www.jmscr.igmpublication.org
Impact Factor (SJIF): 6.379
Index Copernicus Value: 71.58
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v6i5.53

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Prospective Randomised Clinical Trial Study of Diclofenac Sodium 100mg Suppository and Trans Dermal Patch for the Duration of post Operative Analgesia in LSCS Patients Under Going Surgery under Lumbar Subarachnoid Block

Authors
Dr Rajeev D S[1], Dr Harikrishnan S[2]
[1]Assistant Professor, Anaesthesiology and Critical Care, Govt. Medical College Thiruvananthapuram
[2]Associate Professor, Anaesthesiology and Critical Care, Govt. Medical College Thiruvananthapuram
Corresponding Author
Dr Harikrishnan S
Associate Professor, Anaesthesiology and Critical Care, Govt. Medical College Thiruvananthapuram

Abstract
Background: *Post operative analgesia in continuation of lumbar subarachnoid blockade can be effected by several means. But use of non steroid anti inflammatory drugs in various forms is advantageous to the parturient and baby in terms of lack of post operative respiratory depression in mother and baby, It prevents hypoglycemia in the baby, efficient post natal care of the baby by the mother and prevents deep venous thrombosis in the mother by early mobilization of the mother.*
Materials and Methods: *We have investigated a total of 150 patients, with 50 patients in each group constituting three groups: Suppository Group (Group I), Patch Group (Group II) and Control Group (Group III). Duration of post operative analgesia provided by each group and their side effects were studied.*
Results: *Group I (Suppository Group) was most efficient in post operative analgesia of duration of 14.8 hours, with a standard deviation of 1.1. The Patch Group (Group II) showed a mean duration of 4.5 hours while the Control Group (Group III) showed a mean duration of 0.7 hours. The mean dose of the rescue analgesic was lowest for Group I and highest for Group III, showing qualitative analgesia provided by the diclofenac suppository. Mean VAS score was lower for the Group I patients, while it was highest for the Group III patients.*
Conclusion: *Diclofenac suppository can be easily placed by the obstetrician or the paramedical staff post operatively. It was a cost effective and efficient technique compared to the diclofenac patch. We found from this study, which was analyzed via SPSS Version 10.*
Keywords: *Diclofenac Suppository, LSCS Patient, Diclofenac Patch.*

Introduction

In man's constant battle against physical pain the greatest achievement is discovery of anaesthesia. Control of the post operative pain is very important in early postoperative recovery. Diclofenac suppository has been extensively studied for its efficacy and safety as a postoperative analgesic. However the transdermal patch which is less invasive than a suppository has not been studied in detail. Administration of transdermal patch can be done by non-technical or non medical personnel. In contrast, administration

of suppository needs help of a medical personnel. Non steroidal anti-inflammatory drugs make up one of the largest groups of pharmaceutical agents used worldwide. Diclofenac sodium[1] is a versatile NSAID analgesic which can be used orally as tablet, as intramuscular injections, intravenous injections, Transdermal patch, ointment, and as suppository. Rectal suppository[2] of diclofenac reduces patient's opioid requirements with a reduction in side effects of opioids. A single dose of rectal suppository of diclofenac[3] in the post operative period has anti shivering and analgesic action, comparable to pethidine.

Rectal suppository of diclofenac was found more effective than rectal tremadol[4] for post operative pain in post LSCS patients. Opioids used prenatally for management of pain cross placenta and lead to affect the markers[5, 6] of fetal growth such as birth length and birth weight.

Intramuscular injections are very painful, oral preparations associated with gastritis, peptic ulceration and hepatic damage, however preparations like suppository and transdermal patch are relatively free from side effects. Occurrence of pain is associated with physiological adverse effects like increased heart rate, increased blood pressure, decreased cerebral blood flow, increased intracranial pressure, hypoventilation, post operative sputum retention and pulmonary atelectasis. Administration of Diclofenac postoperatively before waning of the spinal anaesthesia after a lower segment caesarian section provides good quality of preemptive analgesia, which helps in early mobilization, healing of the wound, prevents the hemostatic complications of immobilization altogether a good quality postoperative period. Administration of the parenteral opioids is associated with sedation, nausea, vomiting, respiratory depression and constipation in the mother and respiratory depression and inadequate breast feeding in the new born. The goal of treatment with NSAIDS provides pain relief that is effective, well tolerated and which improves parameters of outcome including discharge, street fitness and return to work.

