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Analgesic Efficiency Of Two Different Combinations Of Paracetamol In Management Of Post-Extraction Pain

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Abstract

Aim: To evaluate the analgesic efficiency of two different combinations of paracetamol in management of post-extraction pain.

Materials and Method: Patient who had done therapeutic extraction in our OPD were included in this study. All the volunteers were given a brief explanation of the study, and written informed consent was obtained from all participants before inclusion in the study. 50 patients were selected in total and was randomized into two treatment groups (each with 25 patients: group A received {Meftal Forte; Mefenamic Acid 500mg +paracetamol325 mg} and group B Diclomol {Diclofenac 50mg+ paracetamol 325 mg}, orally. The intensity of pain and durations of analgesia were recorded at the time slot of 30 minutes, 2 hour, 4 hours, and 6 hours. The pain intensity is recorded using a four-point pain intensity scale (verbal rating scale).Also the gastric tolerances of these drugs were also studied.

Results: The duration and range of analgesia produced by both drugs were comparatively equal. But the drug A gave gastric tolerance than drug B.

Conclusion: Both combinations of paracetamol are equally effective in managing post extraction pain. But paracetamol combination with diclofenac is a potential gastric irritant than mefenamic acid.

Keywords: Analgesic efficiency, combinations, paracetamol, post-extraction, pain

Introduction

Dental extraction is a common oral procedure which causes varying degree of pain. So the analgesic efficiency of various NSAIDS available in market can be evaluated by using dental extraction as a model1. In addition to pain edema, trismus etc. are also associated with dental extraction. There is a direct correlation between pain, swelling, trismus and duration of procedure2. The pain elicited by each patient on extraction is varies among persons, and each extraction of an individual may be quite different. Also the response of each patient is variable to the extraction procedures. Many patients avoid dental treatment mainly because of the severe pain experienced after extractions3. It is the responsibility of the oral surgeon to reduce the post-operative effects to a minimum so that the extraction procedure becomes more socially acceptable4,5,6. Dental extraction causes tissue damage and hence inflammation is inevitable secondary to extraction. Various types of anti inflamatory drugs are used for managing the pain and associated sequelae after extraction.

Cylclooxygenase (COX) enzymes, help in converting arachidonic acid to prostaglandins, which generates pain, fever, and inflammation7. NSAIDs inhibit cyclooxygenase enzyme and thus

produces analgesic, anti-inflammatory, and antipyretic effects. COX-1 and COX-2 are the common isomers of cyclooxygenase. While both isoforms catalyse the same reactions, COX-1 is a constitutive enzyme in most cells—it is synthesized and is active in the basal state; the level of COX-1 activity is not much changed once the cell is fully grown. It is believed that eicosanoids produced by COX-1 participate in physiological (house-keeping) functions such as secretion of mucus for protection of gastric mucosa, haemostasis and maintenance of renal function, while those produced by COX-2 lead to inflammatory and other pathological changes8. However, certain sites in kidney, brain and the foetus COX-2 have a physiological role. Lipoxygenase pathway mainly operate in the lung, WBC and platelets. LTs, (generated by 5- LOX) particularly LTB4 (potent chemotactic) and LTC4, LTD4 are the important derivatives of lipooxygenase pathway. They are referred as 'slow reacting substance of anaphylaxis' (SRS-A) and is released during anaphylactic reaction8.

Synthesis of COX products can be inhibited by nonsteroidal antiinflammatory drugs (NSAIDs). Aspirin acetylates COX at a serine residue and thus produces irreversible inhibition while other NSAIDs are competitive and reversible inhibitors. Most NSAIDs are nonselective COX-1 and COX-2 inhibitors, but some later ones like celecoxib, etoricoxib are selective for COX-2. NSAIDs do not inhibit the production of LTs: this may even be increased since all the arachidonic acid becomes available to the LOX pathway.

Materials And Method

Patient seeking dental extraction for orthodontic purpose under age group of 18-23 were included in this study. All the patients who were willing for study were given a brief explanation of the study, and written informed consent was obtained from each participant. The patients not willing for the study, patients with systemic co morbidities were excluded from the study.

Study Design

All the patients were given adequate information about the proposed study. Patients in the study were voluntary, and written consent from the patients was received.

Inclusion Criteria

Patient seeking dental extraction for orthodontic purpose under age group of 18-23. Patients who gave written informed consent

Exclusion Criteria

If during the procedure if any extractions need trans-alveolar extractions they were excluded from the study.

