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TO EVALUATE THE EFFICACY OF TRANSDERMAL DICLOFENAC PATCH IN THE MANAGEMENT OF POST SURGICAL PAIN

Surgery

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ABSTRACT

Postoperative pain is one of the most fearful experience for patients because millions of cells are injured during surgery. The efficacy of pain relief after surgery is one of the most important factors necessary for the discharge of patients from the hospital

Diclofenac sodium, a NSAID, has anti-inflammatory, analgesic and anti-pyretic activity. Oral administration of diclofenac is the route of choice in daily practice but it has few drawbacks like hepatic first pass metabolism, inability of the patient to take it orally in some. The parentral route is irritating and hence painful at the site of administration. Intramusclular injections of NSAIDS have many side effects like erythema, pruritis, oedema, abscess and necrosis.

In transdermal drug delivery system the delivery of the active ingredients of the drug occurs through the skin. The transdermal delivery system has the advantages of therapeutic efficacy and safety of the drugs as the drug is delivered through the skin at a predetermined and controlled rate.

KEYWORDS

Oral surgery. Postsurgical paincontrol .Transdermalpatch .Diclofenac . Dental extraction .

Postoperative pain is one of the most fearful experience for patients because millions of cells are injured during surgery.[1] Postsurgical pain management has always been a big challenge for the surgeons. Different methods to control post surgical pain have been tried from time to time. NSAIDS till today are the most prescribed analgesics for the control of pain after dental surgeries. Among NSAIDS Diclofenac sodium is commonly prescribed. It has anti-inflammatory, analgesic and antipyretic activity.

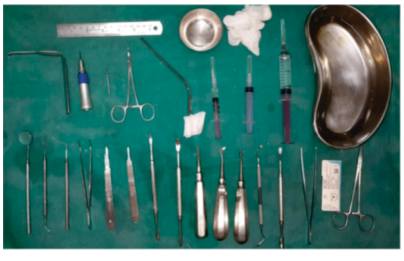
Oral administration of diclofenac is the route of choice in daily practice but due to the first pass metabolism only about 50% of the absorbed dose becomes systemically available. Oral diclofenac also carries the potential for significant adverse reactions due to the high plasma concentrations attained, particularly those involving the gastrointestinal tract.[2]parentral route is irritating and hence painful at the site of administration. Intramuscular injections of NSAIDS have many side effects like erythema, pruritus, oedema, abscess and necrosis.[3]

To overcome these drawbacks newer drug delivery systems such as transdermal patches using pain relieving or modifying agents have emerged. Transdermal drug delivery provide an advantage of controlled drug delivery at the local site, either over the skin or buccal mucosa in the oral cavity. The drug in the transdermal patch enters the body through skin and ultimately diffuses into capillaries for systemic delivery.[4]

MATERIALAND METHODS

The study was conducted on 100 patients who reported to the Department of Oal& Maxillofacial Surgery, Dr HSJ Institute of Dental Sciences, Chandigarh , with impacted mandibular third molars and underwent transalveolar extraction of the same under local anaesthesia. Diclofenac transdermal patch was applied on the ipsilateral shoulder at zero hour postoperatively and changed every 24 hours postoperatively for 3 days. Pain intensity and pain relief was recorded for 3 post operative days using 5 point verbal pain intensity and pain relief score chart (fig 2) Paracetamol was allowed as rescue analgesia in case the pain intensity score is > 3. The following patients were excluded from the study, hypersensitivity to NSAIDS, patients with hepatic, neurological &haemorrhagicdiasthesis, gastric or intestinal ulcers, pregnancy and lactation, asthamatic patients, patients with urticaria, rhinitis or renal disease. Ethical clearance was obtained from institutional Ethical Committe

Frequency distribution scores for visual analogue scale (VAS scale) were used and median values were calculated as the data didn't have normal distribution. The normality of the data was checked using Kolmogorov-Smirnov test. Since distribution was not normal nonparametric test namely Friedmann test was used to compare median pain intensity scores among different time interwals. Wilkoxan sign rank test was used to further compare significant difference between pain intensity scores at different time interwals (one by one comparison). The p value < 0.001was taken as statistically significant. Similar analysis was done for median pain relief scores. Spearman correlation coefficient was also calculated.



Armamentarium used for extraction: fig 1

Fig 2

Patient name:
Age:
Sex:
OPD No:

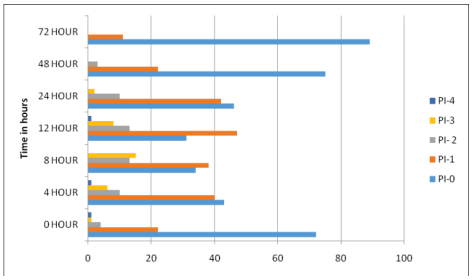
Pain intensity scale
0- None
1- Very mild
2- Mild
3- Moderate
4- Severe