Materials and Methods

This randomized controlled trial was conducted in the department of anesthesiology at Sree Avittom Thirunal Hospital, the women and children wing of Medical College, Thiruvananthapuram during the period 2006-2008. Institutional research committee and ethics committee approval were obtained before conducting the study. Informed consent were taken from all patients enrolled in to the study. We conducted this study in accordance with the principles laid down as per the declaration of Helsinki. In this study, we recruited 150 patients undergoing Lower Segment Caesarian Section under Lumbar subarachnoid (LSAB) block. A priori sample size calculation was done at the protocol stage.

Patients scheduled for elective or emergency LSCS under subarachnoid blockade were randomly recruited in to this study. We included only patients between 18 to 30 years. Only those having a height be ween 155 cm to 175 cm were recruited. ASA grade above III were excluded from the study. In addition, only those case where the duration of surgery was not beyond 90 minutes with Initial Spinal Sensory level above T6 segment were included in this trial. Those cases with failed spinal anesthesia, inadequate spinal sensory level were excluded from the study. Moreover, those with previous hypersensitivity to NSAID, angioedema, urticaria and Bronchial Asthma, bleeding and coagulation disorders, severe renal disease, Congestive Cardiac failure, severe preeclampsia and hepatic insufficiency were excluded as well. In addition we did not included those patients having Acid peptic disease, Gastritis, Malena and history of proctitis or Ulcerative Colitis in this study.

All patients were, in patients. Study was conducted in both emergency and elective caesarian section cases. Thorough preanaesthetic check up and investigations like Blood, Urine routine examinations, VDRL, HIV, HBsAg, Blood grouping and cross matching and bleeding time & clotting time are done prior to surgery. Inclusion and exclusion criteria were strictly followed. All elective cases premedicated with

Ranitidine 150mg and metoclopramide 10mg orally at 10 pm day before surgery and the same repeated at 6 am on the morning of surgery. In emergency caesarian section cases Inj. Ranitidine 50mg 1/V and Inj. Metoclopramide 10 mg were given as premedication immediately before spinal anaesthesia. After premedication baseline blood pressure pulse rate and oxygen saturation were noted. Patients were randomized according to a computer generated random number table. Allocation was concealed. Study, includes three groups of patients group I suppository group. Group II- Patch group. Group III-Control group.

All patients were monitored with noninvasive blood pressure, pulse oximeter and continuous electrocardiography.

Pre-loaded with 250-500 ml normal saline. Patient positioned in the left lateral position, with hip and knee flexed, spine also flexed for administering spinal anaesthesia taking care of the monitors already attached. Patient's back prepared, wiped with iodine solution, followed by spirit, draped sterile under sterile precautions lumbar subarachnoid block at the level of L3-L4 or L4-5 using 23G Quincke needle, after free flow of cerebrospinal fluid. 2ml of 0.5% heavy Bupivacaine administered. Patient immediately turned from the left lateral to supine position. Oxygen is administered via polymask and 15-30° left lateral tilt given.

Spinal Sensory level checked after few minutes and table tilt adjusted to keep sensory level at or above T4 – T6 segment level. Then the surgery started and once the baby delivered, Inj. Midazolam 1mg + I/V plus Inj. Oxytocin 20 units I/V infusion in 500ml normal saline administered via the I/V cannula in mother, were administered for the three study groups. Tilt of table adjust so that patient was in supine position. Rescue analgesic in the form of inj. Morphine 0.05 mgm/kgwt plus or-0.01mgm/kgwt administered if any group of patient complained of pain after noting time ,VAS score and dose of rescue analgesic needed to abolish pain. After closure of the surgical wound in layers up to this step procedure being same for 3 groups of patients under study. At the end of surgery spinal sensory level again checked.

For the group I suppository group clean the area around rectum with mild soap and warm water. Gently dry by patting. Detach one suppository (100mg strength) from the strip. Remove wrapper before inserting suppository by holding suppository up right and carefully peeling wrapper evenly down both sides of suppository. Avoid excessive handling as the suppository is designed to melt at body temperature. Position the patient flat on back or on one side with anal opening exposed. Gently insert the suppository well into rectum use finger tip to complete insertion. If necessary hold buttocks together for 30-60 seconds to keep suppository in place. Time of placement of suppository noted. Given instruction to avoid other analgesic drugs in the form of opioids or NSAIDS.

