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Original Research Article

An Assessment of the Efficacy of Transdermal Diclofenac Sodium Patch versus Transdermal Ketoprofen Patch for Relief of Acute Post-Operative Pain in Laparoscopic Abdominal Surgery: A Randomized Clinical Study

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Abstract

Aim: The present study was undertaken in patients undergoing elective laparoscopic surgeries under general anaesthesia with an objective to evaluate the efficiency of transdermal diclofenac patch with transdermal ketoprofen patch.

Methods: The present study was undertaken at Department of Anesthesiology for one year. Total 100 patients were included in the study after explaining purpose and procedure of study and written informed consent of the patients. All patients were divided equally in two groups, 50 patients in each group.

Results: There was no statistically significant difference between the two groups of patients in terms of age, weight and male/female ratio (P> 0.05). The difference of mean Pulse rate per minute status and systolic and diastolic blood pressure (mmHg) of patients in Group D and Group K was statistically insignificant (p>0.05). The difference was statistically significant at 2 hr, 4 hr, 6 hr, 8 hr, and 12 hr post-operatively. The complications occurrence in both group were insignificant.

Conclusion: We concluded that Transdermal Ketoprofen patch is effective and safe pain relievers in management of acute postoperative pain with early onset of pain relief, longer duration of analgesia, better in reducing the severity of pain in post-operative period, lesser adverse effects in laparoscopic abdominal surgeries under general anaesthesia.

Keywords: diclofenac, ketoprofen, transdermal patch, VAS, abdominal surgery.

Introduction

Pain is a complex experience that consists of a specific sensation and the reactions elicited by that sensation. [1] It is one of the most common symptoms that are experienced after tooth extraction. The successful relief of pain to the patients undergoing any type of dental treatment is of the extreme importance to the dentist. [2] Pain relief offers considerable physiological benefits; therefore, monitoring pain relief has become a crucial postoperative quality measure. Dentist makes every effort to select an analgesic regimen that would provide profound analgesia without any adverse effects. [3]

Various drugs, opioids, and nonopioids have been employed for managing pain. These drugs can be administered by various routes (oral, transdermal, neuraxial, intravenous [IV], and regional). Recently, a concept of transdermal patches is gaining popularity as a new route to achieve analgesia. In this form of drug delivery system is a medicated adhesive patch is positioned over the skin to deliver a selected dose of medication through the skin into the bloodstream. [4] This route of drug delivery is an alternate to oral route and might enhance patients' compliance and tolerance by reducing drug-related side effects. Other than that, it also avoids the pain associated with IV and intramuscular (IM) routes. Topical nonsteroidal anti-inflammatory drugs (NSAIDs) are also available in this form and can be administered systemically in low concentration, thus avoiding upper gastrointestinal complications such as gastric and peptic ulcers and dyspepsia. [5]

Though we have been using parenteral diclofenac (Intramuscular) most often, suppository and intravenous use is also possible. It can be administrated by Transdermal route also. The advantages of this route are painless, non-irritant, increased bioavailability and it can be applied for 24 hours. Though transdermal route has its own advantages there are no studies to compare this route along with intramuscular route. Ketoprofen is a potent non-steroidal anti-inflammatory agent, widely used for the symptomatic treatment of

inflammatory syndromes such as rheumatoid arthritis, osteoarthritis and acute gouty arthritis. Because of its gastric irritation after oral administration, many topical formulations of ketoprofen such as cream and gel were developed. Transdermal drug delivery system is one of the novel drug delivery systems. It has many advantages over the other dosage forms such as providing extended therapy with a single application, thus leading to good patient compliance.

The present study was undertaken in patients undergoing elective laparoscopic surgeries under general anaesthesia with an objective to evaluate the efficiency of transdermal diclofenac patch with transdermal ketoprofen patch.

Materials and Methods

The present study was undertaken at department of Anesthesiology, SKMCH, Muzaffarpur, Bihar, India for one year Normal adult patients of either sex, without any co- morbidity, admitted for elective laproscopic abdominal surgeries between ages of 18 to 60 years with ASA grade: I and II, weight ranging between 40 to 80 kg and duration of surgeries up to 90 minutes were included in the study. Total 100 patients were included in the study after explaining purpose and procedure of study and written informed consent of the patients. Patient with history of alcohol abuse, asthma, underlying neurological, cardiovascular, psychiatric disease, hepatic or renal disorders were excluded from the study.

