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Comparison of Efficacy between Intramuscular Diclofenac and Transdermal Diclofenac Patch for Postoperative Analgesia in Patients Undergoing Lower Limb Surgery Under Sub Arachnoid Block in Jawaharlal Nehru Medical College, Wardha, India

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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ABSTRACT

Background: To compare the analgesic efficacy of transdermal Diclofenac patch (100 mg) with intramuscular Diclofenac sodium (75 mg) for postoperative analgesia and to know the side effects of transdermal Diclofenac patch.
Methods: 60 ASA I and II patients, of either sex, aged 15 and above, scheduled for lower limb surgery under subarachnoid block were included in the study. All were allocated randomly by computer generated randomization sheet into two groups of 30 each. Subarachnoid block was administered using 0.5% hyperbaric Bupivacaine. Participants in the study group were applied with a transdermal Diclofenac patch containing 100 mg of Diclofenac diethylamine at the beginning of the surgery. In the control group 75 mg of Diclofenac sodium was given intramuscularly half an hour before the end of surgery. Pain was assessed postoperatively using visual analogue scale. Injection Tramadol 2 mg was administered intramuscularly as rescue analgesia. The data obtained was analyzed using chi - square test and unpaired student's 't'test.

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Results: The mean time at which rescue analgesia was administered in the control group was 7 hours 28 min and in study group was 20 hours 6min.The time at which rescue analgesics were required in the study group was significantly prolonged ($p<0.0001$). The amount of Inj. Tramadol required as rescue analgesia in the control group was 189.33 mg. ± 16.38 mg. and in study group it was 97 mg. ± 7.24 mg and this was found to be statistically significant ($p<0.0001$). When the side effects were compared they were not significant.

Conclusions: Based on the results obtained we conclude that, the intraoperative application of 100 mg transdermal Diclofenac diethylamine patch significantly prolongs the time at which patient requires rescue analgesia without any significant side effects. Rescue analgesic requirement was also significantly lower in the study group.

Keywords: Postoperative Analgesia; Diclofenac; Transdermal Patch.

1. INTRODUCTION

Pain has been a major concern of mankind since the very beginning and it has been the object of ubiquitous efforts to understand and treat it.

Today the proper management of pain remains one of the most important pressing issues of society in general and the medical community in particular [1-6]. Because pain impairs one's ability to carry out a productive life, pain in general is a serious economic problem as well as a major health problem.

The postoperative period is an integral part of the surgical experience of a patient. If surgery is an injury, then allowing the patient to suffer postoperative pain is like adding insult to injury. Efficient management of postoperative pain is as important as management of intra operative pain however, postoperative pain is not simple due to tissue injury alone but is the final result of various neurophysiological interactions. This makes efficient postoperative pain management much more difficult and an ideal pain management programme is still elusive [7].

Peripheral tissue injury provokes two kinds of modification in the responsiveness of the nervous system. Peripheral sensitization and central sensitization. In peripheral sensitization, there is a reduction in the threshold of nociceptive afferent peripheral terminals. In central sensitization, there occurs an, activity dependant increase in the excitability of spinal neurons. This results in overall hypersensitivity state in the postoperative period. Prevention and establishment of this hypersensitivity could lead to reduced postoperative pain. This formed the basis of preemptive analgesia [7,8].

Nonsteroidal antiinflammatory drugs (NSAIDs) have long been used for preemptive, intraoperative and postoperative analgesia. NSAIDs exert anti inflammatory and analgesic effects through the inhibition of prostaglandin synthesis, by blocking the activity of cyclooxgenase (COX). In the early 1990's COX was discovered to have two isoforms, COX – 1 andCOX–2. Prostaglandins influenced by COX - 1 maintain the integrity of the gastric mucosa. Prostaglandins influenced by COX - 2 mediate inflammatory process. Diclofenac sodium is a commonly used non selective NSAID and is available in various forms for the treatment of pain [9,10]. This includes parental preparation oral tablets, ointments, rectal suppositories and transdermal patch. The Diclofenac transdermal patch is a newly introduced delivery system for Diclofenac and is available in India since 2005. Diclofenac transdermal patch has not been evaluated for the management of postoperative pain in our hospital.