For group II patients once surgery is over Diclofenac Sodium 100mg transdermal patch is peeled off from the silver foil and the exposed patch is pasted 5 cm above the caesarian wound, time noted. Pulse rate and blood pressure are recorded.

In case of group III patients no patch or suppository is placed. After surgery blood pressure and pulse rate and time were noted.

In the post operative period in all the three groups under study, intensity of pain was assessed using VAS scoring system. visual analogue scale which is a 10 cm long horizontal line with no pain at one end and worst imaginable pain at other end. The distance from 'no pain' to the patient's mark numerically quantitates pain. visual analogue scale which is a 10 cm long horizontal line with no pain at one end and worst imaginable pain at other end. The distance from 'no pain' to the patient's mark numerically quantitates pain. VAS score of zero means no pain and score of 9&10 corresponds to severe degree of pain. VAS score of 5&6 indicates moderate degree of pain.VAS > 5 cm in considered as moderate pain and. It is a self assessment method for pain by patient himself when the numerical score is more than 5 patient has moderate pain and rescue analgesic in the

form of inj. Morphine 0.05mgm/kgwt I/V incremental doses until patient is relieved of the pain in all the three groups as suggested by VAS score. Total dose of rescue analgesic needed also recorded in all the three groups. Time at which the rescue analgesic administered also noted, in all the three groups.

Duration of analgesia extends from the time of placement of transdermal patch or suppository, to the time at which patient has moderate degree of pain occurs and rescue analgesic was administered. It was measured in hours.

All the patients in 3 groups were observed for occurrence of nausea, shivering, vomiting, excessive bleeding, itching etc.

All data collected were entered in to a master chart and statistical analysis was done in R statistical software. Descriptive statistics are reported as mean and standard deviation for continuous data and median and interquartile range for non normal data. Categorical data were summarized as percentages and in absolute frequencies. Comparison of outcome between various groups were done with kruskal wallis test and post hoc tests were conducted. A p value less than 0.05 was taken as statistically significant.

Results

A total of 150 patients were recruited in to this randomized controlled trial with 50 patients in each group. The median weight of the patient in the study was 61.0 [60.0;63.0] kg and height 159 [158;162] cm. The Medan duration of analgesic effect in all groups together was 5.00 [0.75;14.5] hours. There were 77(51.3%) in the 18-24 age group and 73 (48.7%) patients in the 25-30 age groups. Baseline characteristics of the patients were comparable across the three groups (table1).

Table1: Baseline comparison across the groups.

	[All] N=150	Control N=50	Patch N=50	Suppository N=50	P.Overall
Weight	61.0 [60.0;63.0]	61.5 [59.5;63.0]	61.0 [59.2;61.0]	62.0 [61.0;63.0]	0.125
Height	159 [158;162]	159 [158;165]	159 [158;162]	160 [158;162]	0.825
Age:					0.602
18-24	77 (51.3%)	28 (56.0%)	26 (52.0%)	23 (46.0%)	
25-30	73 (48.7%)	22 (44.0%)	24 (48.0%)	27 (54.0%)	

There is a statistically significant difference between the duration of analgesia between the three groups (P value <0.001) (Table 2 and Figure1).

Table2: Duration of effects across the three groups.

