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Effectiveness of Diclofenac Suppository in Post LSCS Patients for Immediate Post Operative Analgesia after Lumbar Subarachnoid Blockade

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Abstract
Background: *Pre emptive analgesia following or before lumbar subarachnoid blockade can be instituted through several means. But use of diclofenac suppository is one of the easiest ways to administer in the parturient by the obstetrician or paramedical staff or assisting staff nurse along with the vaginal examination done postoperatively in this category of surgery.*
Materials and Methods: *We have studied a total of 100 patients, 50 patients in each group – Suppository group [Group I], Control group [Group II]. Quality of postoperative analgesia provided effects were studied.*
Results: *Group I [Suppository Group] was more efficient in postoperative analgesia of duration of 14.8 hours with a standard deviation of 1.1 while the control group showed a mean duration of 7 hrs. The mean dose of rescue analgesic was lower for group(I) in comparison to the group(II). Thereby substantiating qualitative analgesia provided by the diclofenac suppository. Mean VAS score was lower for [Group I] patients in comparison to the control [Group II] patients.*
Conclusion: *Diclofenac rectal suppository, being a cost effective and better technique in comparison to the parenteral formulations and opioids.*
Keywords: *Diclofenac Suppository, VAS – Visual Analogue Scale, Pre Emptive Analgesia, Standard Deviation.*

Introduction

In man's major struggle against physical pain the greatest procurement is discovery of Analgesics and Anaesthesia. Control of the post operative pain is very important in early post operative recovery leading to early ambulation and preventing complications like deep venous thrombosis, pulmonary embolism and delayed wood healing.

Diclofenac sodium is an all rounder NSAID, analgesic which can be used orally as tablet, as intramuscular injections, intravenous injections, transdermal patch, ointment and suppository. Intramuscular injections are very painful, oral preparations are associated with gastritis, peptic ulceration and hepatic damage. But suppository and transdermal patch are relatively free from side

effects. It is one of the most potent NSAID analgesic.

The major adverse effects of pain are increased heart rate, increased blood pressure, decreased cerebral blood flow, increased intracranial pressure, hypoventilation, sputum retention and pulmonary atelectasis.

It thereby insists for the importance of an ideal or towards ideal analgesic agent for abating pos operative pain by providing a preemptive analgesic technique whereby analgesic is administered far before the occurrence of pain.

In our study intraoperative analgesia is provided by lumbar subarachnoid blockade. Post operative analgesic can be administered through the diclofenac suppository easily. As the surgeon routinely do P/V examination to detect post partum hemorrhage. Along with this the rectal suppository can be inserted without disturbing the patient. The maternal breast milk[1] levels of diclofenac sodium is insignificant. Diclofenac was detected in in low concentration (<100 nanograms per ml breast milk) which was in significant . 99.7% of diclofenac is bound to plasma proteins mainly albumin (99.4%). Apparent volume of distribution is 0.12-0.17L/Kg wt. Bio transformation diclofenac is by glucuronidation of intact molecule, but mainly by single and multiple hydroxylation and methoxylation reactions resulting in several phenolic metabolites, most of which are glucuronide conjugates. Two of these metabolites are biologically active 60% of administered dose is excreted in urine as glucuronide conjugates <10% excreted as unchanged substance. The rest of metabolites are excreted in bile through faeces. Kounis syndrome with unknown drug is new cardiac adverse effect. NSAIDS are not readily distributed in mother milk because being weak acids are readily in PH range of breast milk according to Lim[2] etal. The advent of opioids for post operative analgesia is associated with respiratory depression in mother and foetus leading to impaired maternal feeding of baby, maternal bonding with baby, maternal constipation and affecting the early ambulation of the mother. Hence a safe alternative to the opioids is the NSAID without these effects. The main target of the treatment with NSAID is the provision of pain relief that is effective, well tolerated and which improves the parameters of outcome including discharge street fitness and return to work. The risk of postpartum haemorrhage in relation to NSAID was reported in many texts considering diclofenac increases bleeding time and platelet aggregation. However diclofenac induced post operative bleeding is a rare phenomenon in clinical practice according to Sia etal[2], 1997; Lim[2] etal 2001, Ambrose[3] 2001; Roseriarius etal[4], 1985;

Duration and therapeutic effect of diclofenac is 3-4 times longer than its t1/2in plasma and release of pain mediating prostaglandin are inhibited and remain so despite decreased plasma concentration but analgesic effect of opioids like pethidine last for 4-6 hours and diclofenac has long duration of action lasting 12-24 hours according to Rashid[5] and Jaruidi; 2000, Diclofenac suppositories are available in strength of 12.5 mg., 25 mg., 50 mg. and 100 mg. Maximum daily dose of suppositories is 150 mg. Each strip contains 5 numbers of suppositories. Suppositories have more rapid onset but slower rate of absorption than enteric coated diclofenac. Many previous studies have shown that pain after LSCS has two components, visceral and somatic respectively due to uterine contractions and surgical wound. Such complex pain managed multimodally managed or combated by a combination of opioids combined with NSAIDS as explained by Olofsson[6] etal 2000; Lim[2] etal.

