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# Global Journal

## of Medical Research: H

# Orthopedic & Musculoskeletal System



Mc-Cune Albright Syndrome

Femoral Supracondylar Amputation

Highlights

Preventing Phantom Limb Pain

Advanced Ayurvedic Detox Program

**Discovering Thoughts, Inventing Future**

VOLUME 20 ISSUE 1 VERSION 1.0

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# Pathological Proximal Femoral Fracture in Mc-Cune Albright Syndrome: A Case Report

By Apoorv Sehgal, Pratyush Shahi & Aarushi Sudan
*University College of Medical Sciences*

*Abstract-* A 25-year-old female present to us in the emergency department with atraumatic fracture of the proximal femur. She had a cafe-au-lait spot on the face and gave history of precocious puberty. A skeletal survey showed polyostotic fibrous dysplasia. A clinico-radiological diagnosis of McCune-Albright syndrome was made which was further confirmed on biopsy. An extra-medullary fixation was done and at 6 months follow-up, the fracture had united and the patient could walk without support.

*GJMR-H Classification: NLMC Code: WE 175*




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# Pathological Proximal Femoral Fracture in Mc-Cune Albright Syndrome: A Case Report

Apoorv Sehgal [α], Pratyush Shahi [σ] & Aarushi Sudan [ρ]

*Abstract-* **A 25-year-old female present to us in the emergency department with atraumatic fracture of the proximal femur. She had a cafe-au-lait spot on the face and gave history of precocious puberty. A skeletal survey showed polyostotic fibrous dysplasia. A clinico-radiological diagnosis of McCune-Albright syndrome was made which was further confirmed on biopsy. An extra-medullary fixation was done and at 6 months follow-up, the fracture had united and the patient could walk without support.**

## I. Introduction

Fibrous dysplasia/McCune-Albright syndrome (FD/MAS) occurs due to somatic gain-of-function mutations of the *GNAS* gene. These mutations cause over activity in the target tissues leading to clinical features that vary in severity and age of onset.[1] Since the disease is rare and can have atypical presentation, the diagnosis can be missed. We report the case of a young female with McCune-Albright syndrome presenting to us with pathological fracture of the proximal femur and highlight the challenges one can face in fixation of such fractures.

## II. Case Presentation

A 25-year-old female patient presented to us with a history of sudden onset of pain in her right hip and inability to bear weight over the affected limb. There was no history of trauma, fever or weight loss. On examination, the right lower extremity was externally rotated and shortened. Movements at the right hip elicited pain. The patient was of short stature and had acafé-au-lait skin macule with jagged, irregular borders (coast of Maine) on her face with short stature.*(Figure 1)* On further inquiry, she gave a history of precocious puberty.

Radiographs revealed lytic expansile lesion with ground-glass appearance and thinning of cortex in metaphyseal region of the right proximal femur associated with a pathological subtrochanteric fracture. Other sites like skull, radius and phalanges also had similar lytic lesions.*(Figure 2)*

Based on clinical and radiological features, a diagnosis of McCune-Albright syndrome with pathological right subtrochanteric fracture was made. The patient was put on skin traction for the right lower limb and advised to undergo surgery for the subtrochanteric fracture of right femur in view of the nature of the fracture and the requirement of early ambulation. After proper consent, the patient was taken up for surgery. Fracture was reduced on a traction table after opening the fracture area. Biopsy was taken from the fracture site followed by reduction and fixation with distal femoral locking plate of opposite side in reverse configuration. The initial plan was of internal fixation with cephalomedullary nail, but due to very narrow diameter of the medullary canal, an extramedullary fixation had to be done. *(Figure 3)* The patient was discharged on post-operative day 5 after confirming healthy state of the wound. She was started on partial weight-bearing with crutches at 2 weeks continuing to full weight-bearing at 6 weeks. At 6 months follow-up, the patient could walk without support and with no residual complaints.

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*Figure1:* Showing the cafe-au-lait spot












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*Figure 2:* (A-D) showing lytic ground-glass lesions in the skull, radius, phalanges and proximal femur, (E) showing a pathological subtrochanteric fracture, (F) after fixation

## III. Discussion

McCune–Albright syndrome is a rare sporadic disease caused by somatic postzygotic activating mutations in the *GNAS* gene. It is characterised by polyostotic fibrous dysplasia, café-au-lait skin spots and variable hyperfunctional endocrinopathies.[2]

A fibrous dysplasia lesion predisposes a person to have a pathological fracture and if involving a large area can lead to deformity of the bone. Although a small lesion can be left as such, a larger lesion causing pain or threatening to fracture should be curetted and bone grafted even though there is a high tendency for it to recur. If the site and extent of the lesion necessitates, prophylactic fixation should be done. The management of fibrous dysplasia becomes more complicated when it is associated with extra-skeletal manifestations.[1,3]

A lesion of the proximal femur causes more pain, fractures and deformity than any other skeletal localization of the disease.[2-5] A pathological fracture of the proximal femur secondary to fibrous dysplasia poses several intra-operative challenges. A surgeon should do proper pre-operative planning and have backup fixation devices. Also, good post-operative wound care and early rehabilitation should be done.

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# Anterior Bowing of Tibia in an Adult

By Pratyush Shahi, Apoorv Sehgal & Aarushi Sudan
*University College of Medical Sciences*

*Abstract-* A 35-year-old female presented to us with anterior bowing of her right tibia. The deformity developed in her adolescence and subsequently had not progressed for nearly two decades. The patient had no functional limitation, her only concern being cosmesis. Radiological investigations suggested either fibrous dysplasia or adamantinoma. Biopsy showed fibrous stroma consisting of myxofibrous tissue and woven bone which was confirmatory of fibrous dysplasia. Keeping in mind that it was a dormant benign lesion not hindering with functionality of the limb, it was decided to keep the patient under observation with regular follow-up.

*GJMR-H Classification:* *NLMC Code: WE 168*




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# Anterior Bowing of Tibia in an Adult

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## I. Introduction

Bowing of tibia can be anterior, anterolateral, anteromedial and posteromedial. Anterior tibial bowing, although rare, can be seen in fibrous dysplasia, osteofibrous dysplasia, adamantinoma, congenital pseudoarthrosis, vitamin D deficiency, syphilis, yaws, Paget's disease of the bone, fluorosis and Weismann-Netter-Stuhl syndrome.

We report a case of anterior tibial bowing in a middle-aged female and aim to highlight the importance of differentiation between benign fibrous dysplasia, potentially pre-malignant osteofibrous dysplasia and malignant adamantinoma in such a case.

## II. Case Presentation

A 35-year-old female presented to us with an anteriorly bowed tibia of the right side. She had started noticing it at the age of 8 years, after which the deformity had progressed for a period of 10 years. It has now remained quiescent over the last 17 years. She complains of occasional pain in the right leg, but has no functional limitation. The overlying skin was normal with no dilated veins. She has normal local temperature, mild tenderness over the apex of the deformity, a shortening of 1.5 cm on the affected side and the range of motion of the knee and ankle joints on the affected side are comparable to the opposite side. Both feet are comparable in size. There is no distal neurovascular deficit. She doesn't have any other deformity or any hyperpigmentation.

