Original Article

Indian Journal of Anesthesia and Analgesia
Volume 8 Number 6 November-December 2021
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.8621.81

Comparison of Transdermal and Intravenous Diclofenac in Acute Post-operative Pain in Intertrochanteric Fractures

Manisha[1], Abhinav Sinha[2], Sashi Aier[3]

Author's Affiliation: [1]Senior Resident, Department of Anesthesia, [2]Associate Professor, [3]Senior Resident, Department of Orthopedics, Lady Hardinge Medical College, Delhi 110001, India.

Abstract

Introduction: Early mobilization is the primary goal after operation of hip fracture in the elderly wherein the main impediment despite adequate fixation being surgical site pain. Prolonged post-operative recumbency due to pain could lead to various complications like venous thrombosis and cardio-pulmonary compromise. Over enthusiastic use of NSAIDs or opioids on the other hand can have its own set of complications. Hence this study was carried out to evaluate effectivity and safety profile of a commonly used drug, diclofenac via transdermal route in comparison to iv diclofenac.

Methods: 30 patients meeting the study criteria were alternatively allocated to either groups of IV diclofenac and TD diclofenac. All patients were informed how to monitor post-operative pain on a VAS scale at 2,4,6 and 12 hour intervals. Group TD was applied Trans Dermal Diclofenac 100 mg patch, 1 hour prior to surgery and repeated at 12 hourly intervals. Group IV was given intravenous diclofenac 75 mg 1 hour prior to end of surgery and repeated at 12 hourly intervals. First rescue analgesic used was Intra Venous (IV) Paracetamol, if VAS was more than 6, if administered Its dosage and timing of administration was noted. IV tramadol was kept as a standby rescue analgesic.

Results: both the groups were comparable with regards to age and ASA scores. Time to first rescue analgesia, IV Paracetamol, in group TD was 10.23±2.42 hours while that in group IV was 8.15±2.48 hours. It was statistically significant($p<0.05$). None of our patients required IV tramadol. The mean VAS scores at 2, 4, 6 and 12 hours were lower in group TD in comparison to group IV. There were no significant side effects noted.

Conclusion: We can conclude that transdermal diclofenac patch group patients had lower VAS scores at all measured intervals compared to IV diclofenac group and a significantly longer time of rescue analgesic use. Thus, it seems a safe and effective choice for post-operative analgesia in orthopaedic patients.

Keywords: Hip fractures; Intravenous; NSAIDs; Transdermal

Key Message: Pre-emptive application of transdermal diclofenac patch in geriatric intertrochanteric fractures provides good analgesia in post-operative period and can reduce requirements of opioids with minimal side effects.

How to cite this article:

Manisha, Abhinav Sinha, Sashi Aier/Comparison of Transdermal and Intravenous Diclofenac in Acute Post-operative Pain in Intertrochanteric Fractures/Indian J Anesth Analg. 2021;8(6):557-561.

Corresponding Author: Abhinav Sinha, Associate Professor, Department of Orthopedics, Lady Hardinge Medical College, Delhi 110001, India.

E-mail: abhinav.kmc@gmail.com

Introduction

Intertrochanteric fractures are common fractures in the geriatric population and with the increase in ageing population, it is one of the most common indication for undergoing emergency orthopaedicsurgery.[1] Hip fracture related pain is usually reported as severe both pre and post-surgery. While the immediate goal of surgery is to shorten the period of recumbency and provide early mobilization, despite adequate surgical fixation these patients are slow in rehabilitation mainly due to pain.[2,3] This also contributes to several other complications like pulmonary compromise, deep venous thrombosis, bed sores etc. A robust pain management plan is therefore important in these patients these patients for early mobilization and recovery.[4] Geriatric population also suffers from several other co-morbid conditions like diabetes, cardiovascular disease, renal and hepatic impairment. Thus pain therapy needs to take into account the safety profile of used drugs. The drug dosages are also modified accordingly and overuse avoided. Inadequate pain management postoperatively in these patients may cause poor or delayed functional recovery, including delayed return to activities of daily living, increased financial burden, or chronic pain, an efficient analgesic regime fastens healing and mobilization, reduces postoperative complications, shortens length of hospital stays, reduces health care costs, and improves patient satisfaction.[4,5,6] Hence we undertook this study to compare the efficacy of transdermal diclofenac with oral diclofenac in providing analgesia postoperatively for 12 hours.