Hence this clinical study was undertaken to evaluate the analgesic efficacy of Diclofenac transdermal patch in patients undergoing lower limb surgery under subarachnoid block during postoperative period.

1.1 Objectives

The objective of the present study is –

a. The Objective of this study was to assess the analgesic efficacy of a transdermal Diclofenac patch (100 mg) vs injectable Diclofenac sodium (75 mg) for postoperative analgesia in patients undergoing lower limb operations under subarachnoid block.

This was a prospective comparative study. The study was conducted on 60 patients aged 15 and older, both sexes, who were scheduled for elective lower limb surgery under subarachnoid block.

1.2 Sample Size Calculation

With a type I error of 0.05 and a statistical power of 90 %, a total sample size of 60 was calculated using the principal variable, visual analogue scale (VAS) ratings for postoperative pain, and a difference of 2 cms as clinically significant (estimated mean standard deviation 1.5 to 2.5cms).

1.3 Inclusion Criteria

a. Participants in the age group 15 and above scheduled for elective surgery of the lower limb under sub-arachnoid block.
b. American society of anaesthesiologist grades I and II.

1.4 Exclusion Criteria

a. Evidence of cardiac, pulmonary, renal, or hepatic pathology, or a history of such pathology.
b. Pregnancy or lactation
c. Clinical evidence of active peptic ulceration within the last six months
d. Aspirin or other NSAIDs have caused bronchial asthma, urticaria, or any other allergic responses in the past.
e. Patients with haemorrhagic diathesis.

1.5 Randomization

A computer - generated randomization table was used to divide the 60 study participants into two groups of 30 each.

1.6 Study Group

Those receiving transdermal Diclofenac patch 100 mg. Control group: Those receiving intramuscular Diclofenac sodium 75 mg.

2. METHODOLOGY

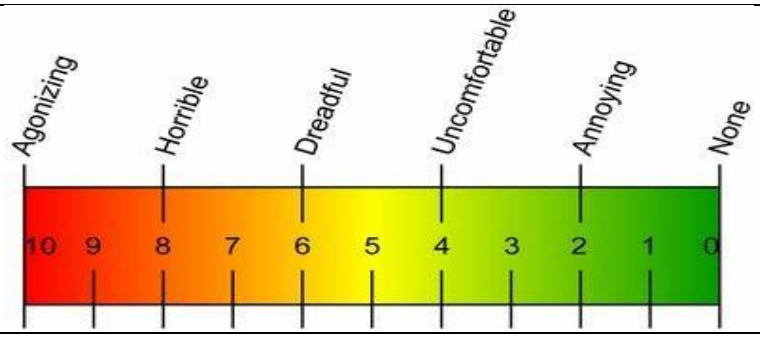
By obtaining a history and doing a clinical examination, a thorough pre - anaesthetic evaluation was completed.

Investigations like complete blood counts blood urea, and serum creatinine were obtained. Random blood sugar, electrocardiogram, chest x - ray were obtained whenever required.

On the day of surgery, the patient was secured with an 18gauge intravenous line and transported to the operating room, where monitors such as a pulse oximeter, electrocardiograph, and blood pressure monitor were attached. All patients received a subarachnoid block in the lateral position with 0.5 percent hyperbaric Bupivacaine and a 23 or 25 gauge Quincke's needle to obtain a sensory level block of T6 - T8.During the surgery, neither group received any intravenous analgesics or sedatives. After subarachnoid block, participants in the study group were given a transdermal Diclofenac patch containing 100 mg of Diclofenac diethylamine at the start of surgery. Half an hour before surgery, 75 mg of Diclofenac sodium was given intramuscularly to the control group. A visual analogue scale was used to assess pain at two, six, twelve, and twenty - four hours after surgery (VAS). If the VAS was greater than or equal to five at any point during the research, injectable Tramadol 2 mg kg^{-1} was given intramuscularly as a rescue analgesic. The time when rescue analgesia was administered was recorded. Amount of rescue analgesia administered to each group and side effects with the use of study drug were also noted.