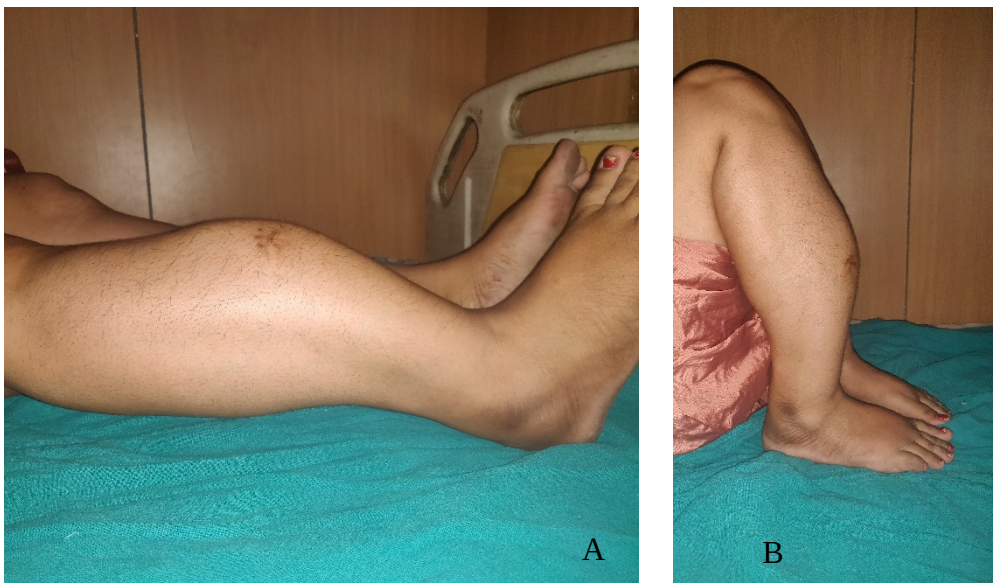



*Figure 1:* A and B showing anteriorly bowed right leg, fairly good motion at knee and ankle joints with minimal shortening

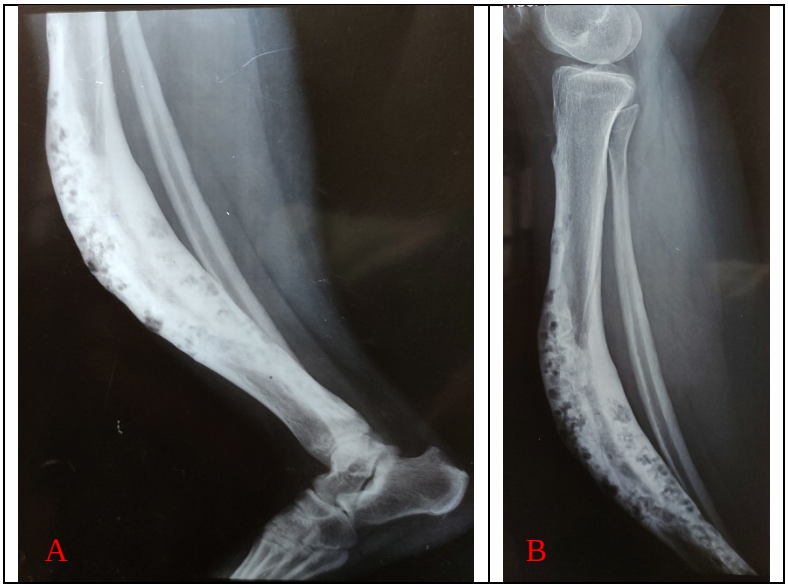
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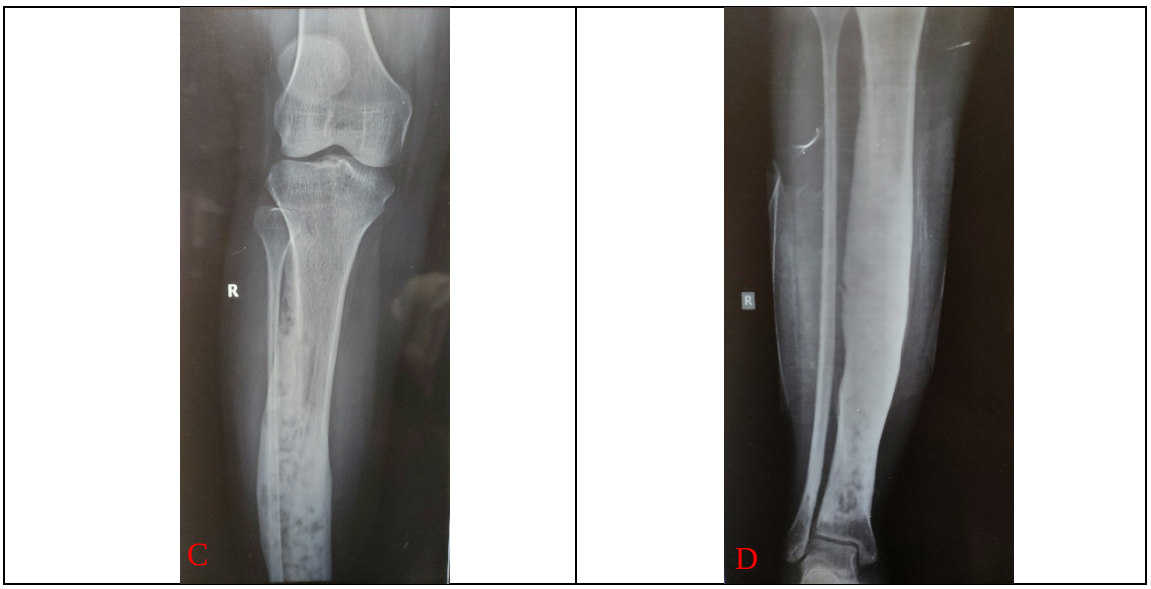


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## III. Investigations

X-ray, CT scan and MRI are shown in the figures. Blood investigations were found to be normal.






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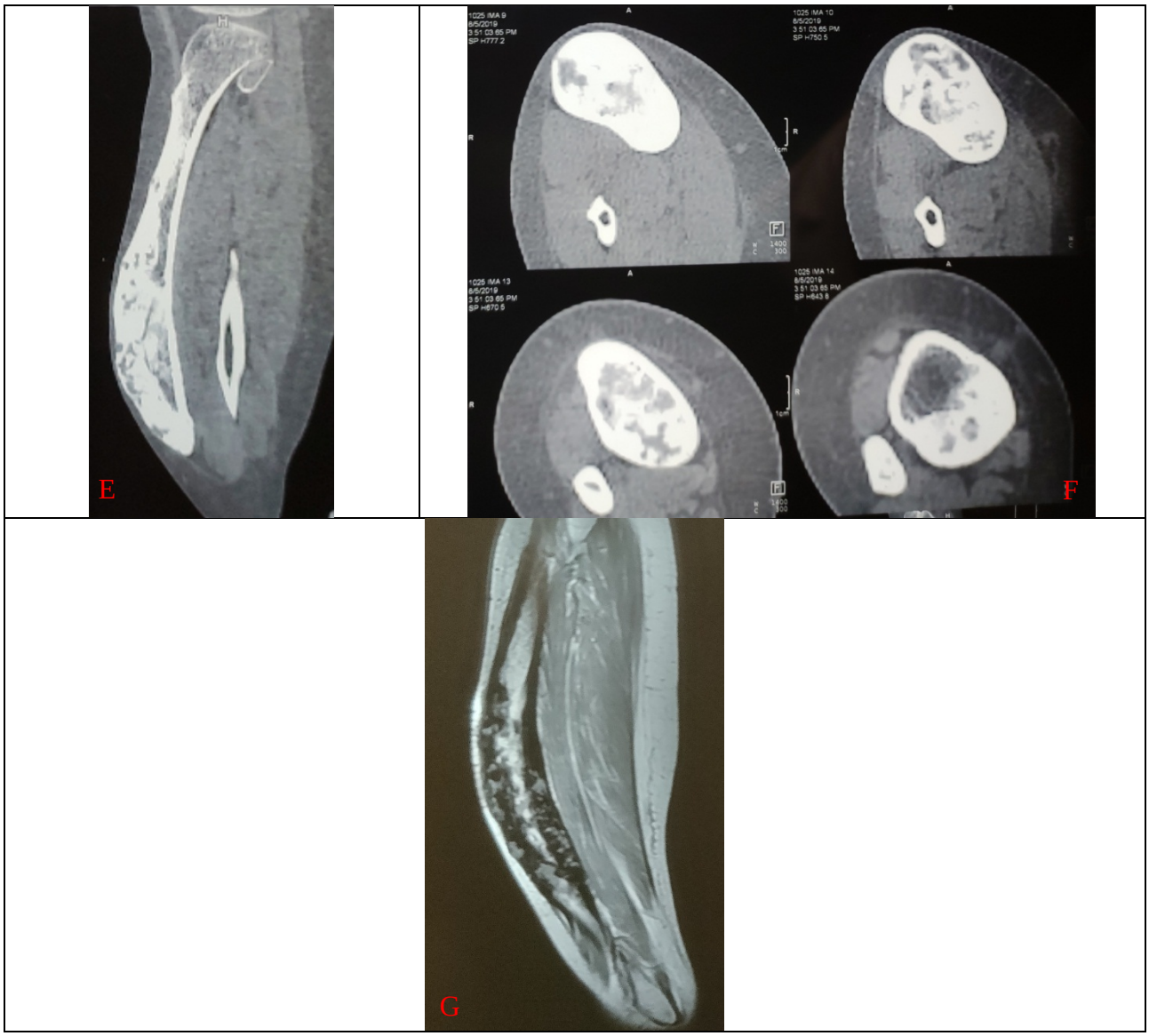



*Figure 2:* A-E showing anterior bowing of tibia, diffuse expansion of tibial diaphysis, loss of cortico-medullary junction, homogenous ground glass opacities and areas of cystic licences, narrow zone of transition with no cortical breach or soft tissue component

## IV. Differential Diagnosis

Based on the radiological investigations, fibrous dysplasia and adamantinoma were kept as the two possibilities. Moth-eaten type of bone destruction and cortical thickening favouradamantinoma. Non-involvement of fibula and no osseous breach favour fibrous dysplasia.