Patients not willing for the study.

Patients with underlying systemic co-morbidities.

Randomization and allocation 50 patients were randomized into two treatment groups (each with 25 patients) by using lottery method: group A received drug A and group B received drug B, orally. All the extractions were done by the same operator and he was blinded about the allocation.

Methodology

After application of topical anesthesia, extractions were performed under same local anesthetic solution(2% lignocaine+1:200000 adrenaline). If during the procedure if any extractions need trans-alveolar extractions they were excluded from the study. After the extraction the patients were kept in observation for 30 minutes who were willing for the study and were provided with the prescribed analgesic. Participants were trained to record the pain intensity scale by a researcher who was also blinded to the groups. All the patients were provided with a VRS and a template to record their score. After 30 minutes the intensity of pain was recorded by the patient in the clinic. The patients were requested to record the durations of analgesia and pain intensity after 2 hour, 4 hours, and 6 hours in the template provided. Post extraction pain was measured using a four-point pain intensity scale (verbal rating scale). The four pain categories were as follows:

0–no

1–slight 2–moderate 3–severe

"Figure 1 : Verbal rating scale"

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After 6 hours patients were called by telephonic conversation to confirm the drug was consumed properly and it was verbally confirmed that the template was properly filled. We have also enquired about the gastric irritation following drug administration and those who reported irritation were advised to consume the H2 blocker which was already prescribed.

"Figure 2 : Randomization and allocation"

Result

"Table 1: Frequency and percentage of Group 1"
"Table 2 : Frequency and percentage of Group 2"

"Table 3 : Comparison of patient score between two groups"

Mann-Whitney U test was used to analyse the differences in scores of patients between groups. The test shows that there is no significant difference in scores of patients at 30 minutes,1 hour, 4 hours and 6 hours follow-ups between groups.

"Table 4 : Comparison of patient score within groups"

The statistical significant difference were determined in patient scores within groups on Friedman test.

"Graph 1 : Graphical comparison between groups"

The pain control in group one was satisfactory except for 3 patients who consumed the second analgesics before 6 hours. Only one patient developed gastric irritation which is not statistically significant.

The pain control was effective in group 2 also. Only 4 patients consumed the second analgesics before 6 hours. But the second group show prominent gastric irritation. 12 patients developed moderate irritation following drug B therapy.

Discussion

The study shows that both combinations of paracetamol were equally effective in managing post extraction pain. But the combination of paracetamol with diclofenac shows moderate gastric irritation. Even though gastric irritation is a common side effect of all the non-selective NSAIDS, drug A shows more gastric tolerance.

Gastric pain, mucosal erosion/ulceration and blood loss are produced by all NSAIDs to varying extents: but main consideration in selecting NSAIDS is relative gastric toxicity. Inhibition of COX-1 mediated synthesis of house-keeping PGs (PGE2, PGI2) is clearly involved, along with local induction of back diffusion of H+ ions in gastric mucosa also plays a role in producing gastric irritation. Deficiency of PGs reduces mucus and $HCO3^{-}$ secrection, which enhance acid secretion, inhibit proper gastric acid neutralisation and may promote mucosal ischaemia. Thus, NSAIDs enhance aggressive factors potentiating gastric ulceration. Paracetamol, a very weak inhibitor of COX is practically free of gastric toxicity and selective COX-2 inhibitors are relatively safer8. Stable PG analogues like misoprostol can be administered concurrently with NSAIDs counteract their gastric toxicity.

Mefenamic acid is analgesic, antipyretic and weaker anti-inflammatory drug, which inhibits synthesis of PGs as well as antagonises some of their actions. Mephenamic acid produces both peripheral and central analgesic action. Diarrhoea is the most important side effect which is often dose-related. Epigastric distress is complained, but gut bleeding is rare. Skin rashes, dizziness and other CNS manifestations are reported. Haemolytic anaemia is a rare but serious complication seen in Mefenamic acid 8,9,10.

Diclofenac sodium is having analgesic, antipyretic and anti-inflammatory effect. It inhibits PG synthesis and is somewhat COX-2 selective8, 11. It has good oral availability, 99% protein bound, metabolized and excreted both in urine and bile. The plasma t½ is ~2 hours. Since it has good tissue penetrability and concentration in synovil fluid they are widely used in joint arthritis. Adverse effects of diclofenac are generally mild: epigastric pain, nausea, headache, dizziness, and rashes. Gastric ulceration and bleeding are moderate. Like many NSAIDs, diclofenac can potentiate the risk of heart attack and stroke. Reversible elevation of serum amino-transferases has been reported more commonly; kidney damage is rare8.

