Research Article

Analgesic Effectiveness of Ibuprofen and Aceclofenac in the Management of Acute Pulpitis - A Randomized Double Blind Trial.

[1]P.Pavithra, [2]M. Dhanraj, [3]Prathap Sekhar*

[1]Under graduate student, Saveetha Dental College, Chennai, India.

[2]Professor and Head of the Department, Department of Prosthodontics, Saveetha Dental College, Chennai, India.

[3]Senior lecturer, Department of Prosthodontics, Saveetha Dental College, Chennai, India.

***Corresponding author's E-mail:** prathapsekhar@gmail.com

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ABSTRACT

Irreversible pulpitis is an acute condition where the patient experiences extreme pain and discomfort in the affected tooth. The management include alleviation of pain followed by endodontic or exodontic management. Non-steroidalanti-inflammatory drugs are the prime choice to manage this pain initially and their effectiveness in combating pulpal pain needs to be investigated further. The aim of this study is to compare and evaluate analgesic effectiveness of Ibuprofen and Aceclofenac in management of acute irreversible pulpitis. The objective is to evaluate the intensity and duration of pain after the drug administration preoperatively, prior to endodontic treatment. 85 patients suffering from acute dental pain due to irreversible pulpitis were enrolled in this study and 50 (29 females, 21 males) patients were found satisfying the inclusion criteria and were recruited. They were randomized into two groups by computer generated random module, Group A receiving 400mg Ibuprofen and Group B received 100mg Aceclofenac respectively. The drugs were identically packaged and administered by an independent operator and pain intensity over time intervals of base time of 15, 30 and 45 minutes were recorded using Visual Analog Scale (0-100) and the observations were statistically analysed. The pain intensity reduced significantly with the ingestion of drugs. At 15 minutes, the pain intensity was 64.28±4.07 for Group A and 62.92±4.613. The pain intensity at 30 minutes was 64.96±3.791 for Group A and 38.48±4.283 for Group B, and pain intensity at 45 minutes was 40.36±4.241 and 9.16±1.57 and independent t test inferred a statistically significant difference between the drugs at the end of all the time intervals of 15 minutes (p=.027), 30 minutes (p<.001), 45 minutes (p<.001) at 5% significance level. Aceclofenac 100 mg demonstrated better analgesic effect than Ibuprofen 400 mg in patients experiencing pain due to irreversible pulpitis.

Keywords: Analgesia, Ibuprofen, Aceclofenac, Visual Analog Scale.

INTRODUCTION

Pain is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.[1] Acute dental pain model has been well established for the assessment of efficacy of analgesics in various short-term studies.[2] Agents such as non-steroidal anti-inflammatory drugs (NSAIDs), cyclooxygenase (COX)-2–selective inhibitors, and opioids are available for the treatment of acute pain.[3] The invention of NSAIDs has significantly improved the management of pain in dentistry.[2] Because of their demonstrated efficacy and safety in relieving moderately severe pain in outpatient setting, dental practitioners now rely completely on NSAID analgesics.[4]

An ideal analgesic should alleviate pain with no undesirable side effects.[5] Combining analgesics offers the possibility of increasing effectiveness without increasing dose.[6,7]

Aceclofenac is an oral NSAID that is effective in the treatment of painful inflammatory diseases and has been used to treat pulpitis widely. It has proved as effective as Diclofenac, Naproxen and Piroxicam in patients with osteoarthritis, Diclofenac, Ketorolac, Tenoxicam and Indomethacin in patients with rheumatoid arthritis and Tenoxicam, Naproxen and indomethacin in patients with ankylosing spondylitis. It also provides effective analgesia in other indications, such as dental or gynaecological pain, lower back pain and ear, nose and throat inflammatory ailments.[8] Aceclofenac appears to be particularly well-tolerated amongst the NSAIDs, with a lower incidence of gastrointestinal adverse effects.[9] This good tolerability profile results in a reduced withdrawal rate and hence greater compliance with treatment.