Materials and Methods

This comparative study 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 100 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 between 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 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 include those patients having Acid peptic disease, Gastiritis, 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. The study includes two groups of patients Group I suppository group and Group II- 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 0.05mgm/kg wt plus or-0.01mgm/kg wt 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 for2 groups of patient's 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 was noted. Instruction to avoid other analgesic drugs in the form of opioids or NSAIDS were given.

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

In the post operative period in the two 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/kg wt I/V incremental doses until patient is relieved of the pain in the two groups as suggested by VAS score. Total dose of rescue analgesic needed also recorded in two groups of .Time at which the rescue analgesic administered also noted, in all the three groups

Duration of analgesia extends from the time of placement of 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 two 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 inter quartile range for non normal data. Categorical data were summarized as percentages and in absolute frequencies. Comparison of outcome between two groups were done with post hoc tests were conducted. A p value less than 0.05 was taken as statistically significant.

Results

A total of 100 patients were recruited in to this study 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. 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 groups (table1).

Table 1: Baseline comparison across the groups.

	Control N=50	Suppository N=50	p.overall
Weight	61.5 [59.5;63.0]	62.0 [61.0;63.0]	0.125
Height	159 [158;165]	160 [158;162]	0.825
Age:			0.602
18-24	28 (56.0%)	23 (46.0%)	
25-30	22 (44.0%)	27 (54.0%)	

There is a statistically significant difference between the duration of analgesia between the two groups (P value <0.001)(table 2 and figure1).

Table 2: Duration of effects across the two groups.

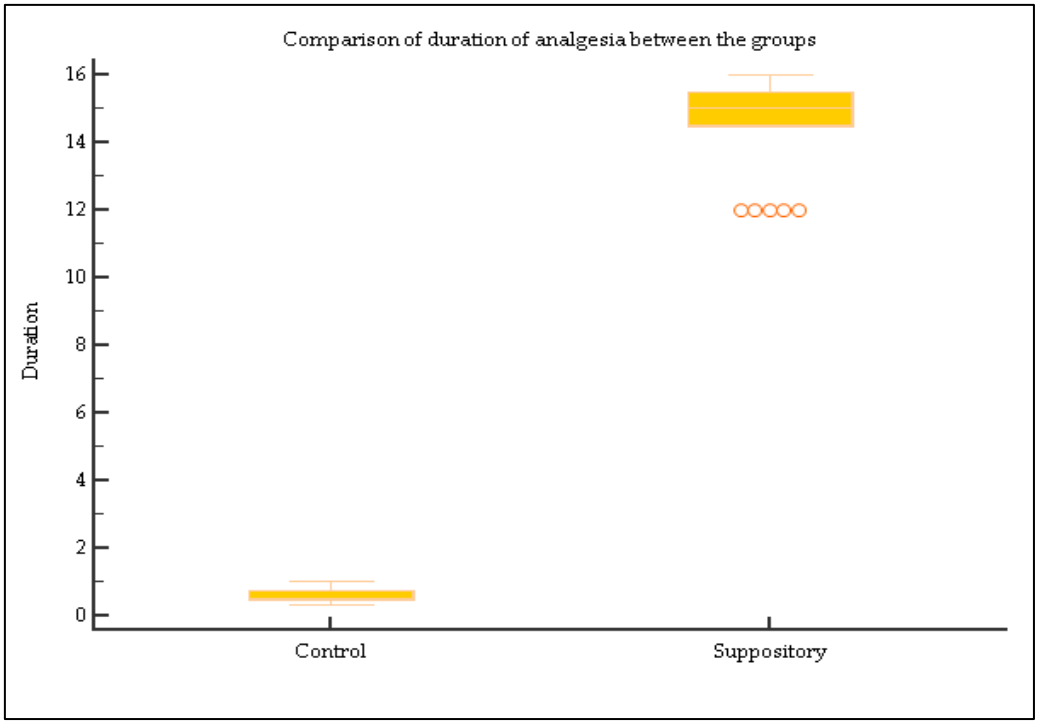
	Control N=50	Suppository N=50	p.overall
Duration	0.75 [0.50;0.75]	15.0 [14.5;15.5]	<0.001

Post hoc analysis showed statistically significant different changes between control and suppository. For suppository, there is significant difference with control

Table 3: Post-hoc analysis

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

Figure 1: Comparison of outcome across the groups.



Discussion

Anesthetist deals with post operative pain and post trauma pain. Pain is associated with increased BP, regional decreases in blood flow, alteration in immune response, increased blood sugar level, negative nitrogen balance and other metabolic changes. Stress response may play a role in post operative morbidity and mortality.

