países en vías de desarrollo.

La Dra. Luvia Curbelo Quiñones⁽⁹⁾ también obtiene que la edad gestacional igual o menor a 32 semanas predomina en el 72,2% de los recién nacidos que desarrollaron ROP. Se observó una asociación significativa entre el peso al nacer y la edad gestacional, y sucede de igual forma en todas las bibliografías revisadas.

Todos los niños estudiados presentaron factores de riesgo al nacer. Esto coincide con el trabajo de Heladia García y cols⁽³⁰⁾ en el que todos los pacientes tienen una o más comorbilidades. También se comporta similar la frecuencia de la oxigenoterapia que fue, con gran diferencia, el más representativo de los factores de riesgo al nacer en este estudio, presente en 26 pacientes. Se coincidió además con la Dra. Luvia Curbelo Quiñones y cols⁽⁹⁾ porque en su trabajo el 94,4% de los pacientes con ROP recibió oxigenoterapia.

Se demostró asociación estadística entre el uso de oxígeno y la aparición de esta complicación, mucho más frecuente en los pacientes que recibieron oxígeno. Globalmente se ha demostrado que a mayor tiempo de oxigenoterapia sin control oximétrico y a mayor concentración de oxígeno inspirados mayores son las posibilidades de padecer la ROP.

Fueron frecuentes también las infecciones, presentes en el 33,33%, lo que coincidió con las Dras. Berta Beauge Valeriano⁽⁵⁾ y Luvia Curbelo Quiñones⁽⁹⁾ porque en sus estudios este es un factor de riesgo encontrado en varios pacientes.

En este trabajo siguió en frecuencia la gemelaridad, presente en el 26,67%; sin embargo, en ninguno de los trabajos revisados se encontró referido este factor de riesgo.

Se encontraron en este estudio otros factores de riesgo al nacer como la hemorragia intraventricular, solamente en un paciente, por lo tanto, es muy infrecuente, lo que está en desacuerdo con lo planteado por la Dra. Luvia Curbelo Quiñones,⁽⁹⁾ que lo señala de alta incidencia en su trabajo, lo que puede estar en asociación con la cantidad de pacientes que estudió nacidos con edad gestacional de 10 semanas o más antes del término porque estos tienen un riesgo más elevado de presentar este tipo de sangrado.

El 60% de los pacientes se clasificaron en el estadio 1 de ROP y solo uno se clasificó en el estadio 4, no hubo ningún paciente en estadio 5. Estos resultados se comportaron de forma muy similar al estudio realizado por Heladia García y cols⁽³⁰⁾, la mayoría de los pacientes presentan estadios 1 y 2, ninguno tuvo ROP 4 y 5.

Referente a la refracción de los pacientes que se relacionó con los estadios de ROP, no se presentó miopía e hipermetropía de forma aislada, siempre estuvo asociada a Astigmatismo, y resultó el más frecuente el astigmatismo hipermetrópico en el 53,33%, seguido del 30% con astigmatismo miopico, con más frecuencia en el estadio 1 y 2 de ROP.

En las bibliografías revisadas hacen referencia a la miopía como el defecto refractivo más frecuente, lo que está en desacuerdo con nuestros resultados. Tal es el caso de la Dra. Berta Beauge Valeriano⁽⁵⁾ que destaca la miopía en 51 niños de su estudio e hipermetropía en 12. Los resultados de este trabajo coinciden con estos al referir la alta incidencia de astigmatismo en la ROP.

De los pacientes el 50% no presentaron lesiones en el fondo de ojo, todos en estadio 1 de ROP, lo que no se comportó de forma semejante al estudio de Brenda Sarita López-Almarala y colaboradores⁽²²⁾ en el que solo un paciente no tiene alteraciones en el fondo de ojo, lo que se debe a la cantidad de niños que en su investigación se clasifican en estadios más graves de ROP.

En este estudio el 23,33% de los pacientes presentaron palidez del disco al examen físico y el 20% ectopia macular, en ambos la frecuencia fue mayor en el ROP en estadio 3. En el trabajo anteriormente mencionado solo un niño presenta ectopia macular.

Secuelas por los tratamientos aplicados se observaron en 5 niños por la crioterapia y en 6 por el tratamiento con láser, resultado muy similar al del estudio referido anteriormente en el que 10 niños presentaron cicatrices provocadas por el láser o la crioterapia.