Ibuprofen is ranked as an NSAID, thereby indicating an "anti-inflammatory" effect.[2] Dionne and Cooper[10] reported on a placebo-controlled study in which the principle objective was to determine whether preoperative treatment with Ibuprofen 400 mg could delay the onset and reduce the severity of pain after third molar removal.[12] Their findings showed that a single dose of Ibuprofen 400 mg, when compared with placebo, delayed the mean time of onset of post-operative pain by 100min.[12]

Pulpal pain is considered one of the most severe types of noxious sensation felt by the patients. NSAIDs play a key role in the management of pulpal pain both pre and post operatively. Rating scales are the most commonly used method of assessing acute pain and its relief. Research on efficacy of different types of measurements of pain has

proved that Visual Analog Scale provided useful measure of pain experience for use in clinical settings.[13]

This study was carried out to evaluate and compare analgesic efficacy of Ibuprofen and Aceclofenac in acute irreversible pulpitis.

The measures that are considered of the evaluation of analgesic efficacy were the onset of analgesia and reduction in intensity of pain.

AIM

The aim of this study is to compare and evaluate analgesic effectiveness of Ibuprofen and Aceclofenac in management of acute irreversible pulpitis.

OBJECTIVE

The objective is to evaluate the duration of pain after the drug administration preoperatively with endodontic treatment using Visual Analog Scale.

Null hypothesis: There is no difference in analgesic effectiveness between Ibuprofen and Aceclofenac in the management of acute pulpal pain.

Alternative hypothesis: There is a difference in analgesic effectiveness between Ibuprofen and Aceclofenac in the management of acute pulpal pain.

METHODOLOGY

85 patients suffering from acute dental pain due to irreversible pulpitis were enrolled in this study. Patients those satisfied the following inclusion and exclusion criteria were included to participate in this study.

Inclusion criteria: patients suffering from acute dental pain due to irreversible pulpitis, both genders, age group between 20 and 50, teeth fit for endodontic therapy and willingness to participate in this study.

Exclusion criteria: patients with pulpitis associated with abscess, pulpitis in third molars, chronic pulpitis with exacerbation, patients with dento-alveolar abscess, pulpo-periodontal lesions, root stumps, pregnant and lactating women, patients under medication with anti-depressents, opiods, anticoagulants, patients with hepatic and renal diseases and known hypersensitivity to Ibuprofen and Aceclofenac.

The study was conducted according to the protocol approved by ethics committees of study centre.

The study was conducted in compliance with the ethical standards laid down in the Declaration of Helsinki, 1964 and its later amendments; Good Clinical Practice (GCP) guidelines issued by the Central Drugs Standard Control Organization (CDSCO), Ministry of Health, Government of India; Ethical guidelines for biomedical research on human participants, Indian Council of Medical Research (2006), New Delhi.

All patients were explained about the procedure clearly and written informed consent was obtained from each participant before their participation in the study. At the time of screening, medical history was obtained; physical examination and laboratory investigations were performed.

A total of 50 out of 85 patients satisfied by inclusion criteria were recruited in the study as per eligibility criteria. The excluded patients were referred for extraction and were prescribed postoperative medication and followed up.

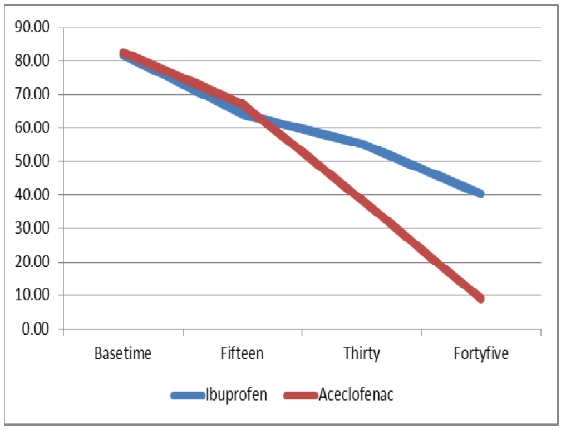
The selected subjects were randomly segregated into two groups, A and B as per computer generated random number module. Group A received a drug of Ibuprofen-400mg random group B received Aceclofenac-100mg. The drugs were packed into identical capsules and identified as X and Y, X denotes Ibuprofen and Y denotes Aceclofenac. Both the drugs were administered to patients preoperatively to endodontic treatment by an independent operator and analgesia denoted as reduction in pain intensity, the primary outcome in this study was determined using Visual Analog Scale (VAS; where 0 indicates no pain and 100 indicates worst pain) at 15 minutes, 30 minutes, 45 minutes time intervals respectively. A proforma was given to the patient and perceived intensity of pain was recorded. The obtained values were tabulated and subjected to statistical analysis with independent sample t test at 5% significance.

