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Research Paper

Comparision of the Efficacy of Ibuprofen to Ibuprofen, Paracetamol and Caffeine Combination in the Control of Postoperative Pain After Periodontal Surgery- A Split Mouth Cross-Over Study"

Medical Science

KEYWORDS : combination of Ibuprofen, Paracetamol and Caffeine, Ibuprofen, post- operative pain and periodontal surgery

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ABSTRACT

Introduction: *The present split mouth cross over study was conducted with an objective to compare combination of Ibuprofen 400 mg, Paracetamol 325mg and Caffeine 25mg (test) to Ibuprofen 400mg (control) in pain management after periodontal surgeries. Method: 25 patients were prescribed test drug after first flap surgery and then control drug after next surgery at a cross-over a period of 3 weeks. Patients were asked to maintain pain chart measuring Numerical Rating Scale (NRS-10) for first 8 hours after surgery, on day 1, 2 and 3 after surgery. Result: Pain scale ratings are significantly less at different timelines for test group as compared to control group (P=0.000). Conclusion: This study showed that the combination drug has better efficacy for pain management as compared to ibuprofen alone and with minimal adverse effects. This combination drug can be routinely prescribed routinely for pain management after periodontal surgery.*

I. INTRODUCTION

Pain is an unpleasant sensory and emotional experience that is associated with actual or potential tissue damage.[1] Tooth pain is second most severe pain after labor pain. Various pains are associated with different periodontal conditions like dull, gnawing pain in chronic periodontitis, throbbing pain in pericoronitis and sharp localized pain in periodontal abscess.[1] Various non-steroidal anti-inflammatory drugs like paracetamol, diclofenac sodium, ibuprofen, aspirin and many more are widely used to minimize pain associated with various periodontal conditions and that after periodontal surgery.[2] Various substances like caffeine, serratopeptidase and other are added to analgesics to increase their efficacy.[3]

Caffeine is one of the most commonly consumed ingredients in the world. It is naturally found in coffee beans, cacao beans, kola nuts, guarana berries and tea leaves. The most prominent sources of caffeine are coffee and tea, Soft drinks, energy drinks and chocolate. Moderate caffeine consumption is considered safe <400 mg/day for healthy adults. Commonly known positive effects of caffeine include physical endurance, reduction of fatigue, enhancement of mental alertness, and assisting in weight loss and management. Less known is the possible analgesic adjuvant effects of caffeine in pain relief medications.[2]

Caffeine has been an additive in analgesics for years. Caffeine is used in combination with each of three over the counter drugs like acetaminophen, ibuprofen and aspirin. **Hernandez G.** et al in 1999 [2] suggested that when caffeine is administered concomitantly, its antinociceptive effect is increased but there is no significant change of NSAID plasma concentrations. The antinociceptive effect of analgesics by caffeine is not likely due to a pharmacokinetic interaction but rather a pharmacodynamic one. Further **Zhang** et al in 2001 [2] suggested that caffeine is adenosine A2 antagonist which in turn leads to COX-2 inhibition; it has its own intrinsic analgesic effects and induces its own central cholinergic analgesia. Caffeine's influence on mood resulting from stimulant properties is considered to be source of pain relief. If caffeine increases the analgesic effects of pain medications, then recommendations for this combination can be considered in clinical practice.

Only, Ibuprofen + Paracetamol + Caffeine and Paracetamol+Caffeine combinations are available in India and as Ibuprofen is potent analgesic as compared to paracetamol, so I have chosen former combination for my study. Moreover, there are very few studies comparing analgesic combination with caffeine in pain management after periodontal surgery. Hence, this study is planned to compare an alternative combination of Ibuprofen 400 mg + Paracetamol 325mg + Caffeine 25mg to Ibuprofen 400mg in pain management after periodontal surgeries.

II. MATERIALS AND METHOD

A split mouth cross-over study was carried out in the Department of Periodontics, K M Shah Dental College and Hospital, Sumandeep Vidyapeeth. The study was started after Institutional Ethics Committee approval was obtained. A total of 25 patients with mean age 41.56 ± 5.687 years were taken according to the sample size calculation by $N = 2*(Z \times SD/d)^2 = 24.653 = 25$ with 99% CI and 80% power.

Recruitment of the participants and sites were as per the following inclusion and exclusion criteria. Informed consent was obtained from each patient. Inclusion criteria: Participants, who are willing and able to read, understand and sign the informed consent form, Age range 20-55 years, systemically healthy, generalized moderate or severe chronic periodontitis and those are indicated for open flap debridement. Exclusion criteria: any periodontal treatment in the preceding 6 months, any allergy to prescribed drugs, Participants with the habit of smoking and chewing tobacco, Participants on any antimicrobial treatment in the previous 6 months or treatment with any medication affecting the serum level of inflammatory markers such as anti-inflammatory, hormone replacement and steroids, stains, immune-suppressants and anti-coagulants and Female participants who are pregnant, lactating or using any acceptable methods of birth control. Exclusions are made to avoid the confounding effects of the diseases/conditions or the medications. All the subjects are informed about the procedure prior to the treatment and a written consent is obtained from them before the inclusion in the study. Following clinical parameters will be recorded before surgery: Probing depth, Clinical attachment level and gingival recession.