Statistical Analysis

Results were analysed statistically using Chi-square test and unpaired Student's "t" test



Visual analogue scale

Fig. 1. Visual analogue score [30]

3. RESULTS

The present study was undertaken in 60 ASA grade I and II patients, of either sex, aged 15 and above scheduled for elective lower limb surgery.

The demographic statistics in terms of age and gender were comparable between the two groups.
ASA grading was also comparable between two groups.

The control group's average surgery time was 1 hr. 58 min. 24.6 min., while the study group's was 2 hr. 10 min. 27 min. There was no significant variation in the length of operation across groups (p value = 0.2295), indicating that there was no significant difference between them. The level of blockade attained by the two groups was comparable.

If the patient had a score of five or higher, rescue analgesia in the form of Injection Tramadol 2 mg kg - 1 was administered. Pain was measured using VAS at two, six, twelve, and twenty - four hours.

At two hours after surgery, 29 of the 30 patients in the control group had no discomfort and one patient had a VAS of two. One patient sought rescue analgesics six hours after surgery, whereas four patients had a VAS of zero, thirteen patients had a VAS of two, and nine patients had a VAS of three. Between the hours of six and twelve, all of the remaining patients were given rescue analgesia. In the control group, the average time to provide rescue analgesia was 7 hours 28 minutes, with a standard deviation of 1 hour 4 minutes. This finding indicates that the analgesia induced by intramuscular Diclofenac is brief, necessitating many injections. The VAS values at 12 and 24 hours were meaningless because the patient had already received rescue analgesia.

In the study group, at two and six hours postoperatively all the 30 patients had no pain, that is, a VAS of zero. At 12 hour postoperatively 14 patients still had no pain, 8 had a VAS of two and seven had a VAS of three. No patient received rescue analgesics till 12 hours postoperatively. The mean time postoperatively at which rescue analgesic were given was 20 hours 6 min. with a standard deviation of 2 hours. At 24 hours postoperatively one patient had a VAS of two and one more patient had VAS of three.

The above observation showed that the time at which rescue analgesics were required in the study group was significantly prolonged (p value less than 0.0001).

Table 1. Duration of Surgery (p value= 0.2295)

Groups	Mean	SD (Min.)
Control group	1 hr. 58 min	24.6
Study Group	2 hr. 10 min	27.0

Table 2. Pain score control group

Score	Time (Hours)			
	2 hours	6 hours	12 hours	24 hours
0	29	4	-	-
1	00	1	-	-
2	01	13	-	-
3	00	9	-	-
4	00	2	-	-
5	00	1	-	-

Table 3. Pain score study group

Score	Time (Hours)			
	2 hours	6 hours	12 hours	24 hours
0	30	30	14	00
1	00	00	00	00
2	00	00	08	01
3	00	00	07	01
4	00	00	01	00
5	00	00	00	00

Table 4. VAS at 2 hours

Groups	VAS		
	0	1	2
Control	29	0	1
Study	30	0	0

At 2 hour postoperatively the VAS was comparable between the groups and was not statistically significant (p = 1.00)

Table 5. VAS at 6 Hours

Groups	VAS					
	0	1	2	3	4	5
Control group	04	01	13	09	02	01
Study Group	30	00	00	00	00	00

At 6 hours postoperatively when VAS was compared between the two groups the study group had significantly lower scores

Table 6. VAS at 12 Hours

Groups	VAS					
	0	1	2	3	4	5
Control group	-	-	-	-	-	-
Study Group	14	00	08	07	01	00

At 12 hours postoperatively 14 patients in the study group had a VAS of zero; eight patients had VAS score of 2
Chi square test 11.333
P value=0.0101 which is significant

Table 7. VAS at 24 Hours

Groups	VAS					
	0	1	2	3	4	5
Control group	-	-	-	-	-	-
Study Group	00	00	01	01	00	00

At 24hour postoperatively one patient had a VAS of two and another patient had VAS of three. At 24 hours postoperatively there was no difference between the groups in respect to pain scores
Chi square test 0.5
P value = 0.4795 which is not significant

Table 8. Time at which rescue analgesia was given and the amount

Groups	Rescue analgesia given at	Tramadol as rescue analgesia(mg)
Control group	7 hours 28 min ± 1 hour4 min.	189.33 ± 16.38
Study group	20 hours 6 min ± 2 hours	97 ± 7.24

The amount Inj. Tramadol required as rescue analgesia was noted in each group. In the control group it was 189.33 mg. ± 16.38 mg. and in study group it was 97 mg. ± 7.24 mg. when it was analyzed using unpaired t test the difference in rescue analgesia required was found to be highly significant.