All patients were divided equally in two groups, 50 patients in each group: GROUP- D (n=50) - Patients received transdermal patch of diclofenac sodium (each patch of 50 cm^2 contains 100 mg) GROUP-K (n=50)-Patients received transdermal patch of ketoprofen (each patch of 70 cm^2 contains 20 mg) Transdermal diclofenac sodium patch/ transdermal ketoprofen patch (in Acute post-operative pain) was applied on intact, clean, dry and hairless skin, before application of patch site was clean with clear water and dried. Patch was applied to either side of chest wall, before extubation or immediately after dressing.

All patients were monitored for haemodynamic changes in pulse rate (per minute), systolic blood pressure (mm Hg), diastolic blood pressure (mm Hg), Respiratory Rate (per minute), SPO2 (%) before premedication, before induction, intra-operatively (at 0 min ,10 min, 20 min, 30 min, 60 min, 90 min, 120 min), post-operatively (at 0 hr, 1 hr, 2 hr, 4 hr, 6 hr,8 hr and 12 hr). Pre-anaesthetic assessment was done (as per proforma) on evening before surgery. A routine examination was done by assessing- General condition, Nutritional status, weight, Airway assessment, complete examination of cardiovascular and respiratory system. Premedication Inj.Glycopyrrolate 0.2mg intramuscular, Inj. Pentazocine 30 mg intramuscular, Inj. Promethazine 25 mg intramuscular and Inj. Ondansetron 4mg intravenous slowly. In operation theatre ECG, NIBP, SpO2 were applied and 18 G intravenous cannula was inserted into a suitable vein and secured. Pre-oxygenation was done with 100% oxygen for 5 minute and Inj. Xylocard 2mg/kg was given intravenous slowly. Inj. Propofol intravenous.2.5mg/kg and Inj. Scoline intravenous 2mg/kg were used as Induction agents. Endotracheal Intubation done with oral portex cuffed endotracheal tube with appropriate size according to glottic opening. Maintenance was done with oxygen [33%], nitrous oxide [66%], Inj. Atracurrium, Inhalational agent, IPPV according to patient need. Reversal of anaesthesia was achieved using inj. glycopyrolate 8 µg/kg + inj neostigmine 0.05 mg/kg intravenous. Endotracheal tube was removed only after establishment of all reflexes, adequate muscle power and consciousness. All patients were monitored for onset of pain relief, duration of analgesia of test drug by visual analogue scale and time when rescue analgesia. Rescue analgesia was given when Visual analogue scale was ≥ 3 then rescue analgesia inj. Tramadol (1mg/kg) was given intramuscularly, post-operatively. Adverse effects (Local -Dermatitis, Erythema, Purities Hyperhidrosis and systemic - Gastritis, Nausea, Vomiting, Dizziness) post-operatively were also observed. Pain scores were evaluated using a 0–10 VAS (0- no pain to 10 - worst pain imaginable). Severity of pain was determined by using the visual analogue scale. It uses a straight line with extremities of pain intensity on either end. The line is typically 10 cm long with one end defined as “no pain” and the other end being “excruciating unbearable pain”. To assist in describing the intensity of pain, words can be placed along the scale (e.g., mild, moderate, or severe). Such descriptors can help to orient the patient for the degree of pain; this particular variation of the VAS has been known as a graphic rating scale. Inj. Tramadol was used as rescue analgesia when VAS score >4.

Statistical Analysis

Statistical analysis was employed using different methods for different data subsets. A comparison of variables between two groups was done by using unpaired Student t- test and Chi- square test to find the p- value. A P-value of <0.05 was considered to be statistically significant.

Results

Table 1: Mean demographic data in group D and group K

Variables	Group D	Group K	P Value
Age (Yrs.)	28.2±8.82	29.4±10.35	0.7
Weight(Kg)	56.4±8.52	53.57±5.35	0.3
Gender(M:F)	40:10	25:25	

There was no statistically significant difference between the two groups of patients in terms of age, weight and male/female ratio (P> 0.05).