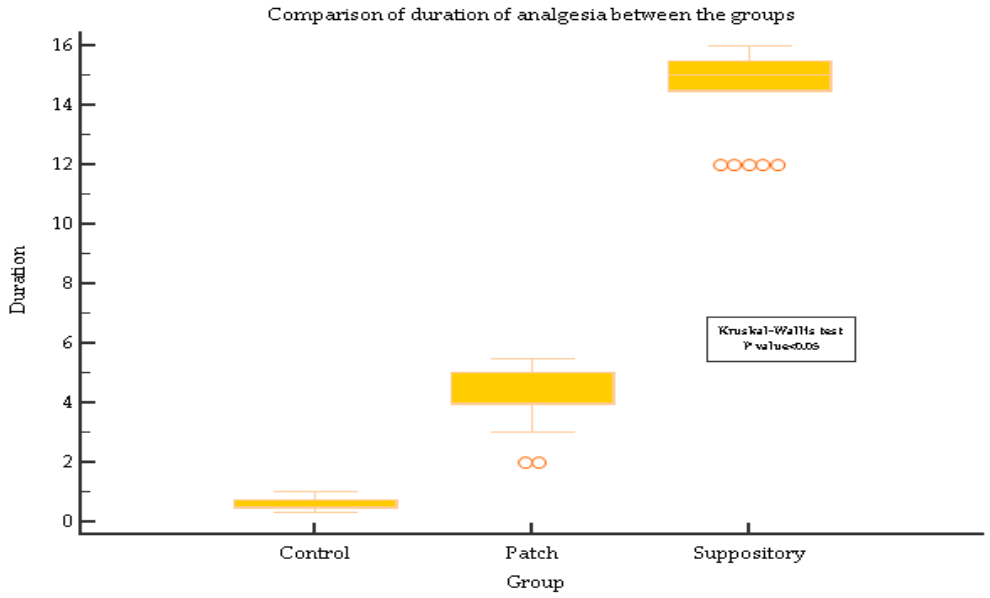
	[All] N=150	Control N=50	Patch N=50	Suppository N=50	P.Overall
Duration	5.00 [0.75;14.5]	0.75 [0.50;0.75]	5.00 [4.00;5.00]	15.0 [14.5;15.5]	<0.001

Post hoc analysis showed statistically significant different changes between patch and control and suppository. For suppository, there is significant difference between control and with patch (Table 3)

Table 3: Post-hoc analysis.

Factor	n	Average Rank	Different (P<0.05) from factor nr
(1) CONTROL	50	25.50	(2)(3)
(2) PATCH	50	75.50	(1)(3)
(3) SUPPOSITORY	50	125.50	(1)(2)

Figure 1: Comparison of outcome across the groups.



Discussion

Pain can be classified according to pathophysiology (e.g. Nociceptice or neuropathic pain), etiology (postoperative or cancer pain) or the affected area (headache or low backache). Acute pain can be defined as pain that is caused by noxious stimulation due to injury, disease process or abnormal function of muscle or viscera. It is nearly always nociceptive. Moderate to severe pain regardless of site can affect nearly every organ function and may adversely influence postoperative morbidity and mortality.

In this study, we studied the duration of analgesia provided by control group, suppository group and patch group. The results of this study showed that there is a statistically significant difference in the duration of analgesia among the three groups and that is more with suppository group compared to patch and control in the post hoc analysis.

Evaluation of preoperative rectal Diclofenac for perioperative analgesia in ENT surgeries was studied by Dr. Hemant Bhagat[7], Dr. Kiran Malhotra, Dr. Chibra Tyag et al GVSM Medical College Kanpur with an aim to reduce the intraoperative use of opioids. Fifty patients of different age groups of both sexes undergoing surgery under GA were randomly selected for double blind study. Diclofenac group received diclofenac suppository 2mg 1 kg body wt. and the control group received placebo. The study concluded that the use of preoperative rectal diclofenac has substantial effect as an adjuant intraoperative analgesic. It considerably delays the onset of post operative pain and is adequate as sole analgesic for early postoperative period.

The route of administration of diclofenac sodium is important in the duration and sustainability of analgesia. Administration through suppository has Major attraction compared to the normal route. The drug is directly absorbed into the system rapidly due to the peculiarity of the vascular supply and anastomosis in the region. Administration per rectally can be done by the person himself. One of the tissues with patch may be reduced absorption from the skin. Moreover the presence of hair may impede with correct application and easy removal. Our study has shown that compared to control and patch, suppository gives prolonged analgesia

In a study by Dr. Nosele Louise8, Siew Home Limi conducted of the General hospital Singapore where two study groups were formed One group received diclofenac suppository and other group didn't receive diclofenac suppository. Both group were compared postoperative for the volume of local anaesthetic (LA) required via patient controlled epidural analgesia (PCEA). Suppository group required less LA value in

PCEA compared to that without suppository. Our study consists of 3 groups of patients but the above mentioned study by Dr. Noelle Louise included only two groups, which was statistically advantageous compared to my study. Fentanyl added in dose of 4mg /ml with local anaesthetic can interfere with the maternal alertness and feeding of newborn baby in comparison to the group 1 and group2 patients in our study.