Pain relief scale
0- None

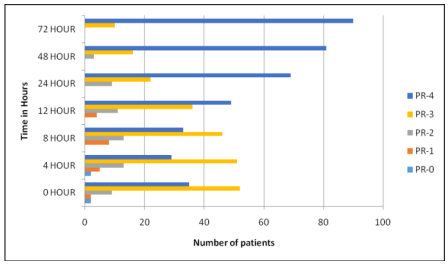
1- A little
2- Some
3- A lot
4- Complete

Rescue analgesia
Yes
No

RESULTS



Graph 1: Frequency distribution of Pain Intensity (PI) Scores at different time intervals



Number of patientsGraph 2- Frequency distribution of Pain Relief (PR) Scores at different time intervals

Number of patients

Graph I describes frequency distribution of pain intensity scores (score 0,1,2,3,4 on 5 point verbal pain intensity scale) at different time intervals namely 0 hours,,8,12,24,48,72 hours

At 0 hours more than 70% of patients reported 0 score (i.e no pain). Number of patients with pain intensity score 1,2, and 3 increased as the time passed till 24 hours and then it started decreasing at 48 hours and the pain intensity score reached 0 for 75% patients, at 72 hours pain intensity score of zero was reported by more than 85% of patients (graph I)

Similarly graph 2 describes frequency distribution of pain relief at different time intervals. At 0 hours more than 50% of patients reported 3 score(i.e a lot of pain relief). Pain relief score of 4 started gradually increasing from 4 hours to 48 hours with more than 80% of patients reporting pain relief 4 at 48 hours. At 72 hours more than 85% of patients reported pain relief score 4 (i.e complete pain relief)(graph 2)

Table 1- Comparison of median Pain Intensity (PI) Scores at different time intervals*

Time in hours		Z score[a]	P- value
0 hour	4	-4.685[b]	<o.oo1**
	8	-5.368[b]	
	12	-5.255[b]	
	24	-3.325[b]	
	48	-0.875[c]	
	72	-3.352[c]	
4 hours	8	-2.559[b]	0.011
	12	-1.779[b]	0.075
	24	-1.128[c]	0.259
	48	-4.858[c]	<0.001**
	72	-6.239[c]	<0.001**
8 hours	12	-0.998[b]	0.318
	24	-3.925[b]	<0.001**
	48	-5.983[b]	
	72	-6.881[b]	
12 hours	24	-4.257[b]	
	48	-6.571[b]	
	72	-7.181[b]	
24 hours	48	-5.423[b]	
	72	-6.503[b]	
48 hours	72	-3.545[b]	

* Friedman test used to find statically significant difference among groups
** statistically significant values at p<- 0.001
a- wilcoxan sign rank test
b- based on negative ranks
c- based on positive ranks

Table 2- Comparison of median Pain Relief (PR) Scores at different time intervals*

Time in hours		Z score[a]	P- value
0 hours	4	-2.079[b]	0.038
	8	-1.371[b]	0.170
	12	-1.357[c]	0.175
	24	-4.367[c]	<0.001**
	48	-6.036[c]	
	72	-6.934[c]	
4 hours	8	-0.498[b]	0.619
	12	-3.520[b]	<0.001**
	24	-5.543[b]	
	48	-6.862[b]	
	72	-7.180[b]	
8 hours	12	-3.284[b]	0.001**
	24	-5.706[b]	<0.001**
	48	-6.796[b]	
	72	-6.921[b]	
12 hours	24	-4.625[b]	
	48	-5.880[b]	
	72	-6.030[b]	
24 hours	48	-3.522[b]	
	72	-4.499[b]	
48 hours	72	-2.683[b]	0.007

* Friedman test used to find statically significant difference among groups
** statistically significant values at p<- 0.001
a- wilcoxan sign rank test
b- based on negative ranks
c- based on positive ranks

Table 1 shows comparison of median pain intensity scores between different time intervals. Wilcoxan sign rank test was used and z scores were calculated. Median pain intensity scores at 0 hours were compared with median pain intensity at 4 hours, 8 hours, 12, 24,48 and 72 hours. Statistically significant difference was observed in all the above comparisons at p value <0.001. Similar comparisons were made for other time intervals. At 4 hours no statistically significant difference was observed in median pain intensity scores when compared with 8,12 ,24 hours. However significant difference was seen when compared with 48, and 72 hours.

At 8 hours no statistically significant difference was observed in median pain intensity scores when compared with 12 hours. However significant difference was seen when compared with 24,48, and 72 hours.

At 12 hours statistically significant difference was observed in median pain intensity scores when compared with 24, 48, and 72 hours.

At 24 hours statistically significant difference was observed in median pain intensity scores when compared with 48, and 72 hours.

At 48 hours statistically significant difference was observed in median pain intensity scores when compared with 72 hours.

Table 2 shows comparison of median pain relief scores between different time intervals. Wilcoxan sign rank test was used and z scores were calculated. Median pain relief scores at 0 hours were compared with median pain reliefat 4 hours, 8 hours, 12, 24,48 and 72 hours. Statistically significant difference was observed when compared with 24, 48 and 72 hours at p value <0.001. However at 4,8,12 hours no

statistically significant difference was observed. Similar comparisons were made for other time intervals.