En este estudio los pacientes fueron derivados a la Consulta de Psicología en la que se le realizaron test psicológicos en dependencia de las posibilidades de cada paciente.

Las alteraciones más observadas fueron los trastornos en la organicidad en el 76,67%, seguidos de los trastornos de memoria y de atención que se observaron en el 56,67%, ambos con mayor frecuencia en los pacientes con ROP 1.

No se encontraron muchos estudios al respecto, pero se tienen resultados similares al realizado por Jorge Alexander Ríos-Flórez y cols⁽²⁶⁾. Refiere que los pacientes presentan criterios de déficit de atención con hiperactividad (la segunda dificultad en frecuencia que se encontró en nuestra investigación) y menciona dificultades en el aprendizaje, presente en 6 de nuestros pacientes. En su estudio los niños sufren de problemas emocionales como conductas de aislamiento, depresión y cuadros de somatización, algo que no concuerda con lo encontrado en este trabajo. Señala dificultades en el ámbito socioafectivo, con lo que sí se coincidió, pues 11 pacientes presentaron problemas de afectividad y 3 de autoestima; este último fue el trastorno con menor frecuencia.

Es de gran importancia conocer estas alteraciones porque provocarán en estos niños mayores dificultades en el desarrollo de habilidades sociales y de compañerismo, tanto en ambientes sociales como familiares.

V. CONCLUSIONES

La ROP se observa con más frecuencia en niños nacidos con edad gestacional de 10 semanas o más por debajo del término, lo que está influenciado por la coexistencia de otros factores de riesgo perinatales, como la oxigenoterapia.

Los niños que presentaron estadios avanzados de la enfermedad fueron los de mayores secuelas en la esfera visual y psicológica, resultó el más frecuente el astigmatismo hipermetrópico, seguido del 30% con astigmatismo miopico, con más frecuencia en el estadio 1 y 2 de ROP.

La esfera psicológica también está alterada, al menos en algún aspecto, en todos los niños, Las alteraciones más observadas fueron los trastornos en la

organicidad, memoria y de atención que se observaron ambos con mayor frecuencia en los pacientes con ROP 1.

Contribución de autores

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Recolección y examen de los datos

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By David G. Morrison & Chrystina Castellon

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Paraneoplastic Syndrome of Myasthenia Gravis Presenting as Isolated Vocal Cord Paralysis in a Patient with Breast Cancer: Case Report and Literature Review

David G. Morrison ^α & Chrystina Castellon ^ο

Abstract- 53-year-old lady presented with progressively worsening loss of voice. Over time she could only be heard upon speaking directly into the ears of her family or physicians. She lost her job as a receptionist due to her loss of voice. She was still on adjuvant treatment for breast cancer. She underwent CT/PET, ENT consultation and a battery of paraneoplastic antibody tests. ENT consultation confirmed vocal cord paralysis. ENT exam and CT/PET found no evidence of vocal cord mass or any lesion compressing the laryngeal nerves. No mass was found in the superior mediastinum. She had a positive antibody test for anti-acetylcholine receptors. Treatment with pyridostigmine reversed her vocal cord paralysis. This is the first report of a patient with breast cancer associated paraneoplastic myasthenia gravis syndrome.

I. INTRODUCTION

Myasthenia gravis is an uncommon disease. MG affects 50 to 200 per million people. It is newly diagnosed in three to 30 per million people per year in the USA (1-3). Isolated vocal cord paralysis (VCP) as the initial manifestation of myasthenia gravis is a very rare event occurring in a large case series in only 7 of over 1500 patients (4). Malignancy associated myasthenia gravis is also relatively rare with thymoma being the most well recognized offender (3,5).

Malignant causes of direct VCP are also uncommon. Breast cancer causing vocal cord paralysis has rarely been reported due to actual metastatic deposits of tumor in the vocal cord or compressing the larynx or laryngeal nerves (6). A prospective evaluation of vocal cord paralysis found left sided non-small cell lung cancer to be the most common culprit. This was most often due to compression of the left recurrent laryngeal nerve. A rare case of breast cancer as the etiology was reported by the same authors. None of their patients who underwent antibody panel assays had positive results. Autopsy series and small case series also indicate metastases to the larynx are very uncommon (8-11). Metastatic involvement of the larynx from distant cancers is rare. Up until 1996 only 143

cases had been reported (8,11). Metastatic tumors account for 0.09 to 0.4% of all laryngeal tumors (10). The most common primary metastatic to the larynx was melanoma followed in descending order by renal cell carcinoma, lung cancer, breast, prostate and colon cancers (8).

