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COMPARATIVE EVALUATION OF THE EFFICACY OF TWO MODES OF DELIVERY OF DICLOFENAC FOR THE MANAGEMENT OF POST ENDODONTIC PAIN- A RANDOMIZED CONTROLLED CLINICAL TRIAL

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Abstract –

Background/purpose: There is a presence of basic relationship among pre and post endodontic torment and roughly 80% of the patients with preoperative agony continue to uncover delicate to serious distress after endodontic treatment. Likewise, counteraction and the board of postoperative torment turns into an imperative piece of endodontic treatment. Showing patients, the ordinary post-employable endodontic aggravation and suggesting medications assemble patients' certainty, limit and can pursue their demeanour towards endodontic treatment. Consequently, utilization of pre-usable pain relieving has displayed to decrease the beginning of postoperative agony.

Aim: The study aims to establish the effectiveness of pre-treatment with diclofenac in managing the post-endodontic pain while comparing two modes of delivery systems of same i.e. oral, and transdermal patch in terms of efficacy.

Materials and methods: a randomized controlled trial was done on180 patients aged 18-65 years with irreversible pulpitis. The patients were aggregated in three groups: oral (group B) and transdermal (group C) administration of diclofenac was done in patient's right before undergoing any endodontic treatment. While in Group A acetaminophen a rescue pill was administered to the patients. A Visual analog scale (VAS) was used to examine the pain and then it was also analyzed statistically.

Results: In each of the three groups, the pain frequency was assessed at intervals of the first 4 hours, 8 hours, 12 hours, 24 hours, and 48 hours following surgery. With statistically significant p values, the transdermal diclofenac patch (group C) appears to be a promising analgesic method for the therapy of endodontic pain.

Conclusion: the study emphasizes the use of preoperative analgesics in reducing post endodontic pain.
KEYWORDS- Analgesics ;Diclofenac ; Endodontic ; Treatment;

Introduction

Pain is a common, irksome emotional or sensory sensation that is mostly linked to existing or potential tissue damage. Pre- and post-endodontic pain have a comparable, substantial association.[1] According to Oliet, Glassman et al. observed a highly varied prevalence of discomfort during root canal therapy ranging from 82.9% to 10.6%. Typically, post-endodontic pain is observed to be more severe in the first 48 hours and lessens with time, going away completely after 7–10 days. While pain is not a symptom of endodontic failure, its alleviation is typically more crucial than the outcome of the procedure. Instrumentation and obturation cause post-endodontic discomfort. It has been noted that when microorganisms are instrumented and extruded, there is an enhanced inflammatory response. Therefore, patients may become dissatisfied if they have ongoing discomfort following endodontic therapy.[2]

Occlusal reduction, local anaesthetic provision of systemic analgesics, anti-inflammatory medicines, or antibiotics are the typical methods used to control pain. The release of inflammatory mediators is inhibited as part of the anti-inflammatory process.[2] Some analgesics may be administered preoperatively to help delay the onset of postoperative discomfort.

When the diclofenac medication was first introduced in 1974, it was mostly used to treat pain in Japan. The 'Australian Therapeutic Guidelines advised using conventional NSAIDs, namely diclofenac, as a second line drug for the treatment of moderate pain following paracetamol. Diclofenac's comparative effectiveness in multiple trials were shown to be among the highest of all NSAIDs. Despite the lack of data supporting the efficacy of diclofenac against placebo, Trelle S et al (2011) undertook research with 100 patients to compare the effects of NSAIDs with placebo. Diclofenac has been the most frequently utilised standard therapy as "Therapeutic goods administration" in clinical studies when COX-2 inhibitors were compared to other treatments.[3]

Endodontic therapy is critically dependent on the prevention and control of postoperative endodontic pain. Due to its antipyretic, anti-inflammatory, and analgesic properties, diclofenac is one of the analgesics that is frequently given to treat pain. It can be used to relieve any pain, including pre- and post-endodontic pain, as an oral tablet or transdermal patch. In order to determine the efficacy of pretreatment diclofenac in the management of post-endodontic pain, this study compared the efficacy of two routes of diclofenac delivery: oral and transdermal patch.

Materials and methods

A full history of the patient's presenting disease and their demographic information were gathered before to therapy in randomised controlled clinical research involving 180 participants between the ages of 18 and 65.