Three individuals experienced abdominal pain (gastritis) and two patients experienced pain at the injection site after taking intramuscular Diclofenac. In the trial group, two individuals had erythema at the patch application site. The GI side effects of IM and oral Diclofenac can be reduced with a transdermal Diclofenac patch. When the side effects were examined between the groups using the test of proportions, it was not significant.

4. DISCUSSION

Over the last decade, our understanding of the mechanisms that cause acute pain has progressed to the point that rational therapy, rather than empirically derived therapy, can be utilized to block the mechanisms that cause

clinical pain. This principle is more applicable to surgical pain management than to any other case.

Pain during the postoperative period is unrelated to the surgical harm. Postoperative pain is always more intense for any surgical injury due to peripheral and central hypersensitivity or the windup phenomenon. In the proper management of postoperative pain, any therapeutic regimen that prevents or modulates this sensitization should be beneficial. One such intervention is pre - emptive analgesia. The essential premise is that therapeutic intervention is undertaken before, rather than after, pain occurs.

Despite the fact that opioids are highly effective analgesics with no analgesic effect ceiling, their tolerability profile might occasionally restrict their efficacy. For the treatment of postoperative pain, multimodal analgesia regimens (a combination of analgesics) are currently advised. Adjunctive treatments such as wound infiltration with local anaesthetics, the use of NSAIDs or corticosteroids, and opioid epidural delivery have all been recommended to relieve postoperative pain. NSAIDs, in particular, have become increasingly popular in the management of postoperative pain.

NSAIDs are effective analgesics with no clinically significant differences in efficacy between different medications. The gastrointestinal system is one of the most common side effects.

Bleeding, renal failure, and platelet failure are all symptoms of platelet dysfunction. Because selective COX - 2 inhibitors are linked to an increased number of thrombotic cardiovascular events, which counteracts the increased number of gastrointestinal side effects seen with NSAIDs, the benefits of COX - 2 inhibitors in treating acute nonspecific pain are questionable [11,1].

Patients undergoing subarachnoid block for lower limb surgery, we compared the analgesic efficacy of transdermal Diclofenac patch vs injectable Diclofenac sodium for postoperative analgesia.

It would be unethical and extremely distressing to the patients to withhold postoperative analgesic medication. Therefore for the control group we administered 75 mg of Diclofenac sodium intramuscularly.

In our study the demographic data were comparable for age and sex in both the groups (Table 1, 2,3).

The control group's average surgery time (Table 4) was 1 hr. 58 min. 24.6 min., whereas the study group's average surgery time was 2 hr. 10 min. 27 min. The length of surgery affects the need for postoperative analgesics because prolonged tissue handling promotes the generation of inflammatory chemicals and oedema, which raises the need for analgesics. The average length of operation in both groups was comparable in our study (p value 0.229).

The duration of postoperative pain varies greatly between people and is determined by a variety of interrelated factors. It is consequently impossible to identify elements that may influence the length of postoperative discomfort.

Compounded on this difficulty is the fact that pain being a multidimensional sensation is not easy to quantify exactly. The visual analogue scale used in this study to measure the severity of pain has its limitations. It was used however because it had some important advantages in our setting. The patients understood it easily and even illiterate subjects could participate.

Pain was measured using VAS at two, six, twelve, and twenty - four hours after surgery, with a VAS of five indicating the need for further analgesics or rescue analgesics. As a rescue analgesic, we employed Inj. Tramadol 2 mg kg^{-1} in this investigation. At any time during the study period when the patients complained that the pain to be uncomfortable, rescue analgesia was given as above.

At two hours postoperatively, 29 of the 30 patients in the control group had no pain (Table 5), and one patient had a VAS of two. One patient sought rescue analgesics six hours after surgery, whereas four patients had a VAS of zero and thirteen patients had a VAS of two. In the control group, the average time to provide rescue analgesia was 7 hours 28 minutes, with a standard deviation of 7 hours 28 minutes.