Table 1: Vas Scores Between the Groups at Time Intervals

Groups		N	Mean	Std. Deviation	Std. Error Mean
Age	Ibuprofen	25	42.92	12.356	2.471
	Aceclofenac	25	41.40	9.018	1.804
Basetime	Ibuprofen	25	81.64	5.147	1.029
	Aceclofenac	25	82.44	4.124	.825
Fifteen	Ibuprofen	25	64.28	4.047	.809
	Aceclofenac	25	66.92	4.163	.833
Thirty	Ibuprofen	25	54.96	3.791	.758
	Aceclofenac	25	38.48	4.283	.857
Fortyfive	Ibuprofen	25	40.36	4.241	.848
	Aceclofenac	25	9.16	1.573	.315

Table 2: Independent Sample Test comparing the Means of Vas Scores

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	Df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Age	Equal variances assumed	1.062	.308	.497	48	.622	1.520	3.059	-4.631	7.671
	Equal variances not assumed			.497	43.919	.622	1.520	3.059	-4.646	7.686
Basetime	Equal variances assumed	.657	.422	-.607	48	.547	-.800	1.319	-3.452	1.852
	Equal variances not assumed			-.607	45.822	.547	-.800	1.319	-3.455	1.855
Fifteen	Equal variances assumed	.120	.731	-2.274	48	.027	-2.640	1.161	-4.975	-.305
	Equal variances not assumed			-2.274	47.962	.027	-2.640	1.161	-4.975	-.305
Thirty	Equal variances assumed	.016	.899	14.406	48	.000	16.480	1.144	14.180	18.780
	Equal variances not assumed			14.406	47.303	.000	16.480	1.144	14.179	18.781
Fortyfive	Equal variances assumed	10.135	.003	34.485	48	.000	31.200	.905	29.381	33.019
	Equal variances not assumed			34.485	30.477	.000	31.200	.905	29.354	33.046



Graph 1: Vas Scores over Varying Time Intervals

RESULTS

In group A, 16subjectes of females and 9 were males and in group B, 13 subjects were females and 12 subjects were males and a total of 29 females and 21 males were selected.

Table 1 provides the details of the group statistics. The pain intensity at baseline with group A was 81.64±4.124.

At 15 minutes, the pain intensity was 64.28±4.07 for group A and 62.92±4.613 for group B. The pain intensity of 30 minutes was 64.96±3.791 for group A and 38.48±4.283 for group B, and pain intensity at 45 minutes was 40.36±4.241 and 9.16±1.57.

Table 2, independent sample t test to compare the differences between the means of Group A and Group B showed a statistically significant differences at 15 minutes, p-value=0.027 and a very highly significant difference with p-value ≤0.001 during 30 and 45 minutes interval respectively.

DISCUSSION

In Irreversible Pulpitis, breakdown of damaged cell membranes and release of arachidonic acid (AA) occurs. This AA is acted on by cycloxygenase (COX) enzyme and gets converted into 20-carbon chain molecules called eicosanoids. These are converted by cell-specific isomerases and synthases to produce five biologically active PGs: PGD2, PGE2, PGF2a, prostacyclin (PGI2), and thromboxane A2 (TxA2). These PGs sensitize nerve endings to bradykinins and histamines and cause the allodynia and hyperalgesia associated with inflammation.

Nonsteroidalanti-inflammatory drugs (NSAIDs), including selective cyclooxygenase (COX)-2 inhibitors, have come to play an important role in the pharmacologic management of arthritis and pain. Clinical trials have established the efficacy of Etoricoxib in osteoarthritis, rheumatoid arthritis, acute gouty arthritis, ankylosing spondylitis, low back pain, acute postoperative pain, and primary dysmenorrhea.