In case of post LSCS patients for post operative analgesia the disadvantages of opioids is that it is secreted in breast milk, produce sedation, nausea vomiting, constipation, respiratory depression, hypoventilation and addition liability in the mother. Significant amount reaching the new born baby leading to reduce the activity, improper feeding, hypoglycemia and respiratory depression in new born.

Moreover, sedative action in the mother post operatively leads to inadequate breast feeding, decreased the alertness and inadequate burping by mother.

NSAID drug on the other hand provide excellent preemptive analgesia, as it is administered before wearing of spinal anaesthesia immediately after surgery. Diclofenac sodium has got anti-nausea effect in addition to its analgesic and anti inflammatory effect. In a cross sectional study conducted at Shaizh[7] Zayed Women Hospital

Larkane, of Pakistan and comprised patients who were admitted to labor room for normal vaginal delivery - A single dose of rectal diclofenac suppository 100mgm was administered to patients post delivery or second stage emergency LSCS. Post procedural pain occurred after12-24hrs. SPSS 16 was used for data analysis use of NSAID suppository was found to be easy and effective modality for combating post operative pain NSAID efficacy of diclofenac rectal suppositories in patients with laparoscopic cholecystectomy patients were studied by Mohammedoreza Arab[8], Hossein Saeedi Motahhar etal, Iran University of Medical Sciences, Tehran at Firozgar Hospital. Diclofenac suppository provided simple pain relief in laparoscopic cholecystectomy. Raghavan etal[9] found that combination of combination of diclofenac suppository and lidocaine perineural blockade provide pain relief during and after a prostatic biopsy. Haq[10] etal found that placement of diclofenac rectal suppository one hour prior to prostatic biopsy alleviated the discomfort associated with the procedure

Effect of preoperative rectal diclofenac suppository on postoperative analgesia requirement in cleft palate repair surgeries. A randomized clinical trial by E.S. Adarsh[11], Rajesh Mane and S.M. Sagar etal. It is observed that preoperative rectal diclofenac provided effective analgesia in immediate post operative period as concluded by reduced the pain scores and reduced opioid requirement.

Fayaz M.K[12]., Able R.J., Pugh SC etal opioid sparing effects of diclofenac and paracetamol had improved outcomes after cardiothoracic surgery, Journal of cardiothoracic vascular Anaesthesia 2004; 18:742-7 (pubmed). The use of rectal diclofenac for post caesarian analgesia Saudi Medical Journal[5] 2000; 21:145-9 (pubmed). Post operative pain and shivering are two post operative challenging components. The evaluation of rectal diclofenac considerably delays the onset of post operative pain and adequate analgesia for early post operative period.

There is reluctance among surgeons to use diclofenac due to its hypothetical risk of bleeding and reopening. But it is an overestimated investigation by a researcher. Diclofenac prevented post operative shivering and pain. It is an accessible and low cost compared to opioids. Preoperative administration of single dose of rectal diclofenac as sole analgesic for early post operative period are done by Ibrahim Alijanpour[13], Ali Jabbri etal, Department of Anaesthesiology and Intensive Care, Babool University of Medical Science, Iran.

Dr. Kiran Malhotra[14] and others GVSM Medical College, Kanpur in their study 'Evaluation of Preoperative Rectal Diclofenac for Perioperative Analgesia in ENT Surgery' proved that diclofenac suppository provided mean duration of postoperative analgesia more than 14 hours. Accessibility to rectal route was good. It considerably delays the onset of postoperative pain and is adequate as sole analgesic for early postoperative period.

It is study where the control patients had injection midazolam postoperatively and the pain score at the time of moderate pain and time of administration of rescue analgesic end point being appreciation of moderate pain grades in the visual analogue scale (>3). End point followed by the rescue analgesic in the form of injection morphine 0.05mgm/kg wt ± 0.01mgm/kg wt increments until stoppage of pain. VAS score, dose of rescue analgesic and time of administration of rescue analgesic and duration between placement of suppository and administration of rescue analgesic noted.

Comparison of duration of analgesia for suppository group and control group showed it to be 14.8 hours and 0.7 hours respectively. Standard deviations are 1.1 and 0.2 respectively for suppository group and control group. Distribution of sample patients according to weight showed P value >0.01. Difference in mean weight was not statistically significant. There was no statistical difference in mean height in the 2 groups, since P value is 0.166. P value for mean duration of

analgesia is 0.00, when it is less than 0.01 it is significant. Thereby showing that the quality of analgesia, duration of analgesia where significant for diclofenac suppository compared to the control group.

Effective preemptive analgesia is being contributed by the administration of NSAIDS. Intravenous opioids in 8 trails compared pre incisional with post incisional administration of various opioids. It was concluded that no overall improvement in postoperative pain control was observed. After preemptive administration of systemic opioids.

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