Evaluation of the Role of Transdermal Diclofenac Patch (Nupatch) in Management of Pain in Postperative Patients

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ABSTRACT

Introduction: The present study was planed and conducted in the surgery Department, Government Medical College and Rajindra Hospital, Patiala to evaluate the role of transdermal diclofenac nupatch in post operative pain management.

Material and methods: The study was carried among 100 adult patients who underwent major surgery. Diclofenac transdermal patch (Nupatch) 50 sq.cm was applied 2-3 cm away from operative site at the zero hour postoperatively on no hariy skin in the recovery room and was changed every 24 hourly postoperatively and following observations were made in all the cases for four days at different time intervals. Intensity and relief was recorded on 4 and 5 point scale observations were drawn. Statistical analysis was carried using Chi-square test with $p<0.05$ as significant value.

Results:34% of patients showed excellent relief of pain while 38% of patients showed good, 27% patients showed fair and only 1% showed poor relief of pain after the application of transdermal diclofenac patch. In 34% of patients no rescue medicine was used while it was used in 66% of patients.

Conclusion: Transdermal patches reduces the side effects related to the oral and parental administration of medication as it bypasses the first pass metabolism and achieves a constant and controlled drug release. Thus, transdermal diclofenac patch (Nupatch) is easy to use and is a painless application that is effective in reducing post-operative pain and also lowers the need of rescue analgesia.

Keywords: Diclofenac sodium; Nupatch; Transdermal Patch;

INTRODUCTION

Surgery results in damage to local tissue with consequent release of analgesic substances (prostaglandins, histamine, serotonin, bradykinin, 5- hydroxytryptamine, substance P) and generation of noxious stimuli that are transduced by nociceptors and transmission to the neuraxis by A delta and C nerve fibers.[1] Diclofenac sodium due to its anti-inflammatory, analgesic and anti-pyretic activity, is a commonly prescribed NSAID post-operatively. However, to the first pass metabolism, the oral route allows only about 50% of the absorbed dose of diclofenac to become systemically available. Also, oral diclofenac carries the potential for significant adverse reactionsdue to the high plasma concentrations attained, particularly those involving the gastrointestinal tract.[2]

In the recent past transdermal patches have been developed as an innovative topical delivery system for diclofenac that offers the advantage of sustained drug delivery. They are defined as a medicated adhesive patch which is applied above the skin to release a specific dose of medicine with a predetermined rate of release through the skin to reach into the bloodstream. These patches due to lower plasma concentrations when compared to oral drugs, decreases the incidence of systemic adverse effects.[3]

The effect of transdermal patches is more than skin deep. According to Morrow T[4] the simply designed transdermal patch has undergone a dramatic transformation over the past decade. All transdermal systems attempt to maintain a balance between various factors including coverage area, size of patch, duration of therapeutic drug level, concentration of the medicine, and use of an enhancer or reserve drug. He further concluded that transdermal patches offers advantage of painless drug delivery, is easy to apply and controllable, provides faster and longer relief, there is no need of bulky delivery devices to manage and have no or few gastrointestinal side effects from the drug itself. The present study was planed and conducted in the surgery Department, Government Medical College and Rajindra Hospital, Patiala to evaluate the role of transdermal diclofenac nupatch in post operative pain management.

MATERIAL AND METHODS

The study was carried among 100 adult patients admitted in surgery department of Rajindra Hospital, attached to Govt. Medical College, Patiala. All the patients undergoing major surgery were selected at random. Patients hypersensitive to NSAIDS; patients with hepatic, neurological and haemorrhagic diasthesis; gastric/intestinal ulcers; pregnancy and lactation; patients with attacks of asthma, urticaria and rhinitis and patients with infective wounds were excluded from the study.

Detailed history of patients was taken and thorough clinical examination and routine investigations were done to rule out clinical abnormality.

Diclofenac transdermal patch (Nupatch) 50 sq.cm was used and applied 2-3 cm away from operative site at the zero hour postoperatively on no hariy skin in the recovery room. Treatment with other NSAIDS or pain killers was stopped and only paracetamol was allowed as rescue medicine. Nupatch is designed to remain at the site of application for 24 hours and changed every 24 hourly postoperatively and following observations were made in all the cases for four days at different time intervals. Intensity and relief was recorded on 4 and 5 point scale observations drawn and conclusions were made and overall assessment of efficacy of transdermal diclofenace nupatch will be made as:

Excellent =Total reduction or near total resolution of pain

Good = Significant resolution of pain

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How to cite this article: Vinod Kumar, Sanjeev Gupta, RenuVerma. Evaluation of the role of transdermal diclofenac patch (nupatch) in management of pain in postperative patients. International Journal of Contemporary Medical Research 2017;4(2):493-496.