Paraneoplastic antibodies against acetylcholine and the the Hu antigen have been reported in patients with thymoma and small cell lung cancer, respectively (7). Paraneoplastic antibody syndromes may precede, occur simultaneously with or follow the occurrence of a malignancy (8). This is the first report of a patient with breast cancer with paraneoplastic myasthenia gravis syndrome causing VCP.

II. MATERIALS AND METHODS

The patient while premenopausal at age 48 developed a mammogram only detected left upper outer quadrant T1bN0M0 well differentiated, Bloom-Richardson 4/9, infiltrating ductal carcinoma that was strongly estrogen and progesterone positive and negative for HER-2-neu expression. Her Oncotype DX score was 12. She had a lumpectomy and sentinel lymph node biopsy followed by adjuvant radiation. She received adjuvant tamoxifen. Three and a half years later she presented to clinic for an unscheduled appointment. She noted severe loss of the ability to speak loud enough to be heard over the phone or by people standing near her. Her only other complaint on extensive review of systems was chronic mild right neck pain for the past 7 years. Her physical exam other than her voice, mammogram and routine labs which included a complete blood count and comprehensive metabolic panel were normal. Thyroid functions were ordered and were normal.

CT/PET was obtained from vertex of skull to midhigh as part of her evaluation with the primary concern being recurrent breast cancer compressing the recurrent laryngeal nerve or directly affecting vocal cord motion. Orthopedic consultation was obtained in view of her neck pain. No direct cause of laryngeal dysfunction was identified by our consultant. ENT consult included direct laryngoscopy. Vocal cord paralysis was observed

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but no mass effect was identified. This was consistent with the CT/PET evaluation. In view of the persistence of her severe lack of ability to phonate despite a period of voice rest, serum was sent to QUEST labs for paraneoplastic antibody evaluation. Direct clinical observation of the patient's voice was used to follow her progress.

III. RESULTS AND DISCUSSION

It was observed that her voice went from barely audible at the start of clinic visits to essentially silent with repeated attempts to speak. Her antibodies against the acetylcholine receptor were positive. After initiation of pyridostigmine her voice became louder, and she did not demonstrate fatigue of her voice during clinical interviews.

VCP in this patient followed resection of the primary cancer by several years. Careful radiographic evaluation and multiple consultants did not identify a direct cause of VCP by tumor or other lesion causing laryngeal muscle or nerve compression. Expanding our differential to include a possible paraneoplastic syndrome led to the recognition of elevated levels acetylcholine receptor antibodies. No other manifestations of MG were observed. Treatment with pyridostigmine has resulted in slow but steady improvement in vocal cord function.

IV. CONCLUSIONS

VCP is a recognized symptom of malignancy, usually lung cancer. Paraneoplastic MG is most often seen with thymoma, however, in view of our recent report it would be prudent to investigate the presence of a paraneoplastic MG syndrome in any patient with a history of cancer who presents with VCP and negative radiographic studies for recurrent laryngeal nerve compression. Her follow up has been adjusted from every 6 months to every 3 months due to concerns that this may herald return of her breast cancer (12) as well as the risk of possible generalized MG (13).

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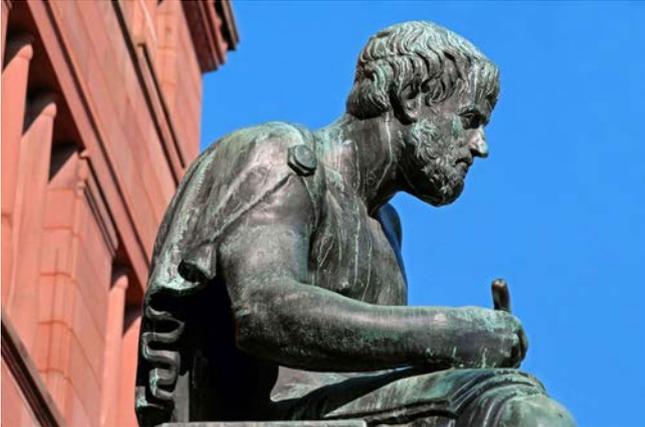
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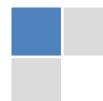
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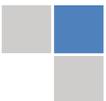
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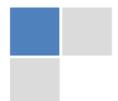
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- The names of first main headings (Heading 1) must be in Roman font, capital letters, and font size of 10.
- The names of second main headings (Heading 2) must not include numbers and must be in italics with a font size of 10.

