COMPARISON OF EFFICACY OF CELECOXIB (SELECTIVE NON STEROIDAL ANTI INFLAMMATORY DRUG) VERSUS NAPROXEN (NON SELECTIVE NON STEROIDAL ANTI INFLAMMATORY DRUG) FOR POST ENDODONTIC PAIN

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ABSTRACT

Objective: To determine efficacy of celecoxib (selective cyclooxygenase - II non steroidal anti inflammatory drug) versus naproxen (non selective cyclooxygenase – I & II non steroidal anti inflammatory drug) for post endodontic pain.

Study Design: Comparative prospective study.

Place and Duration of Study: The study was executed at Department of Operative Dentistry, Armed Forces Institute of Dentistry (AFID), from Apr 2017 to Apr 2018.

Methodology: Total 961 patients (group A Celecoxib n=482 and group B Naproxen n=479) requiring root canal therapy were selected. The patient's record regarding his pain perception using a visual analog scale (VAS) at 6 hours after root canal therapy was recorded. Descriptive statistics were used to calculate mean ± SD. for age and pain, before the procedure and after 6 hours of procedure in each groups.

Results: Total 961 patients were enrolled for the subject study out of which celecoxib group constituted 482 (50.1%) and naproxen group constituted 479 (49.8%) of total. 244 (50.6%) patients in group A (Celecoxib) exhibited adequate pain relief with no gastric discomfort and side effects whereas 195 (40.7%) patients had satisfactory pain relief in group B (Naproxen), however experienced gastric side effects such as nausea and dyspepsia.

Conclusion: Celecoxib was found to be more effective in post – endodontic pain with minimal gastric symptoms, when compared to Naproxen.

Keywords: Celecoxib, Naproxen, Post - endodontic pain.

INTRODUCTION

Endodontic treatment is considered to be an extremely painful experience for patients in dental practice[1]. Pain is already present before initiation of root canal treatment rather it is the presenting complaint compelling patient to seek advice. There is a noteworthy co-relation between pre-endodontic pain and post-endodontic pain. Patient having intense symptoms before treatment have a tendency to experience more distressing operative and postoperative pain sensations in comparison with patients who present with insignificant pain scores[2]. After successful completion of treatment, post endodontic pain resolves in most of the cases however pain perception remains in some of the cases leading to unsatisfactory experience of patient.

Histamine, bradykinin and prostaglandins are leading inflammatory mediators[3]. Prostaglandins are responsible for increased vascular permeability, elevated chemotactic response, manifestation of fever symptoms and pronouce sensitivity of inflammatory mediators at pain receptors. Disease process and Endodontic treatment both produce effects of local trauma and inflammation there by increasing prostaglandin production consequently increasing pain phenomenon.

As per analgesic ladder there are various analgesic groups for control of pain such as opioids, local anaesthetics and non steroidalanti inflammatory drugs. These are employed for control of symptoms considering severity, origin and etiology of pain. Incase of post endodontic pain primary mechanism responsible for pain production is inflammatory and patients are

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Received: 11 Jan 2020; revised received: 04 Mar 2020; accepted: 06 Mar 2020

ambulatory day cases therefore non steroidalanti inflammatory drugs are the most suited one due to possession of anti inflammatory properties inferred by inhibition of activity of cyclooxygenase enzyme thus leading to cessation of prostaglandin production with avoidance of cumbersome side effects such as nausea, vomiting and respiratory depression remarkably associated with opioids.Localanaesthetics are not effective in inflammatory environment therefore making them a poor choice in post endodontic pain. They are principally divided into two groups based on inhibition of cyclooxygenase enzyme (COX) such as non selective cyclooxygenase I & II inhibitors (COX–I & II)and selective cyclooxygenase inhibitor (COX-II). COX-I is responsible for the production of prostaglandins which protect the mucosal lining of gastrointestinal tract particulary stomach and maintenance of renal functions within normal limits. COX-II is prime agent in inflammation and cell growth due to its relation with pro inflammatory cytokines. Advent of COX-II led to the emergence of analgesics such as celecoxib which provide analgesia without compromising renal and gastrointestinal safety [4] .

Naproxen is a time tested and potent analgesic used commonly for pain but is has significant side effects including duodenal and gastric ulcers and upper GI bleeding. Celecoxib is a nonsteroidal anti-inflammatory drugfor post-operative pain management in dental surgery models plus its unique ability to protect stomach ulcers and bleed as experienced with conventional NSAIDS[5,6]. Holstein *et al* in their systemic review of evaluation of NSAIDS for treating post-endodontic pain demonstrated that 54% patient with celecoxib and 46% patients naproxen achieved at least 50% pain relief over 6 hours compared with placebo[7].

Celecoxib has the additional benefit of being stomach friendly (especially in patient with gastric and duodenal ulcers) as well as it is a painkiller. The rationale of this study was to determine whether celecoxib will diminish post-endodontic pain, in comparison to naproxen in our outpatients with added safety profile[8].