Fair = Some resolution of pain
Poor = No resolution of pain.
Statistical analysis was carried using Chi-square test with $p<0.05$ as significant value.

Results

Age of patients in the presnt study varied from 18-90 years with the mean age of the patients 28.5±2.35.

Table 1 and 2 shows that 43 patients required rescue analgesia at 3 hours post-operatively. At 12 hours postoperatively 17 patients required analgesia, 15, 13, 12, 12 and 2 patients required rescue analgesia at 0, 24, 6, 9, and 48 hours intervals post-operatively whereas none of the patients required rescue medicine at 72 and 96 hours. Statistical analgesic requirement at various time intervals is non significant at 6 hours interval, significant at 24 hours interval and highly significant for 3, 9, 12 48, 72 and 96 hours time interval. 34% patients post operatively needed no rescue analgesia, 38% patients needed single injection, 27% patients needed rescue medicine two times and only 1% patients needed rescue medicine three times at different time interval.

Table 3 and 4 shows that the mean pain intensity at 0, 3, 6, 9, 12, 24, 48, 72 and 96 hours intervals was 2.98, 2.55, 2.03, 1.86, 1.48, 1.09, 0.97, 0.48 and 0.13 respectively. Statistical analysis shows that the difference at 3 hours is not significant whereas at 6, 9, 12, 24, 48, 72 and 96 hours is highly significant.

Table 5 shows that the mean pain relief at 0, 3, 6, 9, 12, 24, 48, 72 and 96 hours intervals was 0.41, 0.92, 1.26, 1.92, 2.25, 2.78, 2.92, 3.58, and 3.97 respectively. Statistical analysis (table 6) shows that difference at 3 hours is non significant and highly significant at 6, 9, 12, 24, 48, 72 and at 96 hours.

The table 7 shows that at 96 hours postoperatively all the patients were relieved of pain. At 72 hours 85% patients were relieved of pain. At 48 hours, 24 hours, 12 hours, 9 hours, 6 hours, 3 hours and zero hour postoperatively the number (%age) of patients which were relieved of pain after daily nupatch application was

Time Interval (hrs)	No. of Patients	% age	Mean±SD
0	15	15	15±7.5
3	43	43	43±6.8
6	12	12	12±3.37
9	12	12	12±3.56
12	17	17	17±8.91
24	13	13	13±7.51
48	2	2	2±0.56
72	0	0	0±0
96	0	0	0±0

Table-1: Comparison of rescue analgesia at different time intervals

Comparison	't' value	'p' value	Sig.
0 vs 3	13.26	>0.05	NS
0 vs 6	2.11	>0.05	NS
0 vs 9	7.26	>0.05	NS
0 vs 12	6.51	>0.05	NS
0 vs 24	3.31	>0.05	NS
0 vs 48	8.56	>0.05	NS
0 vs 72	27.11	>0.05	NS
0 vs 96	18.19	>0.05	NS

Table-2: Statistical analysis of analgesia at 0 hours with different point of time

Time Interval (hrs)	Range	Mean±SD
0	2-3	2.98±1.16
3	2-3	2.55±2.17
6	2-1	2.03±1.06
9	2-1	1.86±2.13
12	0-2	1.48±1.37
24	0-2	1.09±1.57
48	0-1	0.97±1.16
72	0-1	0.48±1.03
96	0-1	0.13±0.99

Table-3: Comparision of pain intensity at different time intervals

Comparison	't' value	'p' value	Sig.
0 vs 3	1.26	>0.05	NS
0 vs 6	2.58	<0.05	HS
0 vs 9	3.11	0.05	HS
0 vs 12	3.57	0.05	HS
0 vs 24	4.81	0.05	HS
0 vs 48	5.97	0.05	HS
0 vs 72	6.82	0.05	HS
0 vs 96	7.26	0.05	HS

Table-4: Statistical analysis of pain intesnity at different levels

Time Interval (hrs)	Range	Mean±SD
0	0-1	0.41±3.17
3	0-1	0.92±0.98
6	0-2	1.26±2.17
9	1-2	1.92±1.18
12	1-3	2.25±0.95
24	1-3	2.78±0.44
48	2-3	2.92±0.87
72	3-4	3.58±1.06
96	3-4	3.97±1.03

Table-5: Comparision of pain relief at different time intervals

Comparison	't' value	'p' value	Sig.
0 vs 3	0.95	0.05	NS
0 vs 6	2.41	0.05	HS
0 vs 9	3.01	0.05	HS
0 vs 12	4.16	0.05	HS
0 vs 24	5.12	0.05	HS
0 vs 48	5.35	0.05	HS
0 vs 72	5.97	0.05	HS
0 vs 96	6.24	0.05	HS

Table-6: Statistical comparison of pain relief at different point of time

Time Interval (hrs)	No. (%) of Patients
0	10
3	15
6	22
9	45
12	57
24	65
48	72
72	85
96	100

Table-7: Distribution of patients according to pain relief at various time intervals

72%, 65%, 57%, 45%, 22%, 15% and 10% respectively.