## V. Histopathology

Characteristic findings indicative of fibrous dysplasia include fibrous stroma consisting of myxofibrous tissue and woven bone.[1]The histologic diagnosis of adamantinoma is made when epithelial-like cells arranged in pallisading nests andstrands of cells are identified. Fibrous tissue is abundant in both, so anadamantinoma can remain masked if biopsy is taken from a single lesion site.[2] Precaution must be taken to take samples from lytic as well as dense regions.

Following these principles, we took biopsy with a core biopsy needle. Histopathology was suggestive of fibrous dysplasia.



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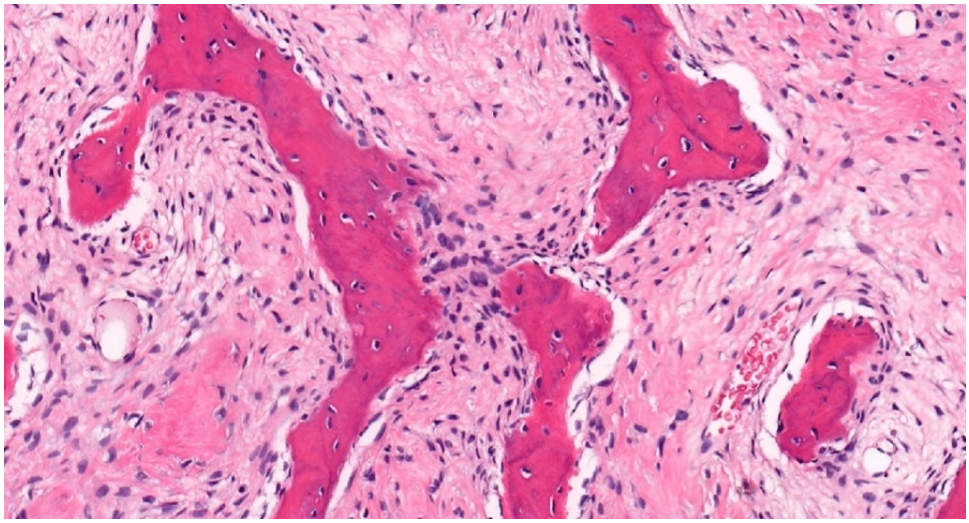


*Figure 3:* Showing trabeculae of woven bone with fibroblastic stroma and no osteoblastic rimming

## VI. Management

Considering the facts that it was a benign lesion, the deformity had not progressed over the last 20 years, patient had no functional limitations or any significant limb length discrepancy, has had no pathological fracture and the lesion was involving almost the whole of tibia making a reconstruction difficult, we decided to keep the patient under observation. We would look for any change in her symptoms or an increase in the deformity and also get yearly X-rays and MRI to look for any enhancement of the lesion. Meanwhile, we started the patient on bisphosphonates and analgesics.

## VII. Discussion

Differentiation between fibrous dysplasia, osteofibrous dysplasia and adamantinoma is vital in such a case.

Fibrous dysplasia (FD) is a benign intramedullary fibro-osseous lesion where normal bone is replaced by fibrous tissue. It can involve a single bone (monostotic), a single limb (monomelic) or multiple bones (polyostotic). It is generally an incidental finding.[3] Radiologically, the lesion is intramedullary, expansile and well-defined with an intact cortex. Although typically having a ground-glass appearance, it can also be completely lytic or sclerotic.[4] Characteristic histologic findings indicative of fibrous dysplasia include fibrous stroma consisting of myxofibrous tissue and woven bone.

Osteofibrous dysplasia (OFD) is a bone-forming lesion in the ventral, intracortical area of the tibial shaft with histology different from fibrous dysplasia. Contrary to fibrous dysplasia, the formed, woven trabeculae in osteofibrous dysplasia are rimmed by cuboidal osteoblasts.[5] There is a separate entity called OFD-like adamantinoma, which some believe to be a regressive form of adamantinoma and others believe to be a precursor of adamantinoma.[6]

Adamantinoma is a primary low-grade malignant bone tumor most commonly seen involving the tibia. Histologically, adamantinoma shows a biphasic pattern of intermingled epithelial and osteofibrous components. Immunohistochemistry should be done to confirm the diagnosis.[7]

It is important to differentiate between the three entities to decide the further line of management. Fibrous dysplasia is a benign lesion, with rare incidences of malignant transformation, and the patient can be kept under observation.[8]Osteofibrous dysplasia has been shown to carry a small but significant risk of containing co-existing adamantinoma or developing into adamantinoma, hence a wide resection of the lesion has been advocated by some.[6]Adamantinoma is a slow-growing, malignant bone tumour and necessitates a wide extraperiosteal resection to prevent recurrence.[9]

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# Effectiveness of Perineural Dexmedetomidine and Ropivacaine on Preventing Phantom Limb Pain in Patients Undergoing Femoral Supracondylar Amputation

By MD. Ramírez-Jaime, MD. Estrada-Sara & MD. Martínez-Raquel
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*Abstract-* *Background:* Phantom limb pain is a frequent complication after limb amputation, its pathophysiology is complex and includes changes in the peripheral nerve, dorsal root ganglia, spinal cord, cerebral cortex, and thalamus. At this time, there is not an effective drug for treatment and prevention of phantom limb pain. Perineural local anesthetic infiltration has obtained different results in the prevention of phantom limb pain, so we propose to combine an α2 agonist in peripheral nerve block to assess its effectiveness in preventing postoperative pain.

*Keywords:* *phantom limb pain, analgesia, dexmedetomi-dine, periferial nerve block, supracondylar amputation.*

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# Effectiveness of Perineural Dexmedetomidine and Ropivacaine on Preventing Phantom Limb Pain in Patients Undergoing Femoral Supracondylar Amputation

MD. Ramírez-Jaime [α], MD. Estrada-Sara [σ] & MD. Martínez-Raquel [ρ]

*Abstract-* ***Background:*** Phantom limb pain is a frequent complication after limb amputation, its pathophysiology is complex and includes changes in the peripheral nerve, dorsal root ganglia, spinal cord, cerebral cortex, and thalamus. At this time, there is not an effective drug for treatment and prevention of phantom limb pain. Perineural local anesthetic infiltration has obtained different results in the prevention of phantom limb pain, so we propose to combine an α2 agonist in peripheral nerve block to assess its effectiveness in preventing postoperative pain.

***Methods:*** This was a prospective, double-blind, controlled, and simple randomized study. We included 30 patients undergoing surgery for supracondylar femoral amputation, older than 18 years, ASA I-III, in a sample calculation of 95% in Confidence Interval and 80% of statistical power. We included 15 patients per group managed with subarachnoid neuraxial block, and a perineural infiltration before the sciatical nerve section with 10 ml of 0.5% ropivacaine + 50 mcg dexmedetomidine (RD Group), or 0.5% ropivacaine + 0.9% saline solution (Group RS), in both groups We continued a perineural infusion with 0.15% ropivacaine using an elastomeric pump for 24 hours; We evaluated stump pain and phantom limb pain, upon admission to recovery, 8 hrs, 24 hrs, 30 days and 3 months. The data analysis was carried out using the SPSS version 21 program; In all cases, we defined statistical significance when obtaining $p < 0.05$.

***Results:*** This study included a total of 30 patients, 15 patients in the RD group and 15 patients in the RS group. Statistical significance was found in the pain levels of the stump at rest at 24 hours, being lower in the RD group ($p = 0.003$). This intervention also impacted the opioid requirements at 24 hours, requiring tramadol rescue 27% of the patients in the RD group, against 93% of the patients in the RS group ($p = 0.0002$). Regarding phantom limb pain, there was no incidence during the three months of follow-up in the RD group, against three patients who report mild phantom limb pain in the RS group.