Patients reporting with pain and diagnosed with irreversible pulpitis in mandibular molars, which can be treated endodontically in one visit, were part of the study. While, patients with known sensitivity to diclofenac and allergy to any anti-inflammatory drugs, pregnant or lactating females, patients with history of asthma or any stomach and intestinal disorders were excluded from the study. Exclusion Criteria of the study also included teeth with any periapical infections.

After receiving agreement from the patients in writing and approval from the college's ethical committee, the participants who met the inclusion criteria were chosen and divided into one of three groups (60 each).

GROUP A (Control group) patients received simply an over-the-counter pain reliever (Acetaminophen) in the event that they experienced pain following root canal therapy.

GROUP B: Oral diclofenac group, where patients took diclofenac tablet orally right before undergoing root canal treatment.

GROUP C: Transdermal diclofenac patch group, where patients were placed transdermal patch on the arm just before undergoing root canal treatment.

PROCEDURE: All groups underwent a single consultation for root canal therapy, and the intensity of postoperative pain was evaluated using a visual analogue scale score after 4, 6, 8, 12, and 48 hours. In the event that they experienced discomfort, patients were given a rescue medication (Acetaminophen). The patient was given a feedback form (a Visual Analogue Scale), and he or she was contacted by phone to remind them to complete it. A 48-hour follow-up was conducted.

CRITERIA FOR THE ASSESSMENT OF PAIN: Pain was

assessed using Visual Analog Scale (VAS)

• NO PAIN: The treated tooth felt normal. patient did not have any pain. (0)

• DISTRESSING PAIN: Discomforting, but bearable pain. (1- 7)

•SEVERE PAIN: Difficult to bear. (8-10)

Statistical Analysis

The three groups were analysed statistically using Wilcoxon signed ranks test and Mann Whitney test. Intra group comparison at various time interval was done using Wilcoxon Signed Ranks Test. Intergroup comparison was done using Mann Whitney test. For the purpose of statistical interpretation, p value of 0.05 was considered statistically significant.

Results -

TABLE 1	GROUP	N	MEAN RANK	SUM OF RANKS
Change in VAS(BL-4 Hrs)	Control	60	8.60	86.00
	Oral Diclofenac	60	12.40	124.00
	TOTAL	120		
Change in VAS(BL-8 Hrs)	Control	60	9.95	99.50
	Oral Diclofenac	60	11.05	110.50
	TOTAL	120		
Change in VAS(BL-12 Hrs)	Control	60	7.95	79.50
	Oral Diclofenac	60	13.05	130.50

	TOTAL	120		
Change in VAS(BL-24 Hrs)	Control	60	8.05	80.50
	Oral Diclofenac	60	12.95	129.50
	TOTAL	120		
Change in VAS(BL-48 Hrs)	Control	60	7.80	78.00
	Oral Diclofenac	60	13.20	132.00
	TOTAL	120		

TABLE 1: In Group A (Control Group) and B (Oral Diclofenac Patch Group) comparisons

TABLE 2: COMPARINING THE EFFICACY	**VAS :PREOPER - ATIVE**	**VAS :4 HRS**	**VAS :8 HRS**	**VAS :12 HRS**	**VAS :24 HRS**	**VAS :48 HRS**
Mann-Whitney U	31.000	49.000	34.500	26.500	39.500	28.500
Wilcoxon W	86.000	104.000	89.500	81.500	94.500	83.500
Z	-1.473	-.081	-1.215	-1.824	-.828	-1.747
Asymp. Sig.(2-tailed)	.141	.935	.224	.068	.408	.081
Exact Sig. [2*(1-tailed Sig.)]	.165[a]	.971[a]	.247[a]	.075[a]	.436[a]	.105[a]

In table 2, comparison between Control group and oral diclofenac group was done. The pain frequency was measured at 4 hrs., 8 hrs., 12 hrs., 24 hrs. and 48 hrs. postoperatively.