METHODOLOGY

After seeking approval of ethics research committee (ERC 03/01/2017) of Armed Forces Institute of Dentistry this comparative prospective study was conducted. Consentwas taken from participants after elaborating risks and benefits associated with treatment. Time span of study was one year from Apr 2017 to Apr 2018.

Sample size was calculated using WHO sample size calculator, with level of significance 5%, Power of test 80%, anticipated population proportion was P1=46% and P2=54%[4]. Total individuals recruited to study were n=961. Consecutive non probability technique was used for sampling.

Patientswere randomly allocated either of the groups (group A and group B). As per study protocol, patients requiring root canal therapy (RCT) were registered for treatment at AFID they were interviewed and briefed about the procedure followed by informed written consentafter adequately answering queries of the patients. A through history was seeked and clinical examination was performed. Patients requiring root canal therapy who were 18 years or older enrolled fulfilling complete clinical and radiological criteria of symptomatic periapical perionditis, which includes negative response on cold testing (with Endo - Ice), tenderness on percussion and palpation and radiolucency on periapical radiograph. Patients with ischemic heart disease, rheumatic heart disease, untreated hypertension, bleeding disorders, stomach ulcers, renal problems, liver disorders, pregnant or breast feeding, already on non steroidalanti inflammatory drugs (NS aids) having history of peptic ulcer disease and a patients who took analgesics within 6 hours of the scheduled treatment were excluded out of selection criteria.

After diagnosis was established and patient selected for treatment, each patient's initial pain perception was recorded using a visual analogue scale.

Visual analogue scale is psychometric response scale for measurement of response of subjective characteristics of pain that can not be

measured directly. In this scale subjects respond to their level of pain by indicating a position on a continuous line between two end points (fig-1)[9].

Two packets of medicines were prepared. Group A were given Celecoxib 100mg twice daily whereas group B was given Naproxen 500mg twice daily. Standard treatment of root canal was executed in two sessions after initial intraoral examination and explanation of procedure to patient. Inferior alveolar nerve block was administered ruling out allergies effectiveness of local anesthesia was determined by electric pulp tester showing two consecutive negative readings. Tooth was isolated using rubber dam, access

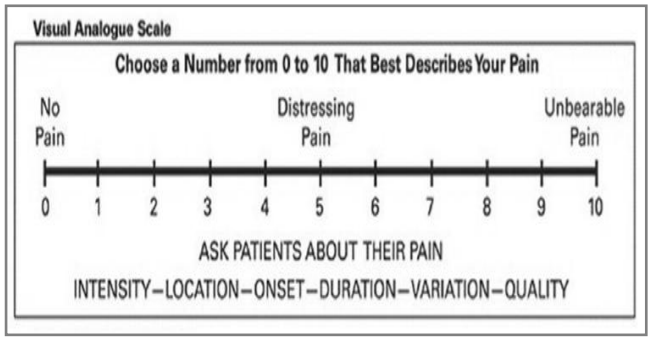

Figure: Visual Analogue Scale[10].

opening was initiated using high speed round diamond bur with air water coolant after complete deroofing canal were located and initial pulpectomy was done using nickel titanium hand files continuous irrigation with 5.25% sodium hypochlorite was carried out throughout the procedure. Working length was established using 4TH generation apex locator and was also confirmed radio graphically. Interappointment intracanal medicament (calcium hydroxide) was placed and tooth was temporarily sealed with zinc oxide eugenol (temporary restorative material). After completion of procedure patient's record regarding his pain perception using visual analogue scale at 6 hours after root canal therapy was recorded on Performa.

Data was analysed by using SPSS-23. Independent sample t test and chi square test was applied for comparison of group A and group B. A *p*-value ≤0.05 was considered significant.

RESULTS

Total number of patients n=961 were enrolled in the study group A - Celecoxib (n=482) and group B -Naproxen (n=479). Upon detailed history following treatment results were that 244 (50.6%) patients in group A exhibited adequate pain relief with no gastric symptoms such as dyspepsia, nausea or vomiting whereas 195 (40.7%) patients had satisfactory pain relief in group-B (table-I). Therefore proving efficacy of Celecoxib over Naproxen in providing analgesia. Total male patients were n=653 and female patients were n=308 with age range of 21-51 years old were recruited in the study (table–II).

Table-I: Comparison of analgesic efficacy of group A & B.

	Group A Celecoxib (n=482)	Group B Naproxen (n=479)	Significance (Pearson chi–square test)
Yes	244 (50.6%)	195 (40.7%)	0.002
No	238 (49.4%)	284 (59.3%)	

Table-II : Distribution of patients.

Gender	Group A Celecoxib (n=482)	Group B Naproxen (n=479)
Male	309 (64.1%)	344 (71.8%)
Female	173 (35.9%)	135 (28.1%)

DISCUSSION

Pain relief is considered as a major challenge in medical field as it accounts for leading cause of failure of treatment and achieving patient satisfaction. Patient comfort and confidence is a prime aim of every physician and surgeon which can be achieved with adequate pain relief. Patients receiving endodontic treatment exhibit greater levels of anxiety and postoperative pain. All these factors contribute to apprehension about dental treatment thereby effecting perception and prospects of dental treatment[11].