In the study group (Table 6), at two and six hours postoperatively all the 30 patients had no pain. But at 12 hours postoperatively 14 patients had no pain, eight had a VAS of two and seven had a VAS of three. No patient received rescue analgesics till 12 hours postoperatively. The mean time postoperatively at which rescue analgesic were given was 20 hours 6min with a standard deviation of 2 hours. At 24 hours postoperatively one patient had a VAS of two and another patient had VAS of three.

The above observation showed that the time at which rescue analgesics were required in the study group was significantly prolonged (p value < 0.0001). Long duration of action seen with transdermal Diclofenac is due to its slow absorption into the circulation.

When we evaluated the VAS between the two groups at two hours, six hours, 12 hours and 24 hours using chi square test, there were no significant difference in the pain scores at two hours but at six hours postoperatively pain scores were significantly less (p value less than 0.0001) (Table 8) in the study group. At 12 hours postoperatively also pain scores were significantly less in the study group (p value of 0.0101). At 24 hours postoperatively there was no difference between the groups with respect to VAS.

The above results show that the transdermal Diclofenac patch is an effective means of providing postoperative analgesia. This is shown by the finding of delayed requirement for rescue analgesia in the study group and a lower VAS during the six and 12 – hour period.

The amount Inj. Tramadol required as rescue analgesia was noted in each group. In the control group it was 189.33 mg. ± 16.38 mg. and in study group it was 97 mg. ± 7.24 mg. The difference in the requirement of rescue analgesia required between the groups was found to be highly significant (p< 0.0001). The lower requirement of Tramadol in the study group is helpful in reducing the opioid associated side effects like nausea, urinary retention and pruritus.

In the search of literature we could find few studies regarding the use of transdermal Diclofenac for postoperative pain relief. We used the mean amount of rescue analgesia required in each group as a criterion to assess the analgesic efficacy of transdermal Diclofenac. In a recent study author have used transdermal Diclofenac patch for postoperative pain relief following laparoscopic chlolecystectomy. They found that 38% patients required no additional analgesic and 48% required one dose parenteral analgesic during 24 hour period.

In another trial, patients having laparoscopic benign gynecologic surgery who received a transdermal Diclofenac patch with a conventional painkiller had a faster rate of discharge than those who received a standard analgesic alone. Hence the results of our study correlate with those of the above listed studies.

Patients who received intramuscular Diclofenac had abdominal pain (gastritis) in three cases and pain at the injection site in two cases, but those who received the transdermal Diclofenac patch had no major side effects except for two cases of redness at the application site. Topical and transdermal formulations are associated with a lower incidence of systemic side effects due to the lower plasma concentration produced by these methods [12].

The transdermal patch's adhesiveness was a concern during the trial, since the patch would lose its adhesiveness and pull off when applied to movable body areas like the arms or gluteal region. As a result, we recommend that the transdermal patch be put to regions of the body that are relatively immobile, such as the front chest wall or the abdomen.

Transdermal formulations maintain a constant plasma concentration while avoiding first - pass metabolism. Diclofenac is a powerful NSAID with anti - inflammatory and anti - edema properties that can aid with postoperative pain relief. However, Diclofenac's negative effects, including as gastric mucosal damage and injection site pain, are common with parenteral formulations [9,11,1]. The use of a transdermal Diclofenac patch can help with these issues.

5. CONCLUSION

Based on the findings of our research, we have come to the following conclusion: the intraoperative application of 100 mg transdermal Diclofenac diethylamine patch significantly prolongs the time at which patient requires rescue analgesia (20 hr. 6 min) compared with 75 mg intramuscular Diclofenac sodium (7 hr.28 min.) without any significant side effects. The amount of Inj. Tramadol required as rescue analgesia was also significantly lower in the study group (97 mg) when compared to the control group (189.33 mg).

Transdermal Diclofenac diethylamine is an effective, non invasive and cost effective way of managing postoperative pain.

CONSENT

As per international standard or university standard, patient’s written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

The study was conducted after receiving institutional ethics committee approval.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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