A Study to Evaluate the Analgesic Efficacy of Transdermal Diclofenac Sodium Patch in Minor Oral and Maxillofacial Procedure

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Abstract

Aims and Objectives: The aim and objectives of this study are to evaluate and determine the efficacy of transdermal diclofenac patch in control of pain following Routine Extractions, Transalveolar extractions, Soft tissue biopsies, to evaluate any adverse reactions following the usage of the transdermal patch and to relate its efficacy to the gender, pre-surgical condition of the patient and time taken for the procedure.

Materials and methods: A clinical study was done in the patients coming to the Oral and Maxillofacial surgery department, Institute of Dental Sciences, SOA University. A total of 537 patients were selected from our patients in Oral and Maxillofacial Surgery department who underwent routine extractions, Transalveolar extractions, Soft tissue biopsies etc.

Results: 500 patients who underwent minor surgical procedures under local anaesthesia with adrenaline. The patient has then prescribed a diclofenac patch for analgesic purpose and the efficacy and tolerability of the patch was evaluated. Using SPSS software, statistical analysis was done. All the patients were evaluated with VAS scale and Wong baker scale on 1st day, 2nd day and 3rd day. The mean age of the patient is 28.2 years and the mean value for the time taken for the procedure is 14.4 min.

Conclusion: Transdermal patch can be effectively used for analgesic effect following minor oral surgical procedures of lesser duration. It is effective for the management of mild to moderate pain relief as it has proved to be a good option as an analgesic especially in patients with gastric problems and for better compliance.

Keywords: *Analgesic Efficacy; Transdermal Diclofenac Sodium Patch; Minor Oral and Maxillofacial Procedure; Transalveolar extractions; VAS scale; Wong baker scale; Pain management; Drug administration*

Introduction

Managing pain is the most substantial problem for any oral and maxillofacial surgeon especially in the post-operative phase. Hence every surgeon should be well prepared to manage pre, intra and post-operative pain for which it is imperative to have in-depth knowledge about the biology of pain and recent theories and its management.[1] Pain can be managed both by pharmacological and non-pharmacological methods out of which post-operative pain management relies heavily on pharmacological methods. There are both opioid and non-opioid drugs to choose for the management of pain. Although opioids are potent analgesics, its drug dependency makes non-opioid a better option for general pain management.[2] Diclofenac sodium is a frequently used NSAID's, as it has antipyretic, anti-inflammatory and analgesic properties. Diclofenac sodium is a phenylacetic acid derivative. Its chemical nomenclature is:

2-[2-(2,6-dichloroanilino) phenyl] acetic acid monosodium salt.

Diclofenac can be administered through various routes such as through oral, intramuscular, intravenous, transdermal and rectal. Oral administration of diclofenac is quite disadvantageous due to the serious side-effects of the drug, which is chiefly due to the poor agent specificity, which results from the drug binding to specific receptors (e.g., prostaglandin). The adverse reaction of the drug mainly affects the gastrointestinal tract. Diclofenac when administered orally is not well tolerated as it can result in severe stomach ulcerations. Hence new methods are being ventured for the administration of the drug to reach the specific therapeutic drug concentration in the tissue without causing any systemic problems. Transdermal delivery is a befitting alternative for the administration where the drug concentration reaches a required therapeutic level in the tissue without reaching the gastrointestinal tract.[3]

Methodology

A clinical study was done in the patients reported to the Oral and Maxillofacial surgery department, Institute of Dental Sciences, Siksha O Anusandhan (Deemed to be University), after getting clearance from the ethical committee. The purpose of the study was explained to all the patients included in the study and written consent was obtained. A total of 537 patients were selected from our patients in the Oral and Maxillofacial Surgery department who underwent following treatment 1. Routine extractions, 2. Transalveolar extractions, 3. Soft tissue biopsies

Materials Used: Diclofenac sodium patch

Inclusion Criteria: ASA-1 category patients, Age – 15 to 50 years, Routine extractions, Transalveolar extractions, Soft tissue biopsies,

Exclusion Criteria: Those patients not fulfilling the inclusion criteria are excluded in the study; patients allergic to diclofenac or any other NSAIDs; those patients who were not willing for the study.