At 4 hours no statistically significant difference was observed in median pain relief scores when compared with 8 hours. However significant difference was observed when compared with 12, 24,48 and 72 hours.

At 8 hours no statistically significant difference was observed in median pain relief scores when compared with 12 hours. However significant difference was observed when compared with 24,48 and 72 hours.

At 12 hours significant difference was observed when compared with 24,48 and 72 hours.

At 24 hours significant difference was observed when compared with 48 and 72 hours.

Table 3- Correlation between Median Pain Intensity (PI) and Pain Relief (PR) at different time intervals*

Time in hours	Variables	Correlation Coefficient Value
4	Pain Intensity And Pain Relief	-0.427
8		-0.465
12		-0.711
24		-0.554
48		-0.558
72		-0.629

*Statistical test used- Spearman Correlation Coefficient, Correlation is significant at the p- value <_ 0.001

Table 3 shows co relation between median pain intensity scores & median pain relief scores at different time interwals. Both were co-related. However there was no statistically significant difference between the two at p value < 0.001

Rescue analgesia was taken by 35 patients and 65 patients were relieved of pain with transdermal patch. For tables 1,2& 3 the patients who used rescue analgesia (35 patients) were excluded from analysis.

3 patients had secondary healing due to early loss of suture.

DISCUSSION

Pain control or pain elimination is considered as one of the most important aspects of practicing dentistry. In the past pain has been so closely associated with dentistry that the words pain and dentistry have become almost synonyms[5]

Patients undergoing removal of impacted mandibular 3rd molars are considered standardised mode for the evaluation of acute surgical pain due to the following characteristics- the surgeries are elective,patients are young and healthy and ambulatory, the performed procedures are consistent and are generally completed within 25 minutes[6]. An estimated of 63.5% of patients experience severe pain at sometime during 1st day for this reason oral analgesic is provided as a standard care for postoperative time periods for atleast 24 hours.In this study< 5% of patients experienced severe pain in first 24 hours, mild pain was reported by 10% at 24 hours and moderate pain was reported by<5 % of patients Non steroidal anti-inflammatory drugs work well to relieve mild to moderate intense postoperative pain caused by 3rd molar surgery[7].

NSAIDS when administered systemically have been implicated in various adverse events due to their inherent mechanism of inhibiting prostaglandin synthesis thereby disrupting the general physiologic system[8]. The local drug application provided an alternative system of administration which may be beneficial in reducing the unfavourable reaction to some extent. Topical formulations of NSAIDS offer advantage of local, enhanced drug delivery to the affected tissues with a lower incidence of systemic adverse affects.

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 the release liner, adhesive serves to adhere the components of the patch to the skin, membrane controls the release of drug from the reservoir and multilayers patches and backing protects the patch from outer environment.[9]The drug (NSAIDS) contained in the transdermal patch enters the body through skin and ultimately diffuses into the capillaries for systemic delivery. The steady permeation of the drug across the skin allows for more consistent serum drug levels often a goal of therapy[4,10]

In the present study 100mg transdermal diclofenac patch was used once daily for 3 post operative days and 65% of the patients were relieved of pain not requiring any rescue analgesia

In terms of safety the patch was well tolerated and did not cause any local or systemic adverse effects. However Agarwal et al[11] reported the occurrence of a localized erythematous rash or pruritis at the site of application of transdermal patch. Safety profile of diclofenac patch has also been emphasized by Mason et al[12], by studies reporting the use of diclofenac transdermal patch in osteoarthritis[13],and its use in sports related injuries.[14]

Gopal swaroop et al[15]in their study reported lesser skin side effects in patch group(2%) as compared to 14% in the injection group. They also highlighted few points like slow onset of action after application of patch and suggested that the patch has to be applied in anticipation to pain and not after the pain sets in. Also the authors reported poor adhesiveness of the patch due to which it loosened and peeled off when applied in summers(due to sweating) or to loose mobile skin parts of the body such as arm or gluteal region. However none of the patients in our study reported any skin problem or loosening of patch.

Patch has following advantages over injection/ oral route like Lesser local side effects like skin erythema,pruritis,oedema,abscess and necrosis. Non invasive and can be self administered, improve patient compliance, can be used in patients who are unable to swallow the oral medication or in whom oral route is to be avoided due to GIT pathologies, avoids 1st pass metabolism in liver as the drug enters systemic circulation directly and drug destruction by stomach and digestive enzymes does not occur.

Limitations of the study

Surgeries were carried out by the post graduate students so the trauma during the extraction can be expected to be more as compared to a trained/ experienced surgeon.

The results were totally dependent on the VAS scores of pain intensity and pain control filled by the patients. Different patients may have different inflammatory/ pain response. The results depend on the information provided by the patients which may not be accurate

CONCLUSION

Side effects related to oral or parentral administration of analgesics are reduced by transdermal patches as it bypasses the hepatic first pass metabolism. Also the drug achieves a constant and controlled drug release. These are easy to use and are effective in reducing the post operative pain. Inspite of so many advantages the patches are not used in routine practice. This may be due to lack of awareness and cost of the patch

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