Paracetamol (acetaminophen) the deethylated active metabolite of phenacetin. It has a central analgesic

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effect with weak peripheral anti-inflammatory activity with a prompt anti-pyretic action. Analgesic action of aspirin and paracetamol is additive. Paracetamol is a good and promptly acting antipyretic. Paracetamol has negligible anti-inflammatory action. It is a poor inhibitor of PG synthesis in peripheral tissues, but more active on COX in the brain8. One explanation offered for the discrepancy between its analgesic-antipyretic and antiinflammatory actions is its inability to inhibit COX in the presence of peroxides which are generated at sites of inflammation, but are not present in the brain. The ability of paracetamol to inhibit COX-3 (an isoenzyme first identified in dog brain) could also account for its analgesic-antipyretic action8. Gastric irritation is insignificant— mucosal erosion and bleeding occur rarely only in overdose. It does not affect platelet function or clotting factors. Also it is not uricosuric. Paracetamol is one of the most commonly used 'over-the-counter' analgesic for headache, mild migraine, musculoskeletal pain, dysmenorrhoea, etc. but is relatively ineffective when inflammation is prominent. It is one of the best drugs to be used as antipyretic, especially in children (no risk of Reye's syndrome). Dose to dose it is equally efficacious as aspirin for non-inflammatory conditions. It is much safer than aspirin in terms of gastric irritation, ulceration and bleeding (can be given to ulcer patients), does not prolong bleeding time. Hypersensitivity reactions are rare; no metabolic effects or acid-base disturbances; can be used in all age groups (infants to elderly), pregnant/lactating women, in presence of other disease states and in patients in whom aspirin is contraindicated. It does not have significant drug interactions.

Efficacy differences among different NSAIDs are minor, but they have their own spectrum of adverse effects17,18,19. They differ quantitatively among themselves in producing different side effects and there are large inter-individual differences. No single drug is superior to all others for every patient. Choice of drug is empirical12. The cause and nature of pain (mild, moderate or severe; acute or chronic; ratio of pain: inflammation) along with consideration of risk factors in the given patient (age, concurrent disease and drug therapy, history of allergy) govern selection of the analgesic13,14,15. Also to be considered are the past experience of the patient, acceptability and individual preference8. The response of patients to different NSAIDs is variable. If one NSAID is unsatisfactory in a patient, it does not mean that other NSAIDs will also be unsatisfactory. Some subjects 'feel better' on a particular drug, but not on a pharmacologically related one8.

Figure 1 : Verbal rating scale

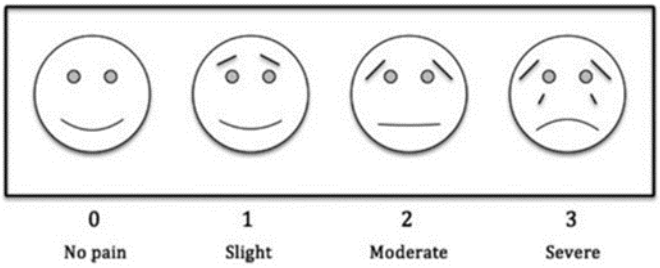

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Figure 2 : Randomization and allocation