500 patients were selected for the study after excluding some of the non-complaint patients. Preoperative radiographs and routine blood investigations were performed before procedures wherever required. The Diclofenac Patch (Dicloplast) 100mg was administered after 30 minutes of the procedure for all the patients. The scheduled regimen for administration of diclofenac patch is Day 1 1st patch after 30 minutes of surgery, Day 2 and Day 3 new patch was given. The patch can be applied to any part of the body, preferably an area devoid of hair (Figure 1). Wong-baker faces pain rating scale and the Visual Analog Rating Scale was used to record the result. The patients will be assigned scores for every parameter at intervals of 6hrs, 12hrs and 24 hrs and 48hrs postoperatively. Furthermore, the subjects will have to set values for a total of 72hrs in the postoperative period.[4]

A special questionnaire was prepared, to record the relevant history. The parameters such as age, gender, pre-surgical condition and the pain rating scales were noted. Each patient received a patch, half an hour post-operatively which was applied over the bare skin of the patient. The patient was explained about the dosage of the transdermal patch and probable side effects of the application. Patients were instructed not to use any other analgesic or anti-inflammatory medications. In the unavoidable situation where they have to take these medications, they are asked to report it on call in which case they were excluded from the study. The amount of pain was recorded with visual analogue pain scale ranging from 0 (least pain) to 10 (maximum pain) and FACES pain rating scale (Wong baker). The patient and their attendant were explained about the ratings. The first rating was recorded by the operator and other ratings were enquired by the attendant over the phone. In case of any incidence where the patient had to take other medications like if the patient complained of fever, the patients were prescribed with other antipyretics. These patients were excluded from the study. Thus, 37 patients were excluded, and statistical analysis was done on the 500 patients. SPSS software was used for purpose of analysis

Ethical Permission and Patient Consent: Approval from the Institutional Ethical Committee of IMS and Sum Hospital, Siksha 'O' Anusandhan (Deemed to be University) was taken before conducting the study. Moreover, prior consent was taken from patients before the study and signature of the patients were taken in the consent form.

Results

In the descriptive study performed on 500 patients who underwent minor surgical procedures under local anaesthesia with adrenaline. The patient has then prescribed a diclofenac patch for analgesic purpose and the efficacy and tolerability of the patch was evaluated using the following parameters

Ø Pre-surgical condition (Symptomatic/ Asymptomatic)

Ø Gender predilection

Ø Duration of the procedure

Ø Visual analogue scale

Ø Wong-baker scale

Using SPSS software, statistical analysis was done. All the patients were evaluated with VAS scale and Wong baker scale on 1st day, 2nd day and 3rd day. The mean rating of Wong baker pain scale for day 1 is 2.6 (Standard Deviation or SD=1.07), day 2 is 0.9 (SD=1.09) and day 3 is 0.07 (SD=0.34). The visual analogue pain scale rating for day 1 is 3.1 (SD=1.35), day 2 is 0.9 (SD=1.07) and day 3 is 0.08 (SD=0.3). The mean age of the patient is 28.2 years and the mean value for the time taken for the procedure is 14.4 min.

As per the study by VAS scale and Wong-Baker scale, there is no statistical significance in comparison of pain rating according to the gender on day 1, 2 & 3 (Table 1 and 2) but as per pre-surgical condition, there is the statistical significance ($p>0.05$) among symptomatic and asymptomatic patients on day 1, 2 & 3 (Table 3 and 4). In contrast, there is no statistical significance on day 1&2 for the time taken during the procedure but significance in day 3 in both scales. There is no correlation between the time taken in minutes and Wong-Baker Pain Rating on Day 1. ($r = -0.01$) There was no statistical significance ($p>0.05$). There is no correlation between the time taken in minutes and Wong-Baker Pain Rating on Day 2. ($r = -0.02$) There was no statistical significance ($p>0.05$). There is a mild positive correlation between the time taken in minutes and Wong-Baker Pain Rating on Day 3. ($r = .133$) There was statistical significance ($p<0.05$). There is no correlation between the time taken in minutes and Visual Analog Scale Pain Rating on Day 1. ($r = -0.02$) There was no statistical significance ($p>0.05$) There is no correlation between the time taken in minutes and Visual Analog Scale Pain Rating on Day 2. ($r = 0.05$) There was no statistical significance ($p>0.05$). There is a mild positive correlation between the time taken in minutes and Visual Analog Scale Pain Rating on Day 3. ($r = 0.167$) There was statistical significance ($p<0.05$).