***Conclusions:*** The combination of ropivacaine with dexmedetomidine appears to be an effective intervention with minimal side effects to prevent the occurrence of acute and chronic pain as well as phantom limb pain in patients undergoing femoral supracondylar amputation as well as reducing the postoperative opioid requirements.

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*Keywords: phantom limb pain, analgesia, dexmedetomidine, periferial nerve block, supracondylar amputation.*

## I. Introduction

Patients undergoing limb amputation surgery are at risk of postoperative pain. Phantom limb pain (PLP) is a painful sensation referred to the absent limb after amputation; but it's not limited to the extremities, phantom pain has also been reported after loosing almost any body part, for example, nose, tongue or breast.[1]

The onset time of PLP varies from days to years, but it´s common to be experienced between the first 24 hours to one week after amputation.[1] In long-term studies, it´s been observed a decrease in the frequency and duration of pain attacks over the years, which is accompanied by a decrement in its intensity, although in some cases, a worsening may occur. [2,3,4]

### *a) Etiology and risk factors for PLP*

Up to date, the exact reason that some patients develop PLP and others do not is unknown. It has been observed that its development is multifactorial, involving from peripheral, central and also psychological mechanisms.[5] There is not a clear relationship between age or sex and the appearance of PLP in the literature, and it's more likely to appear when it's a bilateral amputation and how proximal it is.[6]

There are studies about the influence of previous pain on an extremity as a factor for the development of PLP.[6,7,8] There are reports that more than 50% of patients described PLP as similar to the pain they suffered before amputation.[9,10]

At our country, type 2 Diabetes is the most common pathology causing amputation, referred as vascular diseases, it contributes to 81% of cases. On the other hand, traumatic amputations represent 16%, tumors, and congenital diseases account for 3%.[11]

### *b) Pathophysiology*

We may assume that PLP is an example of neuropathic pain since it occurs mainly as a result of an attempt to reorganize the nervous system followed by



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the deference of all sensory information involving amputation with nerve section.

There are three mechanisms involved: "peripheral" given by the massive lesion discharge and the loss of nerve impulses towards the spinal cord.[12] "spinal" Experimental studies have provided evidence of structural, physiological and neurochemical changes in the deferential neurons of the medullary dorsal horn. And it also causes alterations in "central" processing like transneuronal changes at the level of the nucleus of the thalamus. [1, 13]

There are many pharmacological therapies to treat PLP once it appears, and some others are trying to prevent it, without consistent results that allow us to have a standardized treatment regimen. *Madabhushi et al.* Made a case report of a patient undergoing femoral supracondylar amputation, using bupivacaína (local anesthetic) and clonidine (α2 agonist) with excellent results, the patient didn´t report any pain in the stump and neither PLP 12 months after surgery.[14] There are also systematic reviews about the use of dexmedetomidine (α2 agonist) as an adjuvant to the local anesthetic for neuraxial and peripheral nerve blocks, to prolong the duration of analgesia compared to local anesthetic only. Cataloging Dexmedetomidine as a potential adjuvant and with more favorable pharmacodynamic and safety profile than Clonidine.[15,16]

Due the incidence of chronic pain or symptoms related to phantom limb, which may determine disability, a very poor quality of life by the dependence on consumption of opioid and non-opioid analgesics or neuropathic medications to decrease pain, we proposed preventive analgesia in this case, consisting in the application of an anesthetic and analgesic before the surgical incision of the sciatic nerve with the mainly aim to reduce the magnitude and duration of acute postoperative pain and so, assess the appearance or not of PLP, which it implies a decrease in morbidity and improvement in the quality of life; benefiting the patient, family and health institutions.

## II. Materials and Methods

We carried out this study in Guadalajara´s Civil Hospital ¨Fray Antonio Alcalde¨, México. Our study was a controlled, simple randomized, double-blind, clinical trial, conducted within a period of one year, from January 2018 to January 2019.

*Inclusion criteria:* Adult patients, scheduled for femoral supracondylar amputation, being due to traumatic cause, chronic disease and malignant tumor. Neuraxial block as anesthetic technique. American Society of Anesthesiologists´s physical status I-III. With signed informed consent.

*The exclusion criteria were:* Refusal of the patient to participate, allergies known to any of the medications used, chronic hepatopathy disease, chronic renal disease, branch block or bradycardia and coagulation disorders.

*Sample size calculation.* We considered the total supracondylar amputations (110) performed at the Guadalajara´s Civil Hospital during 2017, and established a significance level of 5% (0.05) and a statistical power of 80%. We obtained a total of 30 patients (15 per group).

*RD Group.* Perineural administration of 0.5% ropivacaine 10 ml adding dexmedetomidine 50 mcg, and maintenance with perineural catheter infusion connected to an elastomeric pump with 0.15% ropivacaine for 24 hours.

*RS Group.* Perineural administration of 0.5% ropivacaine 10 ml adding 0.5 ml saline solution 0.9%, and maintenance with perineural catheter infusion connected to an elastomeric pump with 0.15% ropivacaine for 24 hours.

Prior authorization by the Ethics and Research Committee of our Hospital, we assigned the patients in two groups randomly per sealed envelope.

Anxiolysis was given if required, with IV Midazolam 30 mcg/kg. Antibiotic prophylaxis with Cephalothin 1 gr IV. Preemptive analgesia with Paracetamol 1 gr IV. Subarachnoid neuraxial block was administered, using hyperbaric bupivacaine 30 mcg/kg and intraoperative analgesia Parecoxib 40 mg IV.

After dissection by the surgical team and before the section of the sciatic nerve, they identified the perineurium and infiltrated 10 ml of 0.5% ropivacaine + 50 mcg dexmedetomidine (RD Group) or 0.5% ropivacaine + 0.9% saline solution (0.5 ml). We asked the surgeon to wait 5 minutes before performing the sciatic nerve section. After the amputation of the pelvic limb and before the surgical team closed by planes, a perineural catheter (20 G) was placed and laterally exteriorized through a separate skin incision, connected to an elastomeric pump with 0.15% ropivacaine was placed in both groups for 24 hours.

We measured heart rate, blood pressure, sedation level (Ramsay Scale), at the end of the procedure, at PACU (Post-Anesthesia Care Unit), 8 hours, and up to 24 hours after. Also we recorded the pain in the stump, phantom pain using VAS (Visual Analogue Scale) in case of presenting at PACU, 8 hours, 24 hours, 30 days and up to 3 months after the surgery, all patients were followed by phone call after discharge from hospital. We recorded the rescue analgesia, and it was given with tramadol 1mg/kg when VAS > 4. We also monitored side and adverse effects associated with the use of dexmedetomidine such as bradycardia, hypotension, nausea, vomiting, and respiratory depression in PACU, 1 hour, 8, and 24 hours postoperatively.

We used the *Statistical Package for the Social Sciences version 21* [17] for statistical analysis.

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## III. Results

During January 2018 to January 2019, there were included 30 patients (15 per group) scheduled for supracondylar femoral amputation at our Hospital, under the anesthetic technique of subarachnoid block and perineural block of the sciatic nerve, which met the inclusion criteria from the study.

According to demographic data, of the 15 patients in the RD group were 2 women (13%) and 13 men (87%) with a mean age of 57.4 years (SD 20.7). We classified them according to physical status in ASA I: 1 patient (7%), ASA II: 1 patient (7%), ASA 3: 13 patients (86%), with the following preoperative diagnoses: diabetes mellitus 60%, arterial occlusion 27%, cancer 7%, electric burn 7%.

Of the 15 patients in the RS group, were seven women (47%) and eight men (53%) with a mean age of 60 years (SD 17.4). We classified them according to physical status in ASA I: 2 patients (13%), ASA II: 1 patient (7%), ASA 3: 12 patients (80%), with the following diagnoses: diabetes mellitus 53%, arterial occlusion 33 %, cancer 7%, fracture exposed 7%. (Table 1).