Transdermal drug delivery systems are preferred over other routes of administration because they pose lower systemic risk especially to liver and gastrointestinal tract. It has the potential to yield more stable drug plasma levels and to bypass major organs involved in first-pass metabolism. Our hypothesis was that transdermal diclofenac patch would significantly reduce analgesic requirement over 12 hour post-operative period and might help us in avoiding systemic analgesics like opioids.

Subjects and Methods

We included 60 patients, 30 in each group, in the age group of 50-80 years with stable Intertrochanteric fractures planned for fixation using DHS. Only ASA 1and 2 patients were included in our study. We excluded the following patients from our study:

- Patients having dementia or other neurologic/ psychiatric problems.
- Patients with any bleeding disorders
- Patients with gastric peptic disease
- Patients having chronic hepatic or renal disease
- Patients having known allergy to diclofenac.
- Patients unwilling to cooperate in the study and monitor VAS.
- Surgical duration of more than three hours.

All patients were subjected to routine pre anesthetic evaluation which included detailed history, general physical examination, systemic examination and routine investigations such as complete blood count, random blood sugar, liver function test, renal function test, electrocardiography (ECG), serum electrolytes, prothrombin test (PT) and international normalized ratio (INR). All patients were briefed about the use of Visual Analog Score (VAS). VAS consists of a 10 cm line marked at one end by a label such as "No pain" with a happy face and at other end by a label such as "Worst pain imaginable" and a score of 10.7 All the patients were instructed about VAS and to point out the intensity of pain on the scale. (0-No Pain, 10-Worst Pain). All patients were kept fasted overnight, and given Tablet Alprazolam 0.5mg and Tablet pantoprazole 40 mg on the night before and on the morning of surgery.

The patients meeting the inclusion criteria were distributed into 2 groups using sealed envelopes. Group TD was applied Trans Dermal Diclofenac 100 mg patch, on their left arm 1 hour prior to surgery and repeated at 12 hourly intervals. Group IV was given intravenous diclofenac 75 mg 1 hour prior to end of surgery and repeated at 12 hourly intervals. VAS scores of both groups were noted at 2, 4, 6 and 12 hours postoperatively. First rescue analgesic used was Intra Venous (IV) Paracetamol, in both the groups, if VAS was more than 6. IV tramadol was kept as a standby rescue analgesic, in both the groups, if VAS measured was more than 6 within 6 hours of administration of paracetamol.

Following full aseptic precautions, sub arachnoid block was given in L3-L4 interspace using a 25 Gauge Quincke's spinal needle with patient in sitting position. Bupivacaine heavy (0.5%) was injected into the subarachnoid space after noting the clear free flow of CSF, with the operating table in horizontal position to achieve block level of T6-T8. This was standardized for all patients.

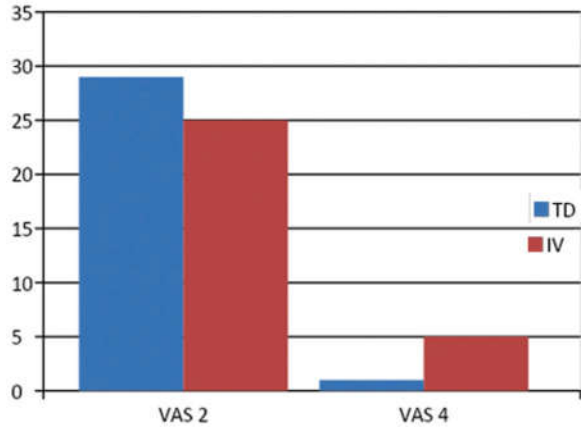
For the statistical analysis, all variables were summarized descriptively. Data was analyzed by software SPSS version 21.0. For continuous variables, the summary statistics of N, mean,

standard deviation (SD) were used. For categorical data, chi square test was use. Unpaired t test was done to compare two group means. P value of less than 0.05 was considered significant.

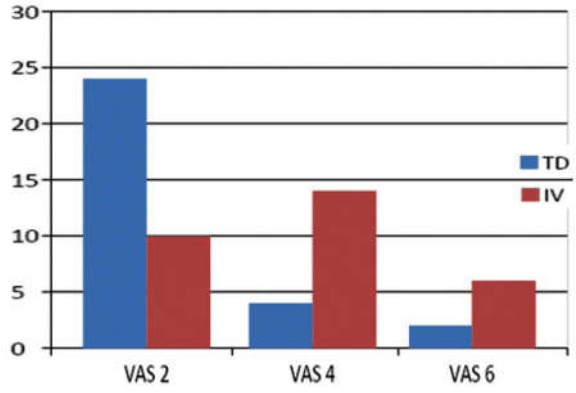
Results

The mean age in group A and B were 63.5±12.2 and 61.8±14.3 respectively and was comparable (p value-0.547). Both the groups were also comparable statistically for gender and ASA grade. The number of ASA grade I patients in group TD was 8 and in group IV was 10. The number of ASA grade II patients in group TD was 22 and in group IV was 20.