In another study Lennart Funk9 et al of Bridge Water Hospital, UK diclofenac transdermal patches for shoulders pain was studied. The patients were randomized into two groups. Group I received diclofenac tablet in addition to paracetamol and codeine.

According to Galer BS[10] Perander J. et al, topical diclofenac patch relieves minor sports injury pain.

The antibacterial action of diclofenac is by virtue of inhibition of DNA synthesis, proved by Dutta NK, Annadurai S[11] et al.

Galezzi M[12] et al proved the efficacy and tolerability of the NSAID drug, DHEP plaster in extra articular rheumatological disease.

Schmit A[13], Bjorkmans. S, Akerson. J studied preoperative diclofenac VS paracetamol for tonsillectomy pain and blood loss and found that increased blood loss, increased duration of analgesia and increased potency was with diclofenac sodium.

Diclofenac has bioavailability 100% with more than 99% protein binding. It is a phenyl acetic acid derivative which is a relatively non selective cox inhibitor. It is metabolized in liver by a cyto P450 co-enzyme of CYP 2C sub family to 4 OH diclofenac, the principal metabolite and other hydroxylated forms after glucuronidation and sulfation. Metabolites are excreted in urine (65%) and bile (35%).

Adverse reaction to diclofenac occurs in 20% patients and 2% discontinue therapy.

In our study, we had a stringent exclusion criteria. This potentially affects the generalizability of our findings. In addition the lack of allocation concealment and masking would have introduced bias in the study. The limitation of the study to a narrow population is another limitation of our study. The limitations in our study need to be considered in the design of related future studies.

Our study suggests that administration of diclofenac per rectally is better compared to transdermal and control groups.

References

1. Thomas G Kantor, MD1986 Vol80 Issue4 Supplement2 Page 64-69
2. Rashid M, Jaruidi H M, Saudi MedJ 2000 Feb; 21(2): 145-149
3. J. Anaesthesiol Clin Pharmacol 2014 April-June; 30(2): 243-247.
4. International J. of Health Care and Biomedical Research Volume: 1 Issue 2. January 2013, P: 32-37.
5. Hendrickon R G, McKeown N J, Is maternal opioid use hazardous to breast fed infants clin toxicol? (Phila) 2012: 50(1); 1-14
6. Spiget O, Hagg S. Analgesic and breastfeeding safety considerations. Paediatr Drugs 2000; 2(3): 223-238
7. Bhagat H, Kiran M, Chitra T, Navneeta G. "Evaluation of y/preoperative rectal Diclofenac for perioperative Analgesia in ENT Surgery". IJA 2003; 147 (6): 463-66.
8. Noelle Louise Siew Hua Lim, Changi General Hospital, Singapore. 'Single dose: Diclofenac suppository reduces post caesarian PCEA requirements.
9. Funk L Umaar R, Molajo A. Diclofenac patches for postoperative shoulder pain. Int J. Shoulder Surg. 2008; 2: 47-48.
10. Galer BS, Rowbotham M, Perander J, Devers A, Friedman E. Topical Diclofenac patch relieves minor sports injury pain: Results of a multicenter controlled clinical trial. J. Pain Symp Manage 2000; 19: 287-94.
11. Dutta NK, Annadurai S, Mazuamdar K, Dastidar SG, Kristiansen JE, Molnar J, Martins M, Amarlal L (2007). Potential management of resistant microbial infec-tions with a novel non-antibiotic: the anti-

inflammatory drug Diclofenac Sodium Int J. Antimicrob agents 30(3): 242-249.

12. Galeazzi M, Marcolongo R. A placebo controlled study of the efficacy and tolerability of a nonsteroidal anti-inflammatory drug DHEP plaster, in inflammatory pain and extra-articular rhematology diseases Drugs Exp Clin Res 1993; 19:107-115.
13. Schmidt A, Bjorkman S, Akeson J. Preoperative diclofenac versus ~ I paracetamol for tonsillectomy induced postoperative pain and blood loss. Acta Anaesthesiologica 2001; 45:48.52; Jenoure P, Segesser B, Luhti U, Gremion G. A trial with J Diclofenac HEP plaster as topical treatment in minor sports injuries. Drug Exp Clin Res 1993; 19:125-31.