Table 1: Comparison of the Mean Wong-Baker Pain rating according to the gender from day 1 to 3.

Wong-Baker Pain Rating	n	Day 1		Day 2		Day 3	
		Mean	SD	Mean	SD	Mean	SD
Male	184	2.67	1.03	0.98	1.07	0.05	0.27
Female	316	2.65	1.11	0.98	1.11	0.09	0.39
Total	500	2.66	1.08	0.98	1.09	0.07	0.35
T-test	T test – p > 0.05, Not Significant			T test – p > 0.05, Not Significant		T test – p > 0.05, Not Significant	

The Mean Wong-Baker Pain rating on Day 1 was 2.67 ± 1.03 among males and 2.65 ± 1.11 among females; Day 2 was 0.98 ± 1.07 among males and 0.98 ± 1.11 among females; Day 3 was 0.05 ± 0.27among males and 0.09 ± 0.39 among females

Table 2. Comparison of the mean visual analogue pain rating according to the gender from day 1 to 3.

Visual Analog Pain Rating	n	Day 1		Day 2		Day 3	
		Mean	SD	Mean	SD	Mean	SD
Male	184	3.14	1.41	0.97	1.06	0.07	0.25
Female	316	3.14	1.33	1.00	1.08	0.09	0.35
Total	500	3.14	1.36	0.99	1.07	0.08	0.32
T-test	T test – p > 0.05, Not Significant			T test – p > 0.05, Not Significant		T test – p > 0.05, Not Significant	

The Mean Visual Analog Pain rating on Day 1 was 3.14 ± 1.14 among males and 3.14 ± 1.33 among females; Day 2 was 0.97 ± 1.06 among males and 1.00 ± 1.08 among females; Day 3 was 0.07 ± 0.25 among males and 0.09 ± 0.35 among females

Table 3. Comparison of the mean Wong-Baker pain rating according to the pre-surgical condition from day 1 to 3.

Wong-Baker Pain Rating	n	Day 1		Day 2		Day 3	
		Mean	SD	Mean	SD	Mean	SD
Asymptomatic	269	2.39	1.01	0.7	1.06	0.03	0.24
Symptomatic	231	2.97	1.08	1.32	1.04	0.13	0.44
Total	500	2.66	1.08	0.98	1.09	0.07	0.35
T-Test	T test – p < 0.05, Significant			T test – p < 0.05, Significant		T test – p < 0.05, Significant	

The Mean Wong-Baker Pain rating on Day 1 was 2.39 ± 1.01 among asymptomatic patients and 2.97 ± 1.08 among symptomatic patients; Day 2 was 0.7 ± 1.06 among asymptomatic patients and 1.32 ± 1.04 among symptomatic patients; Day 3 was 0.03 ± 0.24 among asymptomatic patients and 0.13 ± 0.44 among symptomatic patients.

Table 4. Comparison of the mean Visual Analog scale pain rating according to the pre-surgical condition from day 1 to 3.

Visual Analog scale Pain Rating	n	Day 1		Day 2		Day 3	
		Mean	SD	Mean	SD	Mean	SD
Asymptomatic	269	2.87	1.36	0.74	0.98	0.03	0.23
Symptomatic	231	3.47	1.28	1.29	1.1	0.13	0.39
Total	500	3.14	1.36	0.99	1.07	0.08	0.32
T-Test	T test – $p < 0.05$, Significant			T test – $p < 0.05$, Significant		T test – $p < 0.05$, Significant	

The Mean Visual Analog scale Pain Rating on Day 1 was 2.87 ± 1.36 among asymptomatic patients and 3.47 ± 1.28 among symptomatic patients; Day 2 was 0.74 ± 0.98 among asymptomatic patients and 1.29 ± 1.1 among symptomatic patients; Day 3 was 0.03 ± 0.23 among asymptomatic patients and 0.13 ± 0.39 among symptomatic patients.