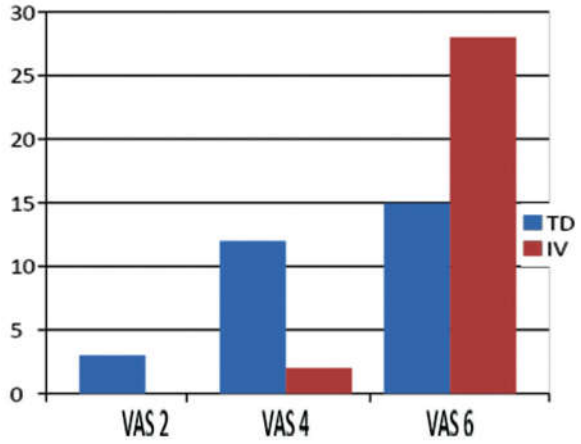
Graph 1: Illustration: 1a VAS scores at 2 hours of both groups.



Graph 2: 1b VAS scores at 4 hours of both groups.



Graph 3: 1c VAS scores at 6 hours of both groups.



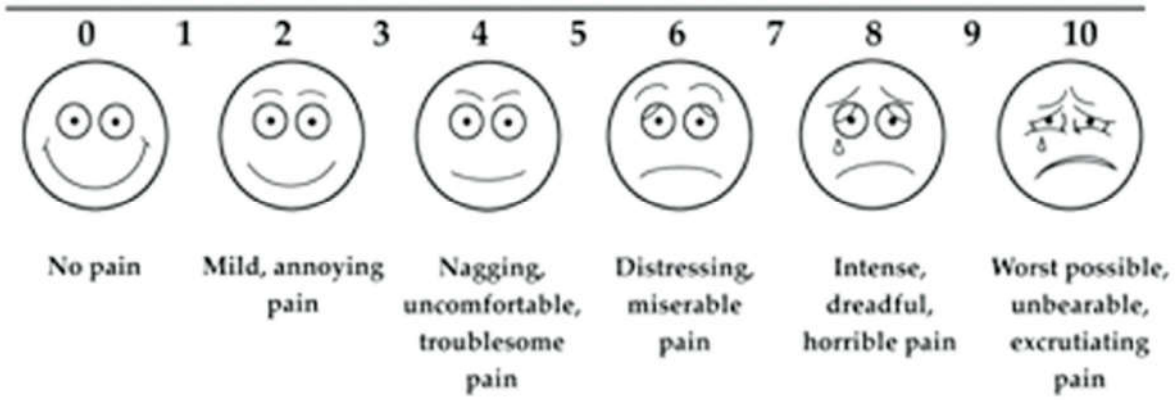


Fig. 1: Visual Analog Scale for pain (VAS).

Time to first rescue analgesia in group TD was 10.23±2.42 hours while that in group IV was 8.15±2.48 hours. It was statistically significant ($p<0.05$). As per our study protocol, IV Paracetamol was the first drug of choice for rescue analgesia when VAS was more than 6. IV tramadol was kept as a standby rescue analgesic if VAS scores were more than 6 within 6 hours of paracetamol administration. None of our patients required IV tramadol. The mean VAS scores at 2, 4, 6 and 12 hours were lower in group TD in comparison to group IV (table 1,2,3,4).

The side effect profiles were not much different in either groups. There were no cases with delirium, disoriented mentation, stomach pain etc. in either

group. Although local site irritation like dryness, erythema is mentioned in literature to be associated with transdermal patch of diclofenac, we did not encounter any such side effects. It might be due to lesser time period of follow up post application of patch in our study.

Discussion

Intertrochanteric fractures are one of the most common indications for orthopaedic surgery in old age patients.[2,3] Postoperative management of pain remains a very important aspect of early recovery and comfortable hospital stay of these patients. The most common drug used for analgesia in the postoperative period in most institutions currently, is diclofenac, administered via various routes most commonly being oral, intramuscular and intravenous. Diclofenac belongs to Non-steroidal anti-inflammatory class of drugs (NSAID) and acts by inhibiting prostaglandin synthesis by blocking the enzyme cyclo oxygenase (COX 1 and COX 2, non-selectively).