Ibuprofen and Aceclofenac are both NSAIDs, they have different chemical structures. Ibuprofen is a non-selective

COX inhibitor and Aceclofenac is a selective COX-2 inhibitor. Ibuprofen also inhibits the migration and other functions of leucocytes, while Aceclofenac reduces intracellular concentrations of free Arachidonates in leucocytes. Aceclofenac and Ibuprofen are relatively safe, fast-acting analgesics that also control inflammation.

The efficacy of Ibuprofen (a propionic acid derivative) in postoperative dental pain is also well established.[14] Aceclofenac (phenylacetic acid derivative) has anti-inflammatory properties similar to those of diclofenac and of indomethacin. In clinical studies, it has been shown to treat dental pain effectively. Aceclofenac (ACF) , [({2-[(2,6-dichlorophenyl)amino]phenyl}acetyl)oxy]acetic acid, has analgesic properties and a good tolerability profile in a variety of painful conditions. It is used for treatment of rheumatic disorders and soft-tissue injuries. ACF inhibits the enzyme cyclooxygenase and thus exerts its anti-inflammatory activity by inhibition of prostaglandin synthesis. Many authors have studied the effects of analgesics in dental pain[14,15] and concluded Ibuprofen is effective against pain.

The mechanism of action of most NSAIDs results by acetylating the cyclooxygenase enzyme, which in turn inhibits the synthesis of prostaglandins.[16] Thus, NSAIDs non-specifically prevent both the COX-1 and COX-2 isoenzymes from forming arachidonic acid metabolites. Because there is induction of COX-2 at sites of inflammation, it is believed that the therapeutic properties of NSAIDs account primarily for the inhibition of COX-2.[16] Aceclofenac [[2-(2', 6'-dichlorophenyl) amino] phenylacetoxyacetic acid] is a phenylacetic acid derivative belongs to the group of non-steroidal anti-inflammatory drug (NSAID).[17] It is a pro-drug of diclofenac and decomposed under hydrolytic stress (neutral, acidic, and alkaline) and also on exposure to light (in solution form). The compound is stable to oxidative stress, heat, and photolytic stress (in solid form). It is a white crystalline solid, practically insoluble in water, freely soluble in acetone and soluble in ethanol (96%).[18,19] It is well absorbed orally (60-70 % of bioavailability following oral administration) and undergoes hepatic first pass metabolism.[20] It is 99% bound to plasma protein extensively with albumin.[21] The elimination half-life is 4 hrs and volume of distribution is 25 litres.[22,23] The pharmacodynamics profile is similar to indomethacin and diclofenac and, being superior to naproxen and phenylbutazone.[24]

400 mg of Ibuprofen and 100 mg of Aceclofenac were administered in this study and Ibuprofen is considered the control. Both the patients and the operator were blinded in this study. For patients still experiencing pain after the administration of the drugs, local anaesthesia was kept ready as rescue regimen to alleviate pain, but was not required since the patients experienced sufficient analgesia with the drugs. Rating scales are the most commonly used method of assessing acute pain and its relief. Research on efficacy of different types of measurements of pain has proved that visual Analog scale provided useful measure of pain experience for use in clinical settings and hence visual analogue scale was used in this study.

The results of this study negated the null hypothesis and Aceclofenac was observed superior than Ibuprofen in providing analgesia by reducing the intensity of pain in patients with irreversible pulpitis.

Both the analgesics exhibited significant amount of analgesia when compared with pre-operative values. There was no difference in the amount of analgesia between the genders.

Both the genders responded similarly to the experimental analgesics. There was a progressive and faster cessation of pain with Aceclofenac than Ibuprofen in all the time intervals observed. This could be attributed to faster dispersion of drug from gastro intestinal tract into the blood in effectively reaching the target site with better bioavailability. The possible confounders in the study could be the diet taken by the patients before ingestion of the drug and anxiety threshold levels. When these NSAIDs were augmented with paracetamol and other synergistic combinations the analgesic effectiveness may show clinical variation.

CONCLUSION

Within the limitation of the study, it could be concluded that Aceclofenac is superior to Ibuprofen in providing analgesia in patients with acute irreversible pulpitis and Aceclofenac could be preferred in clinical practice in the management of inflammatory pulpal disease.

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