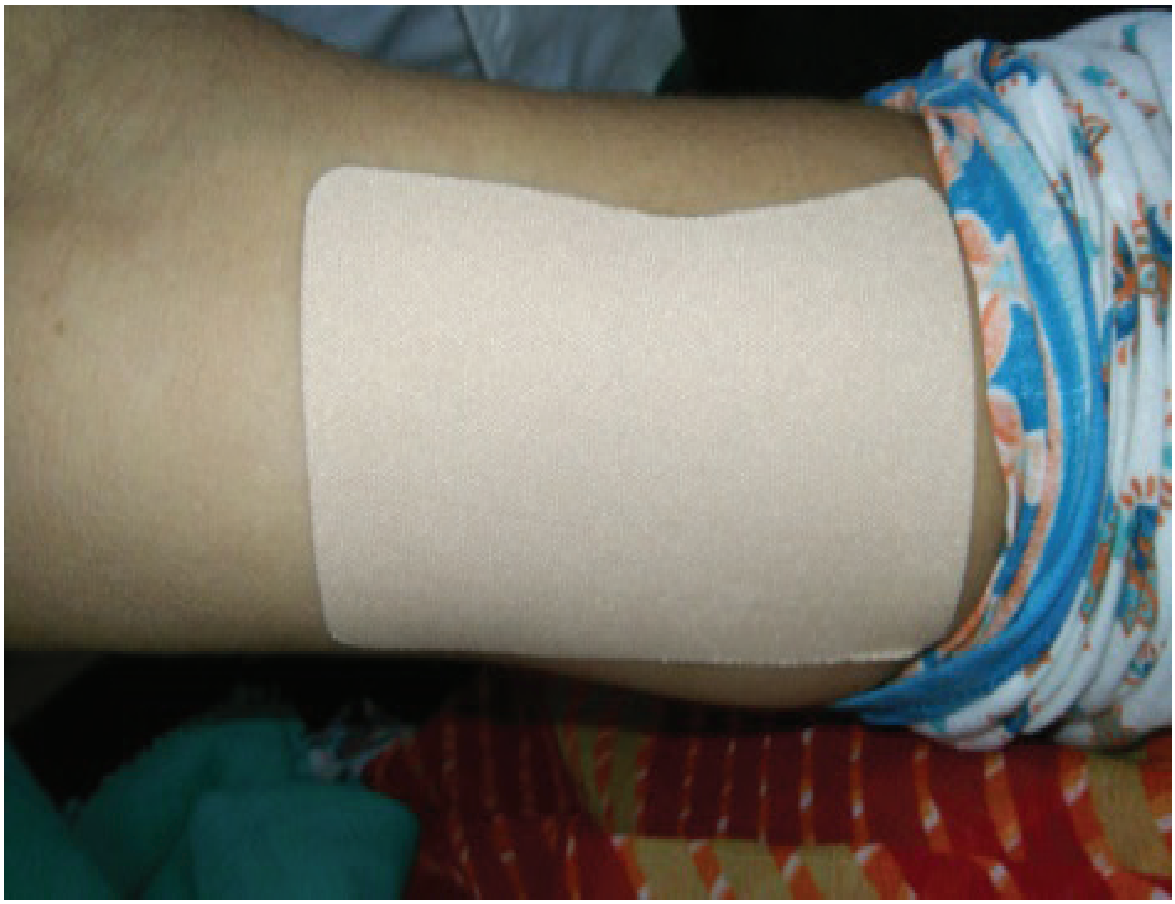

Figure 1: Applied Diclofenac Transdermal patch

Figure 2. Comparison of pain rating according to the time taken for the surgery

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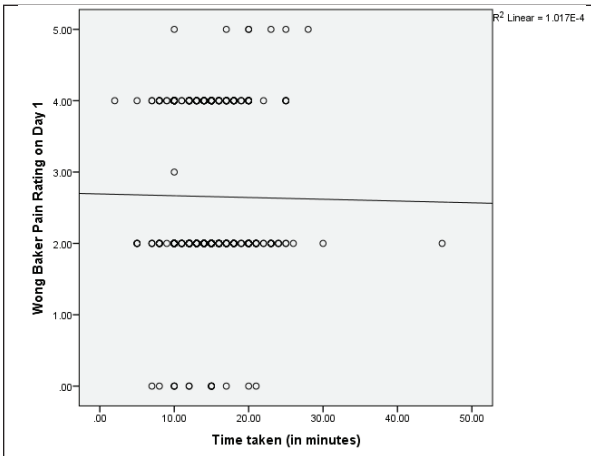
<td> 
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<td>There is no correlation between the time taken in minutes and Wong-Baker Pain Rating on Day 1. (r = -0.01) There was no statistical significance (p>0.05).</td>
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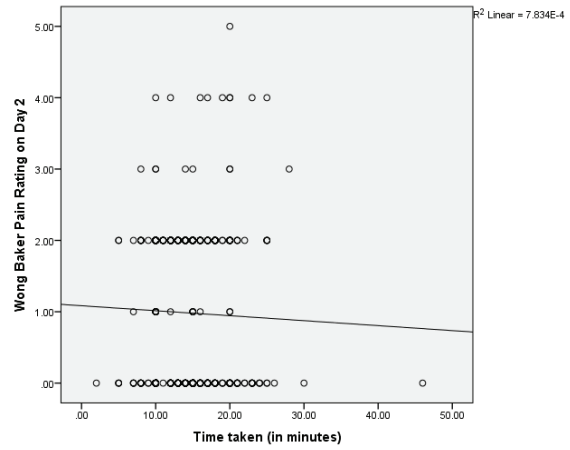
<td> 
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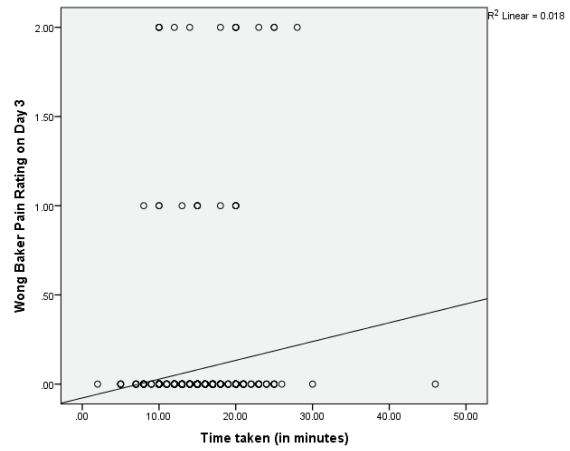
<td> 