Topical diclofenac is a new preparation that can be used for analgesia and is available in various forms like transdermal patch, ointment or cream. It has various advantages over other routes. Systemic side effects are significantly lower due to low and sustained plasma concentrations compared to other routes like oral and parenteral. An update on NSAIDs noted that parenteral route had similar side effect profile including gastrointestinal symptoms like oral route while topical route was an exception and had considerably fewer side effects.[8]

Gastrointestinal symptoms seen with NSAIDs are mainly dyspepsia and peptic ulcers. Other common side effects include cardiovascular, bleeding disorders due to platelet dysfunction and renal dysfunction. Hepatic dysfunction can also be seen. All these adverse drug effects are less with topical route.[8] The added advantages of topical route include ease of application, patient compliance and easy termination. Topical route bypasses first pass metabolism in liver and is also effective in patients with poor absorption in stomach or in patients who cannot swallow or are not orally allowed. It has better bio availability with no marked peak to trough fluctuations leading to sustained plasma concentrations.[9]

The only catch with this drug delivery system is prolonged onset and offset. Its elimination half time is approximately 12 hours. Thus it has to be given in anticipation of pain and cannot be used as rescue analgesia unlike intravenous or intramuscular route which can be used as and when required. Intravenous, intramuscular and oral, in all these routes, plasma concentrations are achieved within a short time and rapidly decline leading to similar decline in analgesic effects.[10,11,12]

The most common side effects noted with topical route is local site irritation, erythema and dryness. The safety profile of diclofenac patch is studied by Mason et al.[12] Roth and Fuller analysed pooled safety data from two randomized trials which showed topical diclofenac solution to be superior to oral tablets in tolerability profile with respect to gastrointestinal symptoms and derangement in renal and hepatic variables after long term use. Topical solution was also found to be similar in efficacy to oral and therefore presented a useful alternative especially in older patients.[13]

Various studies have been done to compare topical with intramuscular and oral routes but we found very few studies comparing topical with intravenous route in orthopaedic surgeries. Thus we conducted this study to evaluate the same. We found transdermal route to be more efficacious in terms of reduced VAS scores than intravenous route at all times. It might be because we correctly timed the patch to be placed preoperatively so that adequate therapeutic levels were achieved after completion of surgery. The total number and dose of rescue analgesics used in transdermal group was also lower than the intravenous group. Thus we were able to completely avoid opioids and other analgesic drugs use in this group.

Opioids are excellent analgesics but their tolerability is limited due to side effects like nausea, vomiting, pruritus, decrease in bowel motility, constipation and more serious ones like sedation and respiratory depression.[14] It is especially problematic in old age patients who are more susceptible. Also these patients generally have some comorbidities like cardiovascular, hepatic or renal dysfunction. Therefore multiple drugs and higher dosages are better avoided.[15] Taking all these factors into consideration, transdermal diclofenac is an ideal candidate for such patients as a single patch is effective for 12-24 hours with very low but therapeutic plasma levels for sustained duration.[10]

Yadav et al conducted a randomized trial to compare intravenous, transdermal and rectal suppository of diclofenac for postoperative analgesia after gynecological surgeries. They found transdermal patch 200 mg to be comparable to rectal suppository of 200 mg in providing analgesia for 24 hours postoperatively. Both these routes were better than intravenous route for analgesia as found

in our study.[16] Singh et al compared transdermal with intravenous diclofenac for analgesia after head and neck cancer surgeries and found transdermal route to be better than intravenous similar to our study. The intravenous group had faster onset with fluctuating analgesic effects whereas transdermal route had delayed onset but a steady analgesia. Patients were more comfortable in transdermal group.[16]

Krishna et al studied the analgesic effects of transdermal diclofenac patch in patients undergoing elective lower limb orthopaedic surgery under spinal anaesthesia and found it to be comparable. Similarly, Bhargava et al concluded that Diclofenac sodium patch was as effective as intramuscular injection in providing post-operative analgesia. Only concern about patch was that it has longer onset of action, so if applied by proper planning, patch had many advantages.[17]

Conclusion

We can conclude that transdermal diclofenac patch group patients had lower VAS scores at all measured intervals compared to IV diclofenac group and a significantly longer time of rescue analgesic use. Thus, if planned timely TD diclofenac could be a useful option in orthopaedic post-operative pain management and if combined with paracetamol IV as rescue analgesic the need of opioids could be almost negligible. The side effect were also minimal in our study groups however larger scale studies need to be conducted with longer postoperative follow up to evaluate the efficacy and compare safety profile and tolerability of these two routes.