*Table 1:* Demographic data

| Variable | RD Group. Ropivacaína + Dexmedetomidina. N=15 | RS Group. Ropivacaína + Solución Salina. N=15 | P (CI 95%) |
|---|---|---|---|
| | (Mean ± SD) | (Mean ± SD) | |
| Edad | 57.4 ± 20.7 | 60 ± 17.4 | 0.56 |
| Género | | | |
| Masculino | 13 | 8 | |
| Femenino | 2 | 7 | |
| ASA | | | 0.83 |
| I | 1 | 2 | |
| II | 1 | 1 | |
| III | 13 | 12 | |

*Statistical significance when obtaining P <0.05. Abbreviations: N (patients per group); ASA (Classification by the American Society of Anesthesiology); SD (Standard Deviation).*

During the postoperative period, both groups were evaluated for pain intensity, both at rest and in movement, of the stump and phantom limb, from PACU, at 8 hours, 24 hours, 30 days, and up to 3 months.

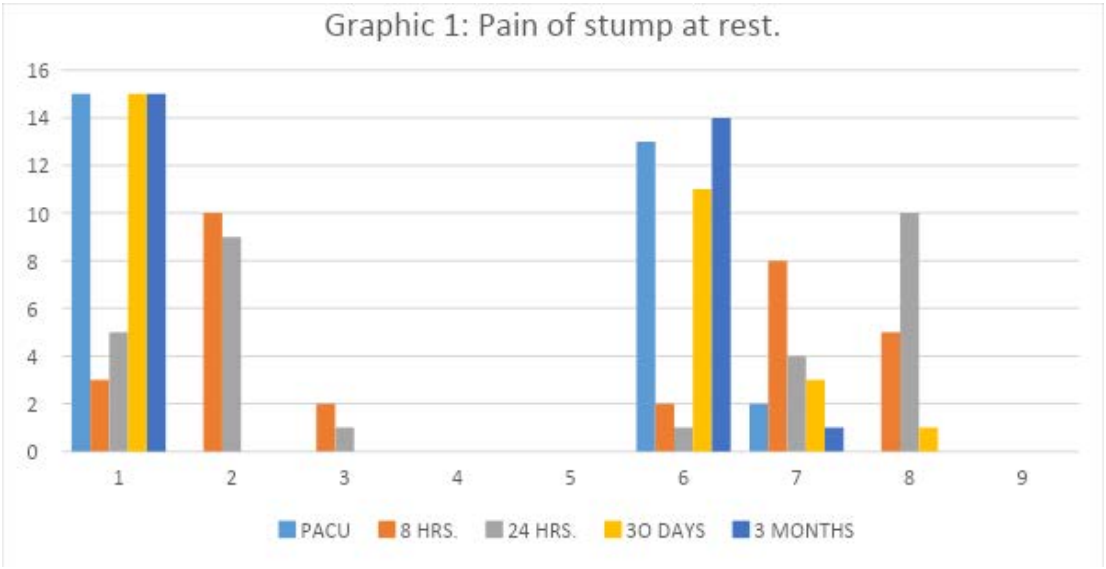
*Table 2:* Pain Assessment (VAS) of the stump at rest and movement

| Variables | Evaluated Period | RD Group N = 15 | RS Group N = 15 | p (CI 95%) |
|---|---|---|---|---|
| Pain Level | | (Main ± SD) | (Main ± SD) | |
| Rest | PACU | 0 | 0.13 ± 0.35 | 0.143 |
| | 8 hrs. | 0.93 ± 0.59 | 1.2 ± 0.67 | 0.426 |
| | 24 hrs. | 0.73 ± 0.59 | 1.60 ± 0.63 | 0.003 |
| | 30 days | 0 | 0.33 ± 0.61 | 0.099 |
| | 3 months. | 0 | 0.06 ± 0.25 | 0.303 |
| Movement | PACU | 0 | 0.20 ± 0.41 | 0.068 |
| | 8 hrs. | 1.40 ± 0.73 | 1.60 ± 0.73 | 0.066 |
| | 24 hrs. | 1.33 ± 0.48 | 1.73 ± 0.45 | 0.022 |
| | 30 days. | 0 | 0.33 ± 0.72 | 0.189 |
| | 3 months. | 0 | 0 | - |

*Statistical significance when obtaining P <0.05. Abbreviations: N (patients per group); VAS (Visual Analog Scale); DS (Standard Deviation); PACU (PostAnesthetic Care Unit) hrs (hours).*



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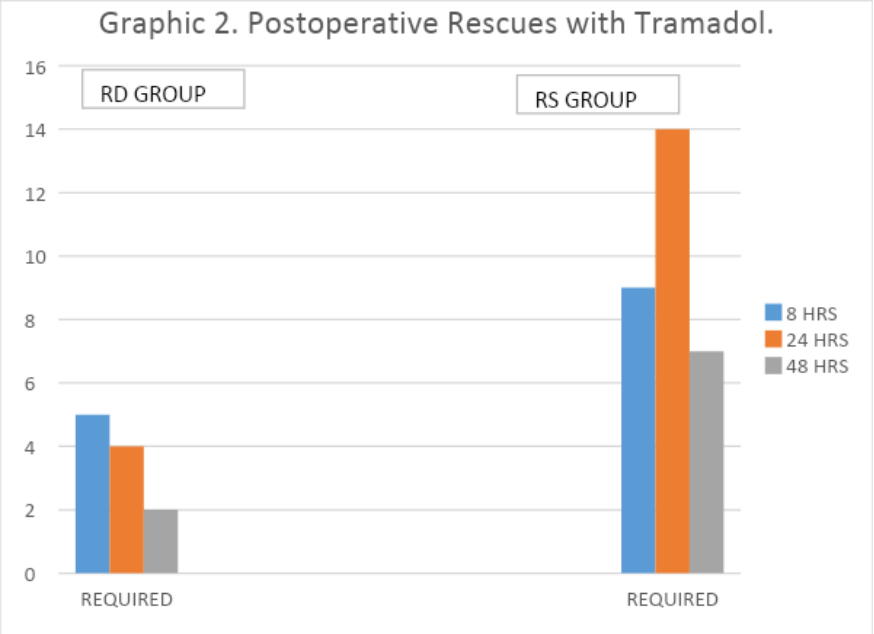

*Abbreviations: RD (Ropivacaine + Dexmedetomidine), RS (Ropivacaine + Saline); PACU (PostAnesthetic Care Unit), Hrs (hours).*

Pain values with VAS 4 and above, had the prescription of rescue with Tramadol at 1mg / kg. In the RD group, at 8 hours, five patients required Tramadol, at 24 hours four patients, and 48 hours 2 of them. In the RS group at 8 hours, nine patients were given tramadol rescue, at 24 hours fourteen patients, and at 48 hours, 7 of them. Then it is possible to demonstrate with statistical significance that the perineural administration of dexmedetomidine does reduce the postoperative opioid requirements. (Table 3, Graph 2).

*Table 3:* Postoperative rescue with Tramadol

| Variables | Evaluated period | RD Grup N = 15 | RS Grup N = 15 | p (CI 95%) |
|---|---|---|---|---|
| Tramadol rescue. | | Percent. | Percent. | |
| | 8 hrs. | 33% | 60% | 0.143 |
| | 24 hrs. | 27% | 93% | 0.0002 |
| | 48 hrs. | 13% | 47% | 0.046 |

*Statistical significance when obtaining P <0.05. Abbreviations: hrs (hours).*




*Abbreviations: RD (Ropivacaine + Dexmedetomidine), RS (Ropivacaine + Saline Solution).*



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We evaluated the appearance of phantom limb pain at rest and movement, which was not reported by any patient of the RD group from the moment of evaluation at PACU up to 3 months of follow-up. It is worth mentioning that two patients of the RD group presented prior amputation, one by contralateral first toe, and another ipsilateral transtibial, none reported previous phantom limb pain.