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<td>There is a mild positive correlation between the time taken in minutes and Wong-Baker Pain Rating on Day 3. (r = .133) There was statistical significance (p<0.05).</td>
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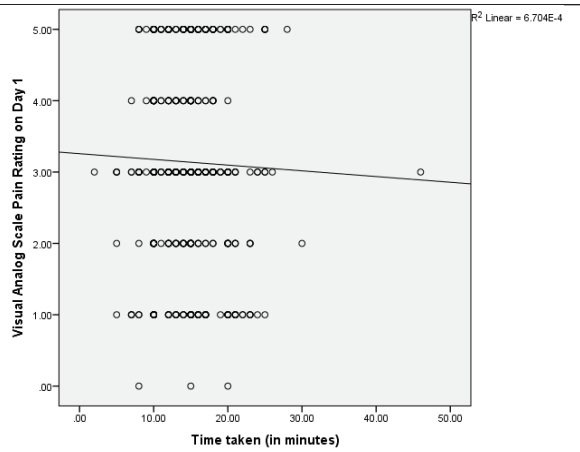
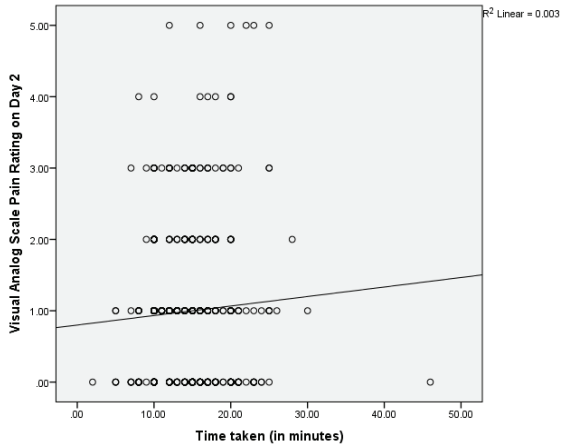
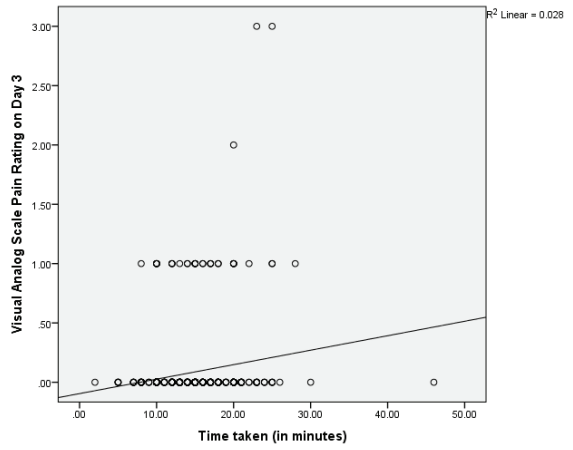
	There is no correlation between the time taken in minutes and Visual Analog Scale Pain Rating on Day 1. (r = -0.02) There was no statistical significance (p>0.05).
	There is no correlation between the time taken in minutes and Visual Analog Scale Pain Rating on Day 2. (r = 0.05) There was no statistical significance (p>0.05).
	There is a mild positive correlation between the time taken in minutes and Visual Analog Scale Pain Rating on Day 3. (r = 0.167) There was statistical significance (p<0.05).