References:

1. Imani, F., 2011. Postoperative pain management. Anesthesiology and Pain Medicine, 1(1), pp.6-7.
2. Imani, F. and Safari, S., 2011. Pain Relief is an Essential Human Right", We Should be Concerned about It. Anesthesiology and Pain Medicine, 1(2), pp.55-57.
3. Räsänen, P., Paavolainen, P., Sintonen, H., Koivisto, A., Blom, M., Ryynänen, O. and Roine, R., 2007. Effectiveness of hip or knee replacement surgery in terms of quality-adjusted life years and costs. Acta Orthopaedica, 78(1), pp.108-115.
4. Barrington JW, Halaszynski TM, Sinatra RS, Expert Working Group On A, Orthopaedics Critical Issues In H, Knee Replacement Arthroplasty FT: Perioperative pain management in hip and knee replacement surgery. American journal of orthopedics (Belle Mead, NJ). 2014, 43:S1-s16.
5. Klug MJ, Rivey MP, Carter JT: Comparison of Intraoperative Periarticular Injections Versus Liposomal Bupivacaine as Part of a Multimodal Approach to Pain Management in Total Knee Arthroplasty. Hospital pharmacy. 2016, 51:305-311.
6. Lonner J: Role of liposomal bupivacaine in pain management after total joint arthroplasty. Journal of surgical orthopaedic advances. 2014, 23:37-41.
7. McCormack HM, Horne DJ, Sheather S. Clinical applications of visual analogue scales: a critical review. Psychol Med. 1988; 18:1007– 19.
8. Ong C.K.S, Lirk P, Tan C.H, Seymour R.A. An evidence based update on non steroidalanti inflammatory drugs. Clinical Medicine & Research. Volume 5, number 1: 19-34
9. Rao et al, Post Operative Pain Relief: A Comparison of Transdermal Diclofenac patch with Intramuscular Diclofenac Injection. Indian Journal of Clinical Anaesthesia 2016;3(1);56-61
10. Alessandri, F., Lijoi, D., Mistrangelo, E., Nicoletti, A., Crosa, M. and Ragni, N., 2006. Topical diclofenac patch for postoperative wound pain in laparoscopic gynecologic surgery: A randomized study. Journal of Minimally Invasive Gynecology, 13(3), pp.195-200.
11. Arthur AM, Bookman, Kate SA, et al. Effect of a topical diclofenacsolution for relieving symptoms of primary osteoarthritis of theknee: a randomized controlled trail. CMAJ. 2004;171(4):333-338.
12. Mason L, Moore RA, Edwards JE et al. Topical NSAIDS for acute pain: a meta-analysis. BMC Family Pract. 2004;5:10.
13. Roth S, Fuller P. Diclofenac topical solution compared with oral diclofenac, a pooled analysis. Journal of Pain Research. 2011;159-167.
14. Garimella, V. and Cellini, C., 2013. Postoperative Pain Control. Clinics in Colon and Rectal Surgery, 26(03), pp.191-196.
15. Pergolizzi, J., Böger, R., Budd, K., Dahan, A., Erdine, S., Hans, G., Kress, H., Langford, R., Likar, R., Raffa, R. and Sacerdote, P., 2008. Opioids and the Management of Chronic Severe Pain in the Elderly: Consensus Statement of an International Expert Panel with Focus on the Six Clinically Most Often Used World Health Organization step III Opioids (Buprenorphine, Fentanyl, Hydromorphone, Methadone, Morphine, Oxycodone). Pain Practice, 8(4), pp.287-313.
16. Yadav et al. An Evaluation and comparison of the various preparations of intravenous injection, Transdermal patch and rectal suppository of diclofenac sodium in the pain management after gynaecological surgery: A randomized trial. Indian Journal of Applied Research. 2016;421-425.
17. Rohith K, Madagondapalli SN. Efficacy of a single dose of transdermal diclofenac patch as pre-emptive postoperative analgesia: a comparison with intramuscular diclofenac. South African J AnaesthAnalg 2012;18(4):194-197.