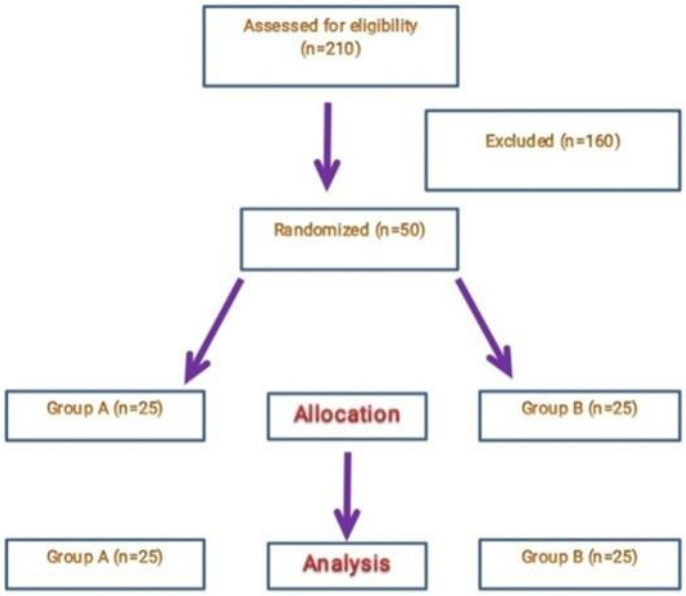

Table 1 : Frequency and percentage of Group 1

Group 1	30 minutes	1 hour	4 hours	6 hours
No pain	15(60)	1(4)	0(0)	0(0)
Slight	10(40)	7(28)	3(12)	0(0)
Moderate	0(0)	13(52)	9(36)	5(22.7)
Severe	0(0)	4(16)	13(52)	17(77.3)

Table 2 : Frequency and percentage of Group 2

Group 2	30 minutes	1 hour	4 hours	6 hours
No pain	16(64)	3(12)	1(4)	0(0)
Slight	8(32)	12(48)	6(24)	3(14.3)
Moderate	1(4)	6(24)	7(28)	4(19)
Severe	0(0)	4(16)	11(44)	14(66.7)

Table 3 : Comparison of patient score between two groups

Time	Group 1	Group 2	P value

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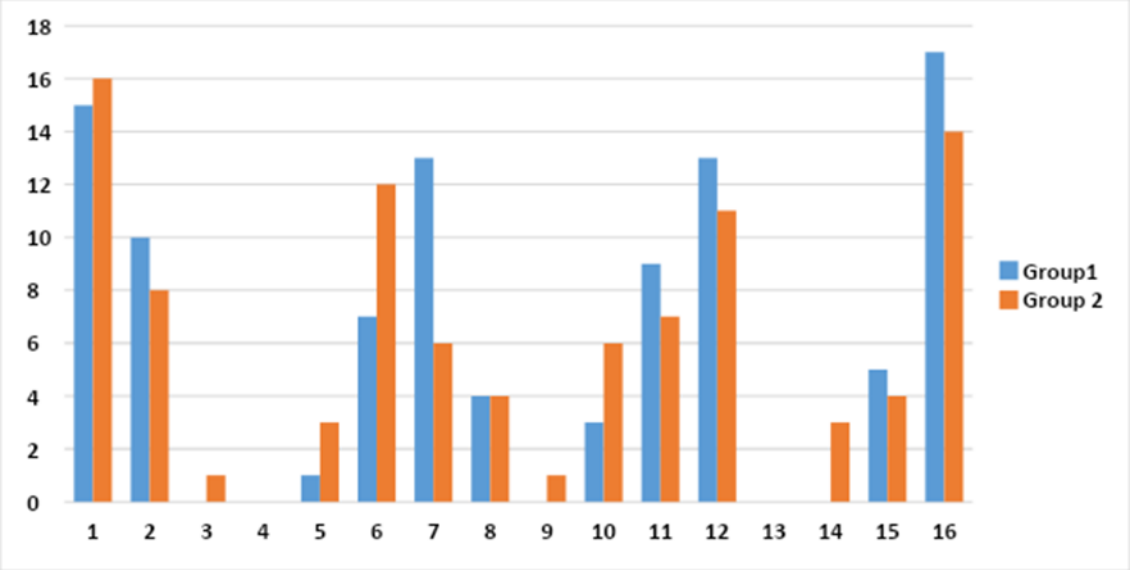
30 minutes			
Mean±SD	0.41±0.50	0.28±0.46	0.318
Median(IQR)	0(0-1)	0(0-1)	
1 hour			
Mean±SD	1.64±0.65	1.14±0.65	0.863
Median(IQR)	2(1-2)	1(1-2)	
4 hours			
Mean±SD	2.32±0.71	1.95±0.92	0.108
Median(IQR)	3(2-3)	2(1-3)	
6 hours			
Mean±SD	2.77±.42	2.57±0.81	0.479
Median(IQR)	3(2.75-3)	3(2-3)	

Table 4 : Comparison of patient score within groups

Groups	30 minutes	1 hour	4 hours	6 hours	Chi-Sq	P value
Group 1	0(0-1)	2(1-2)	3(2-3)	3(2.75-3)	57.606	<0.0001
Group 2	0(0-1)	1(1-2)	2(1-3)	3(2-3)	55.164	<0.0001

Graph 1 : Graphical comparison between groups



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