In this study of 180 patients, 60 patients were studied in each of the three groups. The efficacy of drugs was measured in all the three groups. The pain frequency was measured at 4 hrs., 8 hrs., 12 hrs., 24hrs. and 48 hrs. postoperatively. The above statistics shows that at 4 hrs., 8 hrs., 12 hrs., 24 hrs. and 48 hrs. postoperatively the p value was found to be 0.935, 0.224, 0.068, 0.408, and 0.081 respectively. All the values were found to be statistically insignificant for all the groups

TABLE 3:	GROUP	N	MEAN RANK	SUM OF RANKS
Change in VAS(BL-4 Hrs)	Oral Diclofenac	60	11.50	115.00
	Diclofenac Transdermal Patch	60	9.50	95.00
	TOTAL	120		
Change in VAS(BL-8 Hrs)	Oral Diclofenac	60	8.25	82.50
	Diclofenac Transdermal Patch	60	12.75	127.50
	TOTAL	120		
Change in VAS(BL-12 Hrs)	Oral Diclofenac	60	10.00	100.00
	Diclofenac Transdermal Patch	60	11.00	110.00
	TOTAL	120		
Change in VAS(BL-24 Hrs)	Oral Diclofenac	60	8.40	84.00
	Diclofenac Transdermal Patch	60	12.60	126.00
	TOTAL	120		
Change in VAS(BL-48 Hrs)	Oral Diclofenac	60	10.50	105.00
	Diclofenac Transdermal Patch	60	10.50	105.00
	TOTAL	120		

TABLE 3: In Group B (Oral Diclofenac Group) and C (Transdermal Patch Group) comparisons

TABLE 4: COMPARINING THE EFFICACY	VAS :PREOPERATIVE	VAS :4 HRS	VAS :8 HRS	VAS :12 HRS	VAS :24 HRS	VAS :48 HRS
Mann-Whitney U	49.000	46.000	23.000	43.000	26.000	41.500
Wilcoxon W	104.000	101.0	78.0	98.0	81.0	96.5

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Z	-.082	-.326	-2.103	-.568	-1.882	-.661
Asymp. Sig. (2-tailed)	.935	.744	.035	.570	.060	.508
Exact Sig. [2*(1-tailed Sig.)]	.971[a]	.796[a]	.043[a]	.631[a]	.075[a]	.529[a]

In table 4, comparison between group oral and diclofenac transdermal patch was done. The pain frequency was measured at 4 hrs., 8 hrs., 12 hrs., 24 hrs. and 48 hrs. postoperatively with p-values of 0.744, 0.035, 0.570, 0.060 and 0.508 and was statistically insignificant.

TABLE 5: In Group A (Control Group) and C (Transdermal Patch Group) comparisons

TABLE 5:	GROUP	N	MEAN RANK	SUM OF RANKS
Change in VAS(BL-4 Hrs)	Control	60	8.85	88.50
	Diclofenac Transdermal Patch	60	12.15	121.50
	TOTAL	120		
Change in VAS(BL-8 Hrs)	Control	60	7.00	70.00
	Diclofenac Transdermal Patch	60	14.00	140.00
	TOTAL	120		
Change in VAS(BL-12 Hrs)	Control	60	7.25	72.50
	Diclofenac Transdermal Patch	60	13.75	137.50
	TOTAL	120		
Change in VAS(BL-24 Hrs)	Control	60	5.70	57.00
	Diclofenac Transdermal Patch	60	15.30	153.00
	TOTAL	120		
Change in VAS(BL-48 Hrs)	Control	60	5.85	58.50
	Diclofenac Transdermal Patch	60	15.15	151.50
	TOTAL	120		

TABLE 6: COMPARININGTHE EFFICACY	**VAS :Preopera-tive**	**VAS :4 HRS**	**VAS :8 HRS**	**VAS :12 HRS**	**VAS :24 HRS**	**VAS :48 HRS**

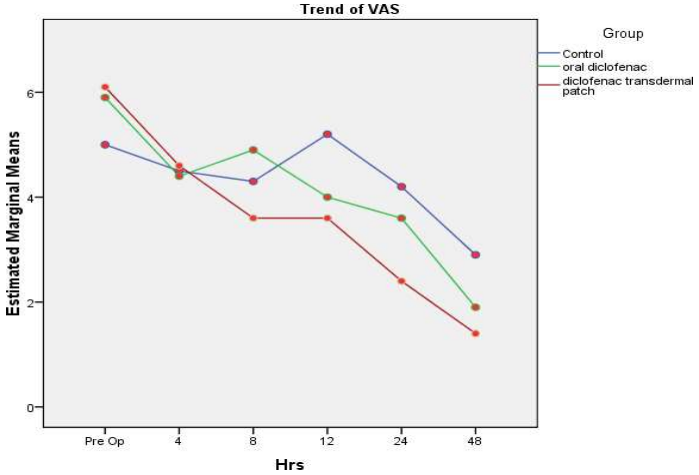
Mann-Whitney U	20.500	40.500	26.000	16.000	4.000	8.500
Wilcoxon W	75.500	95.500	81.000	71.000	59.000	63.500
Z	-2.378	-.781	-2.069	-2.655	-3.623	-3.294
Asymp. Sig. (2-tailed)	.017	.435	.039	.008	.000	.001
Exact Sig. [2*(1-tailed Sig.)]	.023[a]	.481[a]	.075[a]	.009[a]	.000[a]	.001[a]