Discussion

Management of pain is one of the frequently found complications associated with dental practices, mainly by oral and maxillofacial surgeons. Patients are sometimes coming with painful problems, and most of the times the treatment rendered causes pain postoperatively. Every surgeon must be ready to deal with pre-operative, intra-operative and postoperative pain and its treatment. To do this successfully it is necessary to know the biology of pain, recent theories and practices for its management.[5] Treatments for pain can be classified as pharmacologic and non-pharmacologic. Non-pharmacological approaches for the treatment of pain are psychological approaches, physical rehabilitation and surgical approaches. Pharmacological management is the mainstay of pain therapy. Drugs available for

management of pain belong to two major groups: The Non-Narcotic analgesics (NSAIDs and acetaminophen) and The Opioids (or Narcotics). Various formulations of Diclofenac are present for topical administration; Diclofenac sodium, Diclofenac diethylamine (DEA), and Diclofenac Epolamine (EPA).[6] The potassium salt of diclofenac (DFK) which was also administered orally was also checked for skin penetration capabilities. In comparison to the free acid than these salts, they have higher aqueous solubility as the previous is to have a solubility of 60 mm in the water at 25 °C and an intrinsic solubility value of 1.03 _ 0.7 mg/mL, as determined by using acid-base titration.[7,8] Diclofenac exercises analgesic, antipyretic and anti-inflammatory activities by COX 1& COX-II inhibitor with 4-fold advanced discrimination for the latter.

Transdermal patches are nowadays used in various treatment modalities including cosmetic purposes. The patch emerged as a product of various developments in the technology of skin science. Transdermal delivery at the earliest was studied and recognized by Dale Wurster. Most of his studies regarding proper dose, area of application, vehicle and device of the transdermal delivery system are significant.[9] Presently, it has been recommended that the vasculature of the dermis provides the main course to the deeper tissues to transfer anti-inflammatory drugs which are tightly bound. A rate-controlling membrane was used to regulate the rate of delivery of transdermal medications from a bandage to the skin for systemic circulation.

The major disadvantage of transdermal patches is the adverse skin reactions it causes, especially when it is used for a long period which results in extended contact with the skin. Two types of skin reaction have been observed by using patches, that is irritant contact dermatitis and allergic contact dermatitis out of which the former is more commonly seen. Most of the time it is the drug which causes the reaction rather than the other components of the patch. This kind of reaction causes poor patient compliance leading to the discontinuity of the treatment.[10,11]

There are various advantages of transdermal delivery over the oral route. First and foremost, it is used when there is a first-pass metabolism effect of the liver which impulsively metabolize the medications. Over hypodermic injections they have the advantage of being painless, not generating any kind of dangerous hospital waste and avoidance of any chances of transmission of diseases cross-contamination rendered from needle reuse.[12]Additionally, transdermal patches are non-invasive and can be self-applicable increasing the patient compliance. They provide extended-release of the drug for a longer period.

A disadvantage of the transdermal delivery system is that only a few numbers of drugs which can be administered by this route. Recent advances have enabled transport of molecules of molecular mass up to few hundred Dalton, which exhibit octanol-water partition coefficients that highly favour lipids and need doses of milligrams /day or less.[13] Transdermal delivery of peptides macromolecules, including recent genetic method employing DNA or siRNA (small-interfering RNA), has also been studied. The other usage of transdermal delivery includes delivery of vaccines, patient-regulated drug delivery system of fentanyl moderated by electricity to reduce pain (iontophoresis), extracting molecules (analytes) via skin e.g. Extraction of interstitial fluid for glucose monitoring.