DISCUSSION

Transdermal systems for NSAIDs are an innovative delivery mechanism replacing oral and other traditional forms of drug administration. The drug in the transdermal patch enters the body through skin and ultimately diffuses into capillaries for systemic delivery.[5]

The major components of transdermal patch are drug, liner, membrane, adhesive and backing. Liner safeguards the patch during storage and is removed prior to use, drug contains the drug solution in direct contact with release liner, adhesive serves to adhere the components of the patch together along with adhering the patch to the skin, membrane controls the release of the drug from the reservoir and multi-layer patches and backing protects the patch from the outer environment.[6]

Morrow T[4] reported that all transdermal systems attempt to create a balance between number of key factors including size of patch or coverage area, concentration of the drug, duration of therapeutic drug level and use of an enhancer.

The present study evaluated the role of transdermal diclofenac nupatch in post operative pain management. Pain intensity and pain relief on 4 and 5-point scale showed that the efficacy of transdermal diclofenac patch was excellent in 34 patients and good in 38 patients while it was fair in 27 patients and poor in 1 patient. It was further observed that no rescue medicine was used in 34 patients while it was used in 66 patients. 57% patients got pain relief after 12 hours of applying transdermal patch. 65% patients after 24 hours and 72% patients were relieved of pain after 48 hours of applying the transdermal patch.

Verma R et al[6] compared the usefulness and safety of ketoprofen and diclofenac transdermal patch as a postoperative analgesia, and concluded that both ketoprofen and diclofenac transdermal patch are effective for postoperative analgesia but rescue analgesic was required in less number of patients in ketoprofen group. Funk L et al[7] observed that diclofenac transdermal patches provided a significantly better pain relief as compared to oral diclofenac tablets postoperatively, in the early period following arthroscopic shoulder surgery. Krishnan R et al[8] also revealed that intraoperative application of a single dose of 100 mg transdermal diclofenac patch is as effective as a single dose of intramuscular diclofenac (75 mg).

Agarwal et al[9] conducted prospective randomized, double blind placebo controlled study on evaluation of a diclofenac transdermal patch for the attenuation of venous cannulation pain and reported that the application of a diclofenac transdermal patch at the cannulation site appears to be effective in decreasing cannulation pain. Bradley et al[10] conducted a study among patients who had suffered a painful minor sports injury within the prior 72 hours of study entry. Measures of pain intensity were performed in a daily diary and at clinic visits on days 3,7 and 14.They concluded that diclofenac patch was superior to placebo patch in relieving pain. No statistically significant differences were seen in any safety or side effect measures with the diclofenac patch as compared to the placebo patch. They further concluded that diclofenac epolamine patch is an effective and safe pain reliever for treatment of minor sports injury pain. They further said that advantages of this novel therapy include its ease of use and lack of systemic side effects.

Predel et al[11] studied clinical efficacy and safety of diclofenac patch in the topical treatment of blunt injuries and concluded that diclofenac patch was significantly more effective than placebo as the diclofenac patch resulted in pain relief in a short time as revealed by the time to resolve pain at the injured site which was significantly shorter compared to placebo ($p<0.0001$) and the patch was well tolerated.

Alessandri et al[12] compared pain management of standard analgesic and standard analgesic plus transdermal patch in patients who undergo laparoscopic gynecologic surgery and reported that diclofenac transdermal administration seems a valid help to standard analgesic treatment in prospective pain control and could also help to reduce the period of hospitalization of patients who undergo laparoscopic benign gynecologic surgery. The transdermal diclofenac patch is a promising analgesic modality for the management of mild to moderate pain following surgery providing the evidence of its established analgesic potency with a lower incidence of systemic adverse effects.[13]

CONCLUSION

Transdermal patches reduces the side effects related to the oral and parental administration of medication as it bypasses the first pass metabolism and achieves a constant and controlled drug release. Thus, transdermal diclofenac patch (Nupatch) is easy to use and is a painless application that is effective in reducing post-operative pain and also lowers the need of rescue analgesia.

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Source of Support: Nil; **Conflict of Interest:** None

Submitted: 30-01-2017; **Published online**: 13-03-2017