Table 2: Comparison of mean Pulse rate per minute status of patients in Group D and Group K

Variables	Group D	Group K	P Value
Before Premed	85.5±12.6	83.7 ±8.2	0.5632
Before induction	94.2±15.2	90.3±9.41	0.2432
Intra-operative			
0 min	96±16	96±9.4	1
10 min	88.2±12.8	92.4±10.4	0.2434
20 min	86±12	90±12	0.0700
30 min	86±13	89±11	0.3734
60 min	87±11	92±12	0.1432
90 min	82.8±15.6	88.2±12.4	0.076
Post-operative			
0 hr	88±12	86±14	0.5340
1 hr	83±14	82.8±9.11	0.6624
2 hr	78.6±10.4	76.8±7.75	0.4040
4 hr	75±9.18	75.4±6.84	0.7342
6 hr	76.04±12.48	76.54±6.830	0.8230
8 hr	78.4±15.4	75.5±7.23	0.3330
12 hr	72.8±7.73	74±6.44	0.9534

The difference of mean Pulse rate per minute status of patients in Group D and Group K was statistically insignificant (p>0.05).

Table 3: Comparison of mean Systolic blood pressure (mmHg) of patients in Group D and Group K

Variables	Group D	Group K	P Value
Before Premed	124±8.62	120±6.74	0.1625
Before induction	125±8.4	121±6.69	0.1327
Intra-operative			
0 min	123±11	124±6.4	1.0
10 min	119±10.2	120±6.94	0.6534
20 min	118±8.2	117±6.4	0.6223
30 min	117±8	116±6.5	0.6234
60 min	116±7	119±6.4	0.5945
90 min	115±7.3	117±3	0.2224
Post-operative			
0 hr	122±7.68	122±6.74	1.0
1 hr	118±7.43	118±3.97	0.5202
2 hr	115±7.15	116±4.66	0.5212
4 hr	114±7.2	115±5.7	0.5510
6 hr	115.5±7.25	115.4±5.3	0.7116
8 hr	116±4	116±6.54	1.0
12 hr	112±7.33	112±6.74	0.2716

The difference of mean Systolic and diastolic blood pressure (mmHg) of patients in Group D and Group K was statistically insignificant (p>0.05).

Table 4: Comparison of mean Diastolic blood pressure (mmHg) of patients in Group D and Group K

Variables	Group D	Group K	P Value
Before Premed	78±4.06	77.4±5.4	0.4045
Before induction	79±4.05	78±5.1	0.5046
Intra-operative			
0 min	78±4.4	77±3	1
10 min	77.3±4.26	76.2±4	0.8636
20 min	76±4.2	76±4.5	0.3740
30 min	75±4	75±4.6	1.0
60 min	76±4.3	76±6	1.0
90 min	78±1.5	78.2±3.7	0.3844
Post-operative			
0 hr	76.4±4.16	76±4.96	0.8002
1 hr	75±4.26	75±4.56	0.2920
2 hr	74.1±4.76	74±4.6	0.3722
4 hr	72.3±3.77	74±5.3	0.0914
6 hr	73±4.36	74±4.6	0.2634
8 hr	74±4.46	74.6±4.54	0.4436
12 hr	72±4	74±4.6	0.765

The difference of mean Diastolic and diastolic blood pressure (mmHg) of patients in Group D and Group K was statistically insignificant (p>0.05).

Table 5: Mean visual analogue scale (VAS) data in Group D and Group K

Variables	Group D	Group K	P Value
0 hr (VAS)	1.6±0.4	1.6±0.6	0.0530
1 hr (VAS)	0.8±0.3	0.6±0.5	0.0948
2 hr (VAS)	0.6±0.54	0.24±0.46	0.0454
4 hr (VAS)	1.12±0.98	0.52±0.62	0.007
6 hr (VAS)	1.15±1.05	0.62±0.81	0.0306
8 hr (VAS)	2.25±1.35	1.00±0.93	0.0012
12 hr(VAS)	1.85±0.76	1.16±0.37	0.0224

The difference was statistically significant at 2 hr, 4 hr, 6 hr, 8 hr, and 12 hr post-operatively.