Approximately 20% patients experience pain of varying intensity after endodontic treatment[12]. During procedure pain relief and patient comfort can be achieved adequately by local anaesthesia and conscious sedation but real challenge is faced during post operative period. Due to lack of close surveillance of dental patients post operatively, analgesics such as opioids can not be used gene-

rously due to side effects such as drowsiness, nausea and vomiting. Dentists can make use of non steroidalanti inflammatory drugs (NS aids) for analgesic and anti inflammatory purpose although their benefit is limited due to gastrointestinal and renal side effects in addition to tendency of platelet aggregation inhibition[13]. These limitations led to search of newer practice with minimal side effects ensuring more patient comfort and safety. Celecoxib (COX – II Inhibitor) holds therapeutic benefits as of conventional NS aids with fewer side effects as associated with COX -I / COX -II inhibitors.

NS aids exert their therapeutic and adverse effects due to inhibition of COX - I & II enzymes. Inhibition of COX-I results in gastrointestinal bleed and ulceration whereas inhibition of COX-II leads to inhibition of pain, inflammation and fever mediating prostaglandins .

Celecoxib is selective COX-II inhibitor indicated for treatment of acute pain, osteoarthritis, rheumatoid arthritis, ankylosing spondylitis and primary dysmenorrhea. It is not to be used in patients with hypersensitivity reaction e.g. asthma, ischaemic heart disease, cerebrovascular disease, compromised renal function. Side effects experienced with celecoxib are raised blood pressure, headache, dizziness, sodium and fluid retention. At higher doses celecoxib can inhibit COX-I resultantly can manifest gastrointestinal effects.

Naproxen is COX-I & II inhibitor indicated for treatment of acute pain, fever, inflammatory diseases such as rheumatoid arthritis, ankylosing spondylitis and primary dysmenorrhea. It exhibit its effects by inhibition of prostaglandins responsible for inflammation and pain. Side effects manifested are heart burns, stomach pain, bruising, gastrointestinal bleed and cerebrovascular accidents.

Studies had been carried out which proved that Celecoxib provide adequate analgesia and anti inflammatory results in post endodontic patients with added advantage of reduced gastrointestinal effects. Similar studies on other drugs of COX-II inhibitors had also proved superiority of COX-II inhibitors over COX-I inhibitors in terms of analgesia and protection from gastrointestinal manifestations.

Gopikrishna *et al* compared Rofecoxib (COX-II inhibitor) with Ibuprofen (COX-I & II inhibitor) and placebo. Both drugs had higher analgesic activity as compared to placebo, however after 12 and 24 hours rofecoxib produced significant analgesia as compared to other two groups[14].

Bombardier *et al* compared rofecoxib (COX–II inhibitor) with naproxen (COX-I & II inhibitor) in terms of gastrointestinal effects and concluded that incidence of gastrointestinal perforation, gastrointestinal hemorrhage or peptic ulcer was 4.5% in naproxen group and 2.1% in rofecoxib group[15].

Rosenberg *et al* compared safety and efficacy of lumiracoxib with NSAIDs and found that lumiracoxib selective COX–II inhibitor has greater analgesic efficacy with limited gastrointestinal and cardiovascular adverse effects[16].

Akinbade *et al* determined analgesic efficacy and tolerability of celecoxib and tramadol on postoperative pain after mandibular third molar extraction in a double blinded randomized controlled trial. As per study results analgesic efficacy of celecoxib given at a dose of 400 mg initially then 200 mg 12 hourly was greater than that of tramadol at a dose of 100 mg 8 hourly for 48 hours after surgical extraction of mandibular third molar. Moreover celecoxib was more tolerable than tramadol in regards of side effects[17].

Chao *et al* compared celecoxib with placebo, study suggested that celecoxib (200mg orally once daily) when compared with placebo results in greater pain relief with acceptable adverse effects for the treatment of OA pain[18].

ACKNOWLEDGEMENT

Authors are grateful to the seniors for guidance, colleagues &staff of the department for assistance in data collection and smooth conduction of research.

LIMITATION OF STUDY

Our study had limitation that it was not multi centred and was not double blinded therefore exceptional level of accuracy could not be achieved. In addition cost of celecoxib over traditional Nsaids limits its use in setups where limited financial resources are available.

CONCLUSION

This comparative prospective study concluded that celecoxib was more effective in post–endodontic pain relief, when compared to naproxen furthermore celecoxib provides an additional benefit of prevention of gastric symptoms which is a cumbersome side effect experienced by patient while using COX–I & II inhibitors. COX-II inhibitors are of therapeutic benefit in population having bleeding tendencies as celecoxib does not prolong bleeding time. However cost of celecoxib over conventional NSaids limits its use and availability.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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