Table 6 represents the comparison between groups: control group and diclofenac transdermal patch. The pain frequency was measured at time intervals of 4 hrs with p-value of 0.435 which was insignificant, 8 hrs., 12 hrs., 24hrs. and 48 hrs. postoperatively of p value, 0.039*, 0.008* and 0.000* respectively which were statically significant

Inference of Line Diagram

In control group, the pain frequency first decreases from preoperative period to 8 hrs. but after 8 hrs. it increases till12 hrs. and then decreases till 48 hrs. In oral diclofenac, the pain frequency, first decreased from preoperative period to 4 hrs., then increased from 4 hrs. to 8 hrs. and then again decreased from 8 hrs. till 48 hrs. In diclofenac transdermal patch group, the pain frequency was continuously found to decrease from preoperative period till 48 hrs.

Line Diagram



Discussion

Transdermal patches are preferred over oral route of drug administration to the systemic circulation for several reasons including the bioavailability which is increased and improved. Patients, who have difficulty in swallowing tablets and capsules, tempt to crush tablets to assist in swallowing which destroys the controlled release characteristics of the tablets. In such cases transdermal patches prove to be effect, safe and efficient in providing analgesic effect.

In our study, it was discovered that group B had less post-endodontic pain than group A (i.e., Group A > Group B), and this was because oral diclofenac has a quick beginning of effect due

to its quick absorption into the body. Derry et al. (2015) also observed clinical benefits of utilising diclofenac potassium that dissolves quickly and is absorbed, which provides more effective pain relief than diclofenac potassium that is absorbed more slowly.[4] [5] [8]

Dhiman S et al in 2011 stated that first pass metabolism in transdermal patches, was an additional limitation to oral drug delivery, which can be avoided with transdermal administration. A Transdermal patch also known as Skin patch uses a specialized membrane t which controls the rate at which the liquid drug contained in the reservoir of the patch can pass through the skin and into the bloodstream in a coordinated manner. Also, its action is prolonged due to its improved bioavailability, more uniform plasma levels, longer duration of action resulting in a reduction in dosing frequency, reduced side effects and improved therapy by maintaining plasma levels till the end of the dosing interval. At 12 hrs., 24 hrs., and 48 hrs. postoperatively the p value were 0.570, 0.060 and 0.508 respectively which were statistically insignificant. Dhanpal S in 2016 stated that the 50-sq. cm patch contains 100 mg of Diclofenac Diethyl amine as its active agent which permits sustained release of the drug hence offering better pain relief. The same size of patch was also been used in our study. Patel D et al (2012) stated that transdermal patch uses a specialized form of membrane which controls the rate of flow of drug from the reservoir within the patch to the skin and then to the bloodstream.A randomized control trial done by Mangal et al, concluded that transdermal patches of diclofenac was equally effective as an orally administered diclofenac. [1] [6] [7] [12]

When comparing group C with group A, the pain frequency was assessed at 4 hours. At 8 hours, 12 hours, 24 hours, and 48 hours, the p-value was 0.435, which was statistically insignificant. Postoperatively, the p values changed to have values of 0.039, 0.008, 0.000, and 0.001 correspondingly, making them statistically significant. In research by Pradel et al. (2004), diclofenac patch was used to treat acute traumatic blunt soft tissue injuries. It was shown to be very effective and well tolerated.[10] Mason et al. (2004) in their systematic assessment of topical NSAID usage in the UK and by papers describing the use of a diclofenac transdermal patch in osteoarthritis and sports-related injuries.[8] [9] [11]

Conclusion

Within the limitations of this present vivo study it was concluded that preoperative analgesics play an important role in reducing post endodontic pain. Transdermal patches containing diclofenac shows a promising analgesic modality managing endodontic pain. However, further studies having larger patient samples are required to explore the delivery of anti-inflammatory drugs through transdermal patches for the management of post endodontic pain.

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