Structure and Format of Manuscript

The recommended size of an original research paper is under 15,000 words and review papers under 7,000 words. Research articles should be less than 10,000 words. Research papers are usually longer than review papers. Review papers are reports of significant research (typically less than 7,000 words, including tables, figures, and references)

A research paper must include:

- a) A title which should be relevant to the theme of the paper.
- b) A summary, known as an abstract (less than 150 words), containing the major results and conclusions.
- c) Up to 10 keywords that precisely identify the paper's subject, purpose, and focus.
- d) An introduction, giving fundamental background objectives.
- 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.
- f) Results which should be presented concisely by well-designed tables and figures.
- g) Suitable statistical data should also be given.
- h) All data must have been gathered with attention to numerical detail in the planning stage.

Design has been recognized to be essential to experiments for a considerable time, and the editor has decided that any paper that appears not to have adequate numerical treatments of the data will be returned unrefereed.

- i) Discussion should cover implications and consequences and not just recapitulate the results; conclusions should also be summarized.
- j) There should be brief acknowledgments.
- k) There ought to be references in the conventional format. Global Journals recommends APA format.

Authors should carefully consider the preparation of papers to ensure that they communicate effectively. Papers are much more likely to be accepted if they are carefully designed and laid out, contain few or no errors, are summarizing, and follow instructions. They will also be published with much fewer delays than those that require much technical and editorial correction.

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



FORMAT STRUCTURE

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

All manuscripts submitted to Global Journals should include:

Title

The title page must carry an informative 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) where the work was carried out.

Author details

The full postal address of any related author(s) must be specified.

Abstract

The abstract is the foundation of the research paper. It should be clear and concise and must contain the objective of the paper and inferences drawn. It is advised to not include big mathematical equations or complicated jargon.

Many researchers searching for information online will use search engines such as Google, Yahoo or others. By optimizing your paper for search engines, you will amplify the chance of someone finding it. In turn, this will make it more likely to be viewed and cited in further works. Global Journals has compiled these guidelines to facilitate you to maximize the web-friendliness of the most public part of your paper.

Keywords

A major lynchpin of research work for the writing of research papers is the keyword search, which one will employ to find both library and internet resources. Up to eleven keywords or very brief phrases have to be given to help data retrieval, mining, and indexing.

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

Choice of the main keywords is the first tool of writing a research paper. Research paper writing is an art. Keyword search should be as strategic as possible.

One should start brainstorming lists of potential keywords before even beginning 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 a research paper?" Then consider synonyms for the important words.

It may take the discovery of only one important paper to steer in the right keyword direction because, in most databases, the keywords under which a research paper is abstracted are listed with the paper.

Numerical Methods

Numerical methods used should be transparent and, where appropriate, supported by references.

Abbreviations

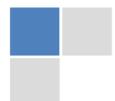
Authors must list all the abbreviations used in the paper at the end of the paper or in a separate table before using them.

Formulas and equations

Authors are advised to submit any mathematical equation using either MathJax, KaTeX, or LaTeX, or in a very high-quality image.

Tables, Figures, and Figure Legends

Tables: Tables should be 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. Authors must submit tables in an editable format and not as images. References to these tables (if any) must be mentioned accurately.



Figures

Figures are supposed to be submitted as separate files. Always include a citation in the text for each figure using Arabic numbers, e.g., Fig. 4. Artwork must be submitted online in vector electronic form or by emailing it.

PREPARATION OF ELETRONIC FIGURES FOR PUBLICATION

Although low-quality images are sufficient for review purposes, print publication requires high-quality images to prevent the final product being blurred or fuzzy. Submit (possibly by e-mail) EPS (line art) or TIFF (halftone/ photographs) files only. MS PowerPoint and Word Graphics are unsuitable for printed pictures. Avoid using pixel-oriented software. Scans (TIFF only) should have a resolution of at least 350 dpi (halftone) or 700 to 1100 dpi (line drawings). 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: Authors are advised 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. Also, you can email your editor to remove the color fee after acceptance of the paper.