From the RS group, up to 30 days, one patient reported mild phantom limb pain and one more patient moderate resting pain; on movement three patients reported mild pain at 30 days and only one patient mild pain at 3 months, who we referred to the Hospital Pain Clinic for evaluation and treatment. Without being these statistically significant values. (Table 4)

*Table 4:* Assessment of phantom limb pain at rest and movement

| Variables | Evaluated period | RD Group N = 15 | RS Group N = 15 | p (CI 95%) |
|---|---|---|---|---|
| Pain Score | | (Main ± SD) | (Main ± SD) | |
| Rest | PACU | 0 | 0 | - |
| | 8 hrs. | 0 | 0 | - |
| | 24 hrs. | 0 | 0 | - |
| | 30 days. | 0 | 0.20 ± 0.56 | 0.343 |
| | Three Months. | 0 | 0.13 ± 0.51 | 0.309 |
| Movement | PACU | 0 | 0 | - |
| | 8 hrs. | 0 | 0 | - |
| | 24 hrs. | 0 | 0 | - |
| | 30 days. | 0 | 0.20 ± 0.41 | 0.068 |
| | Three months. | 0 | 0.06 ± 0.25 | 0.309 |

*Statistical significance when obtaining P <0.05. Abbreviations: N (patients per group); SD (Standard deviation), PACU (PostAnesthetic Care Unit) hrs (hours).*

We decided to measure the possible side effects of perineurally administered medications on systemic blood pressure and heart rate in PACU, as well as the level of sedation (Ramsay scale) and oxygen saturation in PACU up to 24 hours after surgery.

We didn´t find statistically significant differences in the values of systemic blood pressure, heart rate, and oxygen saturation after the intervention.

About sedation in the postoperative care unit, we found significant difference (p <0.025) with a higher degree of sedation in the RD group with an average of 2.8 on the Ramsay scale. 2.4 in the RS group.

*Table 5:* Side effects on vitals and sedation after perineural block

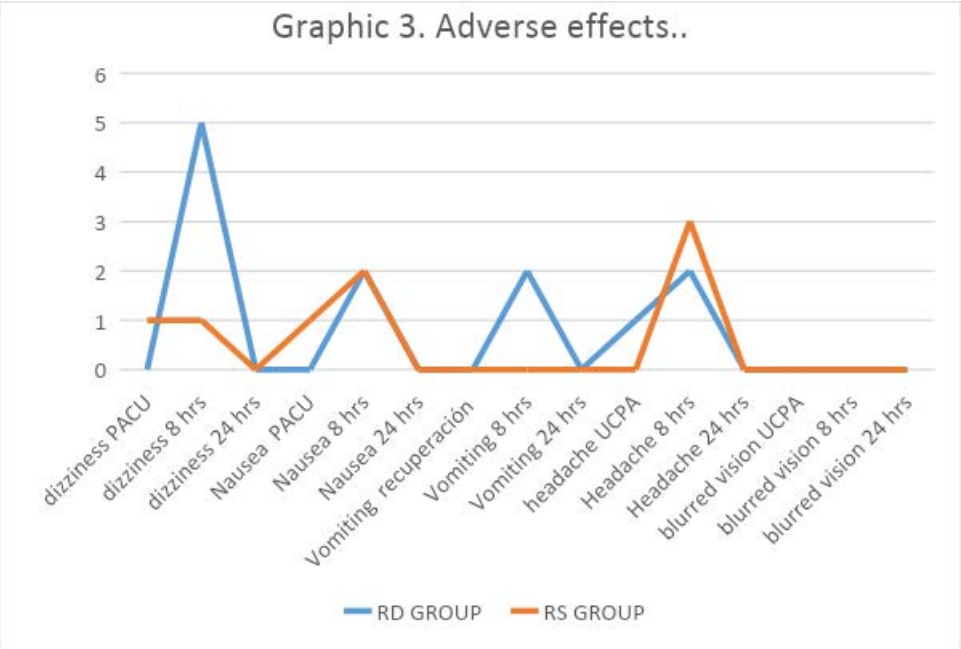
| Variables | Evaluated Period | RD Group N = 15 (Main ± SD) | RS Group N = 15 (Main ± SD) | p (CI 95%) |
|---|---|---|---|---|
| Mean arterial pressure (mmHg) | PACU | 82.9 ± 13.12 | 83.5 ± 12.04 | 0.341 |
| Heart rate (Bpm) | PACU | 75.2 ± 10.56 | 74.0 ± 8.4 | 0.555 |
| Pulse-oximetry (%) | PACU | 96.4 ± 2.02 | 95.7 ± 1.90 | 0.552 |
| | 8 hrs. | 94.93 ± 0.96 | 95.33 ± 0.72 | 0.261 |
| | 24 hrs. | 94.86 ± 0.80 | 95.06 ± 0.59 | 0.057 |
| Sedation (Ramsay) | PACU | 2.80 ± 0.41 | 2.40 ± 0.50 | 0.025 |
| | 8 hrs. | 2.20 ± 0.41 | 2.00 ± 0.41 | 0.068 |
| | 24 hrs. | 2.00 ± 0 | 2.00 ± 0 | - |

*Statistical significance when obtaining P <0.05. Abbreviations: N (patients per group); SD(Standard deviation), PACU (PostAnesthetic Care Unit) hrs (hours).*

Of the possible adverse effects of the drugs used in our study, dizziness, nausea, vomiting, headache, and blurred vision were evaluated the first 24 hours after the perineural block. It was observed mainly in the RD group, dizziness in 13% at 8 hours, against 7% in the RS group (p = 0.068). Nausea in 13% at 8 hours in both groups. And headache 13% in the RD group against 20% in the RS group at 8 hours (p = 0.62). However, we didn´t find statistically significant difference for any of the adverse effects measured.



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*Abbreviations: RD (Ropivacaine + Dexmedetomidine), RS (Ropivacaine + Saline); HRS (hours).*

## IV. Discussion

This study yielded significant data regarding the analgesic intervention of perineural infiltration with the combination of a local anesthetic (Ropivacaine) and an α2 agonist (Dexmedetomidine) since in the published literature there are only isolated reports of clinical cases of this combination, but no clinical trials and much less meta-analysis; there are some others of perineural infiltration with local anesthetic without additive for the prevention of PLP, and other about the addition of an α2 agonist for prolongation of peripheral nerve block, without assessing the impact on the prevention of phantom limb pain after amputation objectively.

Regarding the levels of postoperative pain, at 24 hours lower scores of pain at rest were found using the combination ropivacaine + dexmedetomidine ($p = 0.003$); However, both interventions evaluated in this study with infiltration of local anesthetic and its postoperative infusion by using an elastomeric pump were effective for pain management, coinciding with the study by *Borgh* et al. In which they conclude that the use of a prolonged postoperative perineural perfusion of 0.5% ropivacaine is effective therapy for the treatment of phantom limb pain. [18]

Therefore, postoperative opioid consumption was also reduced as described by *Bosanquet* et al. in a systematic review and meta-analysis on the use of intraoperative placed perineural catheter with infusion of local postoperative anesthetic[19]. In this case, for our study, the addition of dexmedetomidine to perineural infiltration had a statistically significant difference in the reduction of the use of rescue tramadol at 24 hours, compared with the use of only local anesthetic ($p = 0.0002$).

## V. Conclusion

Phantom limb pain, associated with the amputation of a member of the organism, is a frequent complication after each procedure, sometimes reported with very high incidence rates.

In the understanding of the pathophysiology for the development of this neuropathic pain, there were proposed different interventions for its treatment, but few focused on preventing its onset. One of those proposals is perineural infiltration and continuous infusion of local anesthetic adding an adjuvant to mitigate peripheral sensitization in nociceptors at the medullary level and central de-centralization (cortex and thalamus) in a preventive manner, avoiding the development of the PLP, which once it appears is very complex to treat.

In this study, we corroborate and verified the advantages of doing a preventive intervention as described with a local anesthetic but adding an α2 agonist, observing excellent results, and with no significant side effects.

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*Conflicts of interest*
*There are no conflicts of interest.*

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# 'Arthrox' an Advanced Ayurvedic Detox Programfor Knee Osteoarthritis- A Case Report

By Smita Naram, Deepak S. Mahajan, Hemang Parekh & Ronak naik

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*Abstract-* Reported case was a 68 years old Male with Early-stage Osteoarthritis of both knees (Sandhigata Vata), accompanied by reduced medial joint spaces bilaterally, marginal osteophytes. Initially, VAS scale rating was poor. Proven herbal formulations like Painmukti MJ, Painmukti Sandhical, Painmukti cream along with Advance Virechana (Arthrox), Knee Dhara, Yogbasti, and Matrabastitwice a week was given for 16months.Visual analog scale for knee pain and an Ayurveda clinical assessment criteria used to evaluate the effects of Treatment and Herbal remedies monthly basis. After a treatment of 30 days of Advance Virechana (Arthrox), Knee Dharaand Yogbasti, Pain, movement, and stability of the joint was improved at an excellent level. During follow up visit with the help of Matrabasti twice a week, Pain, movement of joint and stability, and even X-ray reading were change. In conclusion, this knee osteoarthritis patient's quality of life improved by Advance Virechana (Arthrox).