Conclusion

This study was done to evaluate the efficacy of transdermal patch of diclofenac sodium in any minor oral surgery. Out of 537 patients who have prescribed the patch, 37 patients were excluded in the study as they took other medications due to either fever or swelling or if the patient were incompliant. The statistical analysis was made on the other 500 patients. The conclusion achieved after the complete study is that, there is no difference in pain relief between male and female patients. Further, there is a significant difference in pain scores between symptomatic and asymptomatic patients. From the graphs, it was evident that on day 1 and day 2 pain relief was better in asymptomatic patients when compared to symptomatic patients whereas on day 3 there is not much difference in scores, but this is significant - due to big sample size. The time is taken for the procedure also did not have much significance on the 1st and 2nd day whereas on 3rd day it had a mild effect. Hence, the transdermal patch can be effectively used for analgesic effect following minor oral surgical procedures of lesser duration. It is effective for the management of mild

to moderate pain relief as it has proved to be a good option as an analgesic especially in patients with gastric problems and for better compliance. The only drawbacks of this patch are that it is not waterproof and any contact of the patch with water will decrease its effectiveness moreover this patch has not shown promising results on symptomatic patients i.e. patients having pain before the surgical procedure. There are only a few clinical trials with larger samples out of which this is one of them, hence there is a need to have more trials in various fields of medicine and dentistry and the third-generation patches should be explored and developed for better transport of the drug transdermally.

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Ethical Permission: Approved

References

1. Predel HG, Koll R, Pabst H, Dieter R, et al. Diclofenac patch for topical treatment of acute impact injuries: a randomised, double-blind, placebo-controlled, multicentre study Br J Sports Med 2004;38:318–323.
2. Agarwal A, Gautam S, Gupta D, Singh U. Transdermal diclofenac patch vs eutectic mixture of local anesthetics for venous cannulation pain. Can J Anesth 2007; 54(3):196-200.
3. Zuniga JR, Phillips CL, Shugars D, Lyon JA, Peroutka SJ, Swarbrick J, Bon C. Analgesic Safety and Efficacy of Diclofenac Sodium Softgels on Postoperative Third Molar Extraction Pain. J Oral and Maxillofac Surg 2004; 62(7): 806–815
4. Krishna R, Nataraj MS. Efficacy of a single dose of a transdermal diclofenac patch as pre-emptive postoperative analgesia: a comparison with intramuscular diclofenac. South Afr J Anaesth Analg 2012;18(4):194-197.
5. Pastore MN, Kalia YN, Horstmann M, Roberts MS. Transdermal patches: history, development and pharmacology British J Pharmacol 2015; 172: 2179–2209
6. Puria A, Murnane KS, Blough BE, Banga AK. Effects of chemical and physical enhancement techniques on transdermal delivery of 3-fluoroamphetamine hydrochloride. Int J Pharma 2017; 528: 452–462
7. Fang JY, Sung KC, Lin HH, Fang CL. Transdermal iontophoretic delivery of diclofenac sodium from various polymer formulations: in vitro and in vivo studies. Int J Pharma 1984; 178: 83–92.
8. Godin B, Touitou E. Transdermal skin delivery: Predictions for humans from in vivo, ex vivo and animal models. Advanced Drug Delivery Reviews 2007; 59: 1152–1161
9. Funk L, Umaar R, Molajo A. Diclofenac patches for postoperative shoulder pain Int J Shoulder Surg 2008; 2(2): 47–48.
10. Rahimi M, Makrem J. Effects of diclofenac epolamine patch on postoperative sore throat in parturients after cesarean delivery under endotracheal general anesthesia Acta Anaesthesiol Taiwan 2000;47(1):17−21
11. Cegu MP, Murthy N. Pre-treatment with chemical penetration enhancers in dermal/transdermal drug delivery J Drug Del Sci Tech 2002; 24 (3) 251-254
12. Bhaskar H, Kapoor P, Ragini. Comparison of transdermal diclofenac patch with oral diclofenac as an analgesic modality following multiple premolar extractions in orthodontic patients: A Cross over efficacy trial. Contempt Clin Dent 2010;1(3):158-63
13. Kogan A, Garti N. Microemulsions as transdermal drug delivery vehicles Adv Colloid Interface Sci 2006;123–126: 369–385