TIPS FOR WRITING A GOOD QUALITY MEDICAL RESEARCH PAPER

1. Choosing the topic: In most cases, the topic is selected by the interests of the author, but it can also be suggested by the guides. You can have several topics, and then judge which you are most comfortable with. This may be done by asking several questions of yourself, like "Will I be able to carry out a search in this area? Will I find all necessary resources to accomplish the search? Will I be able to find all information in this field area?" If the answer to this type of question is "yes," then you ought to choose that topic. In most cases, you may have to conduct surveys and visit several places. Also, you might have to do a lot of work to find all the rises and falls of the various data on that subject. Sometimes, detailed information plays a vital role, instead of short information. Evaluators are human: The first thing to remember is that evaluators are also human beings. They are not only meant for rejecting a paper. They are here to evaluate your paper. So present your best aspect.

2. Think like evaluators: If you are in confusion or getting demotivated because your paper may not be accepted by the evaluators, then think, and try to evaluate your paper like an evaluator. Try to understand what an evaluator wants in your research paper, and you will automatically have your answer. 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.

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

4. Use of computer is recommended: As you are doing research in the field of medical research then this point is quite obvious. Use right software: Always use good quality software packages. If you are not capable of judging good software, then you can lose the quality of your paper unknowingly. There are various programs available to help you which you can get through the internet.

5. Use the internet for help: An excellent start for your paper is using Google. It is a wondrous search engine, where you can have your doubts resolved. You may also read some answers for the frequent question of how to write your research paper or find a model research paper. You can download books from the internet. If you have all the required books, place importance on reading, selecting, and analyzing the specified information. Then sketch out your research paper. Use big pictures: You may use encyclopedias like Wikipedia to get pictures with the best resolution. At Global Journals, you should strictly follow here.



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

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

8. Make every effort: Make every effort to mention what you are going to write in your paper. That means always have a good start. Try to mention everything in the introduction—what is the need for a particular research paper. Polish your work with good writing skills and always give an evaluator what he wants. Make backups: When you are going to do any important thing like making a research paper, you should always have backup copies of it either on your computer or on paper. This protects you from losing any portion of your important data.

9. Produce good diagrams of your own: Always try to include good charts or diagrams in your paper to improve quality. Using several unnecessary diagrams will degrade the quality of your paper by creating a hodgepodge. So always try to include diagrams which were made by you to improve the readability of your paper. Use of direct quotes: When you do research relevant to literature, history, or current affairs, then use of quotes becomes essential, but if the study is relevant to science, use of quotes is not preferable.

10. Use proper verb tense: Use proper verb tenses in your paper. Use past tense to present those events that have happened. Use present tense to indicate events that are going on. Use future tense to indicate events that will happen in the future. Use of wrong tenses will confuse the evaluator. Avoid sentences that are incomplete.

11. Pick a good study spot: Always try to pick a spot for your research which is quiet. Not every spot is good for studying.

12. Know what you know: Always try to know what you know by making objectives, otherwise you will be confused and unable to achieve your target.

13. Use good grammar: Always use good grammar and words that will have a positive impact on the evaluator; use of good vocabulary does not mean using tough words which the evaluator has to find in a dictionary. Do not fragment sentences. Eliminate one-word sentences. Do not ever use a big word when a smaller one would suffice.

Verbs have to be in agreement with their subjects. In a research paper, do not start sentences with conjunctions or finish them with prepositions. When writing formally, it is advisable to never split an infinitive because someone will (wrongly) complain. Avoid clichés like a disease. Always shun irritating alliteration. Use language which is simple and straightforward. Put together a neat summary.

14. 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 for your topic. You may also maintain your arguments with records.

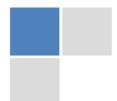
15. Never start at the last minute: Always allow enough time for research work. Leaving everything to the last minute will degrade your paper and spoil your work.

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

17. Never copy others' work: Never copy others' work and give it your name because if the evaluator has seen it anywhere, you will be in trouble. Take proper rest and food: No matter how many hours you spend on your research activity, if you are not taking care of your health, then all your efforts will have been in vain. For quality research, take proper rest and food.

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

19. Refresh your mind after intervals: Try to give your mind a rest by listening to soft music or sleeping in intervals. This will also improve your memory. Acquire colleagues: Always try to acquire colleagues. No matter how sharp you are, if you acquire colleagues, they can give you ideas which will be helpful to your research.