*Keywords:* *osteoarthritis, arthrox, sandhigatvata, virechana.*

*GJMR-H Classification:* *NLMC Code: WE 348*




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# 'Arthrox' an Advanced Ayurvedic Detox Program for Knee Osteoarthritis- A Case Report

Smita Naram [α], Deepak S. Mahajan [σ], Hemang Parekh [ρ] & Ronak naik [ω]

*Abstract-* Reported case was a 68 years old Male with Early-stage Osteoarthritis of both knees (Sandhigata Vata), accompanied by reduced medial joint spaces bilaterally, marginal osteophytes. Initially, VAS scale rating was poor. Proven herbal formulations like Painmukti MJ, Painmukti Sandhical, Painmukti cream along with Advance Virechana (Arthrox), Knee Dhara, Yogbasti, and Matrabastitwice a week was given for 16months.Visual analog scale for knee pain and an Ayurveda clinical assessment criteria used to evaluate the effects of Treatment and Herbal remedies monthly basis. After a treatment of 30 days of Advance Virechana (Arthrox), Knee Dharaand Yogbasti, Pain, movement, and stability of the joint was improved at an excellent level. During follow up visit with the help of Matrabasti twice a week, Pain, movement of joint and stability, and even X-ray reading were change. In conclusion, this knee osteoarthritis patient's quality of life improved by Advance Virechana (Arthrox).

*Keywords: osteoarthritis, arthrox, sandhigatvata, virechana.*

## I. Background

Pain have been regarded as a symptom of an underlying condition.[1]Pain is the main causative factor that forces a person to visit a doctor immediately. The most common symptom as joint pain and stiffness is a diseased condition called Osteoarthritis. Initially, symptoms may occur only following exercise, but over time may become constant. Other symptoms may include joint swelling, decreased range of motion[2].Osteoarthritis is also erroneously called degenerative joint disease, which mostly affects cartilage. Cartilage is the slippery tissue that covers the ends of bones in a joint. Healthy cartilage allows bones to glide over each other, absorb the shock of movement. In osteoarthritis, the top layer of cartilage breaks down and wears away. This breakdown of cartilage allows bones under the cartilage to rub together. The rubbing causes pain, swelling, and loss of motion of the joint.[3]

The management of Osteoarthritis includes Lifestyle management, Physiotherapy, and Medication. The effectiveness of NSAIDs varies substantially. Paracetamol is clinically in effective in symptomatic the treatment of Osteoarthritis, nsaids such as naproxen, while more effective in severe cases, are associated with greater side effects, such as gastrointestinal bleeding.[4] Another class of NSAIDs, COX-2 selective inhibitors (such as celecoxib) are equally effective, and have lower rates of adverse gastrointestinal effects, but higher rates of cardiovascular disease such as myocardial infarction[5] Because oral medication often does not lead to an adequate clinical response in OA, non-pharmacological therapies such as exercise, weight reduction, and physical therapies play role in the long-term management of osteoarthritis and are recommended. In addition, complementary and alternative medicine (CAM) treatments such as acupuncture or herbal medicines are used frequently by OA patients.

Acharya Charaka mentioned Sandhigatavata, which can be compare with Osteoarthritis. *Shula* (pain) is the cardinal feature of the disease associated with *Sandhishotha* (joint inflammation), *Vatapurna-drati-sparsha* (edema palpable as air-filled sac), *Prasaraṇa-akuncanasavedana* (painful movement of the joints), and in the later stage *Hantisandhi* (restricted joint movements).[6]

## II. Case Report

Reported case was a 68 years old Male with Early-stage Osteoarthritis of both knees (Sandhigata Vata), accompanied by reduced medial joint spaces bilaterally, marginal osteophytes, Tibia spiking,and Patellar breaking. When the patient was 65 years old, they developed pain in the right knee, at the age of 65.6 years in the left knee. At the age of around 66 years, he had an X-ray with a diagnosis early-stage osteoarthritis. Therefore the patient took NSAIDs and received conservative treatment and Physiotherapy. However, knee pain increases progressively along with weight; on the other hand, his daily living activities stared decreasing with age. At the age of 68 years, this patient visited Ayushakti Ayurveda Pvt Ltd outdoor unit in Thane, Mumbai, Maharashtra, India branch with a complaint of both knee pain while walking and climbing. The patient got his self-reported visual analog scale (VAS) pain score in-between 8 and 9. On clinical examination, both knees showed mild detectable effusion. As per clinical symptoms and X-ray reporting patient diagnosed as having Osteoarthritis of both knee joints. The patient was convinced to undergo Advance Virechana (Arthrox),*Knee Dhara, Yogbasti,* and Herbal formulations for 20 days, followed by *matrabasti*(60 ml oil enema) twice a week for 12 months along with Herbal formulations. All the test drugs ( table- 01)Pain Mukti MJ 400 mg twice a day after food, Pain MuktiSandhical 720

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mg twice a day after food, Pain Mukti Cream for local Applicationwere prepared byAyushakti Ayurveda Pvt Ltd pharmacy, Plot number 78, Stice, Musalgaon, Sinnar, Nashik- 422112.

*Table 1:* Formulas for the test drug shown in table-01

| Pain Mukti MJ | | Pain MuktiSandhical | | Pain Mukti Cream | |
|---|---|---|---|---|---|
| Ingredients | Quantity | Ingredients | Quantity | Ingredients | Quantity |
| NirgundhiGhan (Vitexnirgundo) | 50 mg | Guggul(Commiphoramukul) | 150mg | Mahanarayan oil | 10% |
| Rasna Ghan (Pluchealanceolata) | 100mg | Asthishrunkhlaghan (Cissusquadrangularis) | 100 mg | Lavang oil (Eugenia aromatica oil) | 0.5 % |
| ShallakiGhan (Boswelliaserrata) | 100mg | Lajjalughana (Mimosa Pudica) | 30 mg | Twak oil (Cinnamomum Zeylanicum oil) | 0.5 % |
| RaktaPunarnavaGhan (Boerhaviadiffusa) | 40mg | Lakha (Lacciferalacca) | 20 mg | Pudinaphool (Menthaspicata) | 5 % |
| Shunthi powder (Zinziberofficinalae) | 25mg | Aswagandha (Withaniasominfera) | 20 mg | ShuddhaGuggul (Balsamodendronmukul) | 1 % |
| Musta powder (Cyprus rotandus) | 75mg | Mukta | 400 mg | Marich ark (Capsicum extract) | 0.1 % |
| | | | | Gandhapurapo oil (Winter green oil) | 10 % |

The first regimen of Advance Virechana (Arthrox) was started for the patient after his informed written consent for the procedure, all the do's and don'ts, all the possible complications during Advance Virechana (Arthrox) procedure explained thoroughly.

## III. Treatment Plan Advance Virechana (Arthrox)

The procedure of Advance Virechana (Arthrox) performed in three steps.

1. *Poorvakarma, ie. Preparatory procedures*- This was performed before therapy, which includes *Deepana* (Appetising drugs) and*Pachana* (Digestive drugs), which was then followed by *Snehapana,*ie. Oral administration of medicated ghee) for 4 days, planned after the examination of *Kostha* (nature of bowels) of the patient until achieving the symptoms of Adequate oleation (Internal consumption of mediacated ghee). Simultaneously *Abhyanga* (external application of Oils) and*Swedana* (Steam) was given for five days.
2. *Pradhankarma, ie. Main procedure*- This was the actual administration of Advance Virechana (Arthrox) herbs, as per *Bala* (Strength*) Kostha*(nature of bowels)of the patient. The herbal combination used was tablet virechana four tablets, manufactured by Ayushakti Ayurveda.
3. *Paschatkarma,ie. Post mainprocedure*- As per the number of bouts of bowel evacuated after giving Advance Virechana (Arthrox), *Sansarjanakrama* with *Mand, Peya*, and *Vilepee* advised for three days.