Table 6: Complications in both Group D and Group K

Variables	Group D	Group K	P Value
Dermatitis	0	0	0
Erythema	0	0	0
Pruritis	0	0	0
Hyperhydrosis	0	0	0
Gastritis	3 (6%)	0	0.48
Nausea	9 (18%)	10 (20%)	1.0
Vomiting	5 (10%)	0	0.22
Dizziness	2 (4%)	0	1.0

The complications occurrence in both group were insignificant.

Discussion

The international association for the study of pain has proposed a working definition of acute post-operative pain. Pain is an unpleasant sensory and emotional experience associated with either actual or potential tissue damage. Most commonly used drugs for postoperative analgesia are NSAIDs worldwide. They can be used orally, intravenously (i.v.), intramuscularly (i.m.) and as transdermal patches. Transdermal delivery drug system avoids the pain associated with i.v. and i.m. routes and is an option for patients who don't tolerate the oral drug especially in postoperative period. Also topical NSAIDs have a reduced risk of upper gastrointestinal complications such as gastric and peptic ulcers, and dyspepsia because of low systemic concentrations. [6]

There was no statistically significant difference between the two groups of patients in terms of age, weight and male/female ratio (P> 0.05). The difference of mean Pulse rate per minute status, Systolic and diastolic blood pressure (mmHg) of patients in Group D and Group K was statistically insignificant (p>0.05). The difference was statistically significant at 2 hr, 4 hr, 6 hr, 8 hr, and 12 hr post-operatively. The complications occurrence in both group were insignificant. In

2010, Bhaskar H et al [7], revealed that there were no significant differences in the pain relief and pain intensity scores between transdermal patches and oral diclofenac sodium. Results of this study indicate that the transdermal diclofenac patch provides potent analgesia as compared to the oral diclofenac tablets with the added advantage of better patient compliance. Oral administration of NSAIDs, however, carries a risk of first pass metabolism with significant amount of the drug being lost before it is systemically absorbed. Oral NSAIDs are also known to cause several adverse effects, particularly gastrointestinal effects, which are dose dependant. Topical formulations of NSAIDs have been developed as alternate routes of drug administration, offering the advantage of local, enhanced drug delivery to the affected tissues with a lower incidence of systemic adverse effects. Topical NSAIDs have thus carved out a niche for themselves as therapeutic analgesic modalities with established benefits and lower incidence of adverse events. Transdermal systems for NSAIDs are an innovative delivery mechanism replacing oral and other traditional forms of drug administration. The drug contained in the transdermal patch enters the body through skin and ultimately diffuses into capillaries for systemic delivery. The steady permeation of drug across the skin allows for more consistent serum drug levels, often a goal of therapy. [8,9]

The transdermal diclofenac patch 100 mg used once daily was found to be as potent as oral diclofenac 150 mg daily for post dental extraction analgesia. These findings are similar to those of Funk et al [10] who reported that when used in patients with post operative shoulder pain, both oral and transdermal diclofenac showed similar analgesic efficacy. Diclofenac patches have also been reported to provide efficient analgesia following laparoscopic surgery. [11] In 2012, Krishna R, Natraj MS et al [12], the mean duration of analgesia in the control group was 7 hours 28 minutes, and in study group, it was 8 hours 6 minutes, which was comparable (p-value < 0.341). Results showed 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) for acute postoperative pain, without any significant side effects. In March 2015, Raichurkar A et al [13] compared the efficacy of diclofenac and ketoprofen transdermal patch with placebo in attenuating intravenous cannulation pain in patients posted for elective surgeries. VAS score 4 hours before venous cannulation and VAS score was observed. VAS score for venous cannulation pain in the ketoprofen group (2.14±0.96) was lower compared with diclofenac (3.14±0.76) and the placebo group (5.18±1.003) which was statistically significant. Transdermal diclofenac and ketoprofen patch significantly decreased both the incidence and severity of pain associated with cannulation without any adverse effects.

Conclusion

From the present study, we concluded that Transdermal Ketoprofen patch is effective and safe pain relievers in management of acute postoperative pain with early onset of pain relief, longer duration of analgesia, better in reducing the severity of pain in post-operative period, lesser adverse effects in laparoscopic abdominal surgeries under general anaesthesia.

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