20. Think technically: Always think technically. If anything happens, search for its reasons, benefits, and demerits. Think and then print: When you go to print your paper, check that tables are not split, headings are not detached from their descriptions, and page sequence is maintained.

21. Adding unnecessary information: Do not add unnecessary information like "I have used MS Excel to draw graphs." Irrelevant and inappropriate material is superfluous. Foreign terminology and phrases are not apropos. One should never take a broad view. Analogy is like feathers on a snake. Use words properly, regardless of how others use them. Remove quotations. Puns are for kids, not grunt readers. Never oversimplify: When adding material to your research paper, never go for oversimplification; this will definitely irritate the evaluator. Be specific. Never use rhythmic redundancies. Contractions shouldn't be used in a research paper. Comparisons are as terrible as clichés. Give up ampersands, abbreviations, and so on. Remove commas that are not necessary. Parenthetical words should be between brackets or commas. Understatement is always the best way to put forward earth-shaking thoughts. Give a detailed literary review.

22. Report concluded results: Use concluded results. From raw data, filter the results, and then conclude your studies based on measurements and observations taken. An appropriate number of decimal places should be used. Parenthetical remarks are prohibited here. Proofread carefully at the final stage. At the end, give an outline to your arguments. Spot perspectives of further study of the subject. Justify your conclusion at the bottom sufficiently, which will probably include examples.

23. Upon 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 through which your research is going to be in print for 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 of 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 criteria peer reviewers will use for grading the final paper.

Final points:

One purpose of organizing a research paper is to let people interpret your efforts selectively. The journal requires the following sections, submitted in the order listed, with each section starting on a new page:

The introduction: This will be compiled from reference matter and reflect the design processes or outline of basis that directed you to make a study. As you carry out the process of study, the method and process section will be constructed like that. The results segment will show related statistics in nearly sequential order and direct reviewers to similar intellectual paths throughout the data that you gathered to carry out your study.

The discussion section:

This will provide understanding of the data and projections as to the implications of the results. The use of good quality references throughout the paper will give the effort trustworthiness by representing an alertness to 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 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 avoid:

- Insertion of a title at the foot of a page with subsequent text on the next page.
- Separating a table, chart, or figure—confine each to a single page.
- Submitting a manuscript with pages out of sequence.
- In every section of your document, use standard writing style, including articles ("a" and "the").
- Keep paying attention to the topic of the paper.
- Use paragraphs to split each significant point (excluding the abstract).
- Align the primary line of each section.
- Present your points in sound order.
- Use present tense to report well-accepted matters.
- Use past tense to describe specific results.
- Do not use familiar wording; don't address the reviewer directly. Don't use slang or superlatives.
- Avoid use of extra pictures—include only those figures essential to presenting results.

Title page:

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

Abstract: This summary should be two hundred words or less. It should clearly and briefly explain the key findings reported in the manuscript and must have precise statistics. It should not have acronyms or abbreviations. It should be logical in itself. Do not cite 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 approaches 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. Use comprehensive sentences, and do not sacrifice readability for brevity; you can maintain it succinctly by phrasing sentences so that they provide more than a 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 limit the initial two items to no more than one line each.

Reason for writing the article—theory, overall issue, purpose.

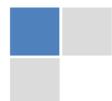
- Fundamental goal.
- To-the-point depiction of the research.
- Consequences, including definite statistics—if the consequences are quantitative in nature, account for this; results of any numerical analysis should be reported. Significant conclusions or questions that emerge from the research.

Approach:

- Single section and succinct.
- An outline of the job done is always written in past tense.
- Concentrate on shortening results—limit background information to a verdict or two.
- Exact spelling, clarity 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 of comprehending and calculating the purpose of your study without having to refer to other works. The basis for the study should be offered. Give the most important references, but avoid making a comprehensive appraisal of the topic. Describe the problem visibly. If the problem is not acknowledged in a logical, reasonable way, the reviewer will give no attention to your results. Speak in common terms about techniques used to explain the problem, if needed, but do not present any particulars about the protocols here.