The assessment of Advance Virechana (Arthrox)based on various parameters termed as*Shuddhi* (cleansing) criteria like *Vaigiki*(number of bouts of stool passed), *Maniki* (quantitative measurements of stool), *Laingiki* (Symptoms), and *Antyaki* (assessment based on end points of purgation).This particular patient had Madhyamshudhhi. In the second regimen, the Advance Virechana (Arthrox) procedure was followed by *Yogbastikrama* (8 enemas) and *Knee Dhara* (pouring of oil on knee anterior and posterior aspect) with *Mahanarayan oil* for eight days. All the test drugs Pain Mukti MJ 400 mg twice a day after food, Pain MuktiSandhical 720 mg twice a day after food, Pain Mukti Cream for local Application was kept continue after that for 16 months. Matrabastitotal of 60 ml (*Mahanarayan oil*-20 ml, *Balada oil*-20 ml, *Jivanyaghrut*-20 ml) twice a week advised for 16 months.

*Table 2:* Schedule of administration of treatment

| Days | Treatment | Drug | Duration |
|---|---|---|---|
| 1-5 days | Dry pindsweda | Shunthi powder (Zinziberofficinalae), Ajwain powder Trachispermumammi | 20 mins |
| 6-10 days | Internal and external snehana (Oleation), Swedana (Steam) | Internal- Mahatiktaghruta<br>External- Mahanarayan oil | 20 mins |
| 12th day | Virechana (Detox) | Special virechana tablet | |
| 13-15 days | Sansarjankrama | Mand, Peya, Vilepee | |
| 13-20 days | Yogbasti Knee dhara | Knee dhara- Mahanarayan oil | 20 mins |
| Onwards | Matrabasti | (Mahanarayan oil-20 ml, Balada oil-20 ml, Jivanyaghrut -20 ml) | Twice a week |

The overall improvement observed with symptoms like Pain (table-3), Swelling (table-4), Akunchana Prasarane Vedana (table-5) difficulty in Walking (table-6) and difficulty in climbing (table-7) and were grades like following-



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*Table 3:* Pain scale

| Symptom | Grade |
|---|---|
| No Pain | 0 |
| Mild pain of bearable nature, comes occasionally | 1 |
| Moderate pain- Slight difficulty in joint movements due to pain , requires medication and may remain throughout the day | 2 |
| Severe Pain- More difficulty in moving the joints and disturbing sleep and requires strong analgesics | 3 |

*Table 4:* Swelling scale

| Symptom | Grade |
|---|---|
| No Swelling | 0 |
| Minimal edema only in joint Capsule | 1 |
| Edema in dependant parts | 2 |
| Massive edema in the limb | 3 |

*Table 5:* Akunchana Prasarane Vedana

| Symptom | Grade |
|---|---|
| No Pain | 0 |
| Pain without wincing of face | 1 |
| Pain with wincing of face | 2 |
| Prevent complete flexion | 3 |
| Does not allow passive movement | 4 |

*Table 6:* Difficulty in Walking

| Symptom | Grade |
|---|---|
| No Effect | 0 |
| Needs Minimal Assistance / Can Stand or walk for 1 Hour | 1 |
| Needs Maximum Assistance / Can Stand or Work for less than 30 Minutes | 2 |
| Almost Not Standing or Walking or Bed Ridden | 3 |

*Table 7:* Difficulty in climbing

| Symptom | Grade |
|---|---|
| No Effect On Climbing | 0 |
| Needs Minimal Assistance | 1 |
| Needs Maximum Assistance | 2 |
| Almost No Climbing or Bed Ridden | 3 |

## IV. Results

During the treatment of the first 30 days, patient experienced gradual improvement. All the symptoms were around 50 % reduced except climbing in first 30 days only (table-8). After the successful completion of all the arthrox treatment patient experienced 100 % relief in all the symptoms. His VAS scale reading was improved significantly. When the patient had his both knee X-ray after 13 months, it showed no abnormality except mildly reduced joint space in medial compartments of both knees (image-1 and image-2).

*Table 8:* Showing difference in symptoms in the first 30 days

| Symptom | BT | AT | Relief in % |
|---|---|---|---|
| Pain scale | 3 | 2 | 33.33333 |
| Swelling | 2 | 0 | 100 |
| AkunchanaPrasaraneVedana | 3 | 1 | 66.66667 |
| Difficulty in Walking | 2 | 1 | 50 |
| Difficulty in climbing | 2 | 2 | 0 |




*Image 1:* Before treatment




After treatment

## V. Discussion

Osteoarthritis *(Sandhigatvata)* is commonly known as wear and tear arthritis. In this natural cushion between the joints, cartilages wears away[7]. There may be inflammation in the joint spaces, which causes symptoms like Pain initially,later Swelling. Due to lack of this cushion and absorption material, inflammation, in Sandhigatvatathe mobility of joints is restricted at the initial stage, and later it is aggravated by anatomical changes in the articular surfaces and joint capsule and the ligamnets[8]. When the patient wants to move his knee



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in his regular daily activities, he experiences the pain, which may cause wincing of the face. All the signs and symptoms noted for the patient, and the assessment was done. The symptoms assessed before starting treatment, after one month, three months, six months and final visit were after twelve months.

The two main events in any degenerative disease described by our Achary as are *Asthidhatukshyaya* and *Vataprakopa*, and according to Samhitas, *Vata* and *Asthi* have *Ashrayaashrayi-sambandh*(connection) in which the herbs are causing *Kshaya* of *Vata* are responsible for *Asthidhatuvriddhi* and vice versa[9].Bastichikitsa is the best panchakarma treatment for vitiated Vata[10]. According to Acharya CharakPanchakarma procedure of Basti is called Ardhchikitsa (Half treatment) for Vata[11]. Virechana increases the absorption of basti to achieve a target of pain relief in a short period. *Virechana* evacuates all morbid *Doshas* from all micro to macro *Dhatu* channels and regulates *Vata*, thus decreasing all symptoms of on *Srotasa* level[12].Painmukti MJ and Painmukti Sandhical are moderately effective and safe herb in chronic arthritic conditions along with painmukti cream for local application and used as an alternative to NSAID's without side effect[13]. Cissusquadrangularis present in Painmukti Sandhicalcan stimulate osteoblastogenesis[14]. Boswelliaserrata blocks an enzyme 5-lipooxygenase that plays a role in the formation of leukotrienes, which stimulates inflammation[15].

## VI. Conclusion

Arthrox plan can be used successfully in knee osteoarthritis for the long term; it can give better relief in Symptoms of Osteoarthritis as well as can reverse the early degenerative changes in X-ray readings.

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Authors can submit papers and articles in an acceptable file format: MS Word (doc, docx), LaTeX (.tex, .zip or .rar including all of your files), Adobe PDF (.pdf), rich text format (.rtf), simple text document (.txt), Open Document Text (.odt), and Apple Pages (.pages). Our professional layout editors will format the entire paper according to our official guidelines. This is one of the highlights of publishing with Global Journals—authors should not be concerned about the formatting of their paper. Global Journals accepts articles and manuscripts in every major language, be it Spanish, Chinese, Japanese, Portuguese, Russian, French, German, Dutch, Italian, Greek, or any other national language, but the title, subtitle, and abstract should be in English. This will facilitate indexing and the pre-peer review process.

The following is the official style and template developed for publication of a research paper. Authors are not required to follow this style during the submission of the paper. It is just for reference purposes.

***Manuscript Style Instruction (Optional)***

- Microsoft Word Document Setting Instructions.
- Font type of all text should be Swis721 Lt BT.
- Page size: 8.27" x 11'", left margin: 0.65, right margin: 0.65, bottom margin: 0.75.
- Paper title should be in one column of font size 24.
- Author name in font size of 11 in one column.
- Abstract: font size 9 with the word "Abstract" in bold italics.
- Main text: font size 10 with two justified columns.
- Two columns with equal column width of 3.38 and spacing of 0.2.
- First character must be three lines drop-capped.
- The paragraph before spacing of 1 pt and after of 0 pt.
- Line spacing of 1 pt.
- Large images must be in one column.
- 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.



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## 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.



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***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 though 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.



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*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.



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**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.

*Please read the following rules and regulations carefully before submitting your research paper to Global Journals Inc. to avoid rejection*.

*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.

*Written material:* You may discuss this with your guides and key sources. Do not copy anyone else's paper, even if this is only imitation, otherwise it will be rejected on the grounds of plagiarism, which is illegal. Various methods to avoid plagiarism are strictly applied by us to every paper, and, if found guilty, you may be blacklisted, which could affect your career adversely. To guard yourself and others from possible illegal use, please do not permit anyone to use or even read your paper and file.

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

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