The following approach can create a valuable beginning:

- Explain the value (significance) of the study.
- Defend the model—why did you employ this particular system or method? What is its compensation? Remark upon its appropriateness from an abstract point of view as well as pointing out sensible reasons for using it.
- Present a justification. State your particular theory(-ies) or aim(s), and describe the logic that led you to choose them.
- Briefly explain the study's tentative purpose and how it meets 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 for every section. If you make the four points listed above, you will need at least four paragraphs. Present surrounding information only when it is necessary to support a situation. The reviewer does not desire to read everything you know about a topic. Shape the theory 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 soundly written procedures segment allows a capable scientist to replicate 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 to give the least amount of information that would permit another capable scientist to replicate 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 section, mention the specific item describing the way, but draw the basic principle while stating the situation. The purpose is to show 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:

Materials may be reported in part of a section or else they may be recognized along with your measures.

Methods:

- Report the method and not the 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—detail how procedures were completed, not how they were performed on a particular day.
- If well-known procedures were used, account for the procedure by name, possibly with a reference, and that's all.

Approach:

It is embarrassing to use vigorous voice when documenting methods without using first person, which would focus the reviewer's interest on the researcher rather than the job. As a result, when writing up the methods, most authors use third person passive voice.

Use standard style in this and 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 as 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. Use statistics and tables, if suitable, to present consequences most efficiently.

You must clearly differentiate material which would usually be incorporated in a study editorial from any unprocessed data or additional appendix matter that would not be available. In fact, such matters should not be submitted at all except if requested by the instructor.

Content:

- Sum up your conclusions in text and demonstrate them, if suitable, with figures and tables.
- In the manuscript, explain each of your consequences, and point the reader to remarks that are most appropriate.
- Present a background, such as by describing the question that was addressed by creation of an exacting study.
- Explain results of control experiments and give 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 manuscript.

What to stay away from:

- Do not discuss or infer your outcome, report surrounding information, or try to explain anything.
- Do not include raw data or intermediate calculations in a research manuscript.
- Do not present similar data more than once.
- A manuscript should complement any figures or tables, not duplicate information.
- Never confuse figures with tables—there is a difference.

Approach:

As always, use past tense when you submit 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 section.

Figures and tables:

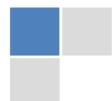
If you put figures and tables at the end of some details, make certain that they are visibly distinguished from any attached appendix materials, such as raw facts. Whatever the position, each table must be titled, numbered one after the other, and include a heading. All figures and tables must be divided from the text.

Discussion:

The discussion is expected to be the trickiest segment to write. A lot of papers submitted to the journal are discarded based on problems with the discussion. There is no rule for how long an 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 implications of the study. The purpose here is to offer an understanding of your results and support all of your conclusions, using facts from your research and generally accepted information, if suitable. The implication of results should be fully 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 the prospect, and let it drop at that. Make a decision as to whether each premise is supported or 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 an experiment might be personalized to accomplish a new idea.
- Give details of all of your remarks as much as possible, focusing on mechanisms.
- Make a decision as to whether the tentative design sufficiently addressed the theory and whether or not it was correctly restricted. Try to present substitute explanations if they are sensible alternatives.
- One piece of 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 other available information. Present work done by specific persons (including you) in past tense.

Describe generally acknowledged facts and main beliefs in present tense.

THE ADMINISTRATION RULES

Administration Rules to Be Strictly Followed before Submitting Your Research Paper to Global Journals Inc.

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Segment draft and final research paper: You have to strictly follow the template of a research paper, failing which your paper may get rejected. You are expected to write each part of the paper wholly on your own. The peer reviewers need to identify your own perspective of the concepts in your own terms. Please do not extract straight from any other source, and do not rephrase someone else's analysis. Do not allow anyone else to proofread your manuscript.

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CRITERION FOR GRADING A RESEARCH PAPER (COMPILATION)
BY GLOBAL JOURNALS

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.

Topics	Grades		
	A-B	C-D	E-F
<i>Abstract</i>	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
<i>Introduction</i>	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
<i>Methods and Procedures</i>	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
<i>Result</i>	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
<i>Discussion</i>	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
<i>References</i>	Complete and correct format, well organized	Beside the point, Incomplete	Wrong format and structuring



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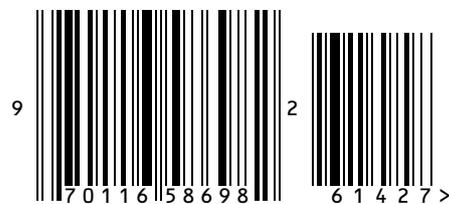
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