All the recordings were done by one examiner. The patients were allocated into two groups and scheduled for open flap debridement surgery following scaling and root planning; surgery for other quadrant will be planned at 3 weeks interval. All the surgeries were done by trained periodontist other than one carrying out this study. Test group (Group A) were administered combination of Ibuprofen 400 mg + Paracetamol 325mg + Caffeine 25mg and control group (Group B) were administered Ibuprofen 400 mg immediately after surgery and 8 hours later. Patients were unaware about drug given to them. For surgery,

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muco-periosteal flap will be raised under local anesthesia (2% lidocaine with 1:100,000 epinephrine) for complete scaling and root planing using Gracey curettes and ultrasonic instrumentation. Interrupted suturing was done. The location and the extent of surgery, volume of the local anesthesia given, and time required to perform the surgical procedure was recorded in the patient file along with any adverse effects to the drugs given. In case if the pain was not subside by the prescribed drug than Diclofenac sodium 50 mg was prescribed for immediate pain relief. Patients were instructed to complete a pain diary chart every hour for 2, 5 and 8 hours after the surgery and at night on the following 2 days. If Diclofenac sodium was prescribed than it was mentioned in pain dairy chart. The clinical pain intensity was recorded using Numeric Rate Scale (NRS). For the NRS-10, the patient rates his/her pain intensity on a numeric scale ranging from 0 to 10. (Fig: 1)

Fig 1: Numeric Rating Scale

III. RESULTS

Table 1: Gender Ratio for Cases and Controls

		Group		Total
		Case	Control	
SEX	F	15	15	30
		60.0%	60.0%	60.0%
	M	10	10	20
		40.0%	40.0%	40.0%
Total		25	25	50
100.0%		100.0%	100.0%	

Table 2: Mean age for Cases and Controls in years

	Group	N	Mean	Std. Deviation
AGE	Case	25	41.56	5.687
	Control	25	41.56	5.687

Table 3: NRS on first day 2 hours after surgery

			Group		Total
			Case	Control	
NRS2	4	Count	1	0	1
		% within Group	4.0%	.0%	2.0%
	5	Count	4	0	4
		% within Group	16.0%	.0%	8.0%
	6	Count	17	6	23
		% within Group	68.0%	24.0%	46.0%
	7	Count	3	15	18
		% within Group	12.0%	60.0%	36.0%
	8	Count	0	4	4
		% within Group	.0%	16.0%	8.0%
Total		Count	25	25	50
% within Group		100.0%	100.0%	100.0%	

Table 4: NRS on first day 5 hours after surgery

			Group		Total
			Case	Control	
NRS5	4	Count	5	0	5
		% within Group	20.0%	.0%	10.0%
	5	Count	11	3	14
		% within Group	44.0%	12.0%	28.0%
	6	Count	7	9	16
		% within Group	28.0%	36.0%	32.0%
	7	Count	2	11	13
		% within Group	8.0%	44.0%	26.0%
	8	Count	0	2	2
		% within Group	.0%	8.0%	4.0%
Total		Count	25	25	50
% within Group		100.0%	100.0%	100.0%	

Table 5: NRS on first day 8 hours after surgery

			Group		Total
			Case	Control	
NRS8	4	Count	8	0	8
		% within Group	32.0%	.0%	16.0%
	5	Count	10	1	11
		% within Group	40.0%	4.0%	22.0%
	6	Count	6	13	19
		% within Group	24.0%	52.0%	38.0%
	7	Count	1	11	12
		% within Group	4.0%	44.0%	24.0%
Total		Count	25	25	50
% within Group		100.0%	100.0%	100.0%	

Table 6: NRS on second day at night after surgery

			Group		Total
			Case	Control	
NRS_2NI	3	Count	3	0	3
		% within Group	12.0%	.0%	6.0%
	4	Count	8	2	10
		% within Group	32.0%	8.0%	20.0%
	5	Count	11	2	13
		% within Group	44.0%	8.0%	26.0%
	6	Count	3	19	22
		% within Group	12.0%	76.0%	44.0%
	7	Count	0	2	2
		% within Group	.0%	8.0%	4.0%
Total		Count	25	25	50

Table 7: NRS on third day at night after surgery

			Group		Total
			Case	Control	
NRS_3NI	2	Count	10	1	11
		% within Group	40.0%	4.0%	22.0%
	3	Count	9	0	9
		% within Group	36.0%	.0%	18.0%
	4	Count	6	9	15
		% within Group	24.0%	36.0%	30.0%
	5	Count	0	7	7
		% within Group	.0%	28.0%	14.0%
	6	Count	0	8	8
		% within Group	.0%	32.0%	16.0%
Total		Count	25	25	50
% within Group		100.0%	100.0%	100.0%	

A total of 25 patients: 15 males and 10 females (Table: 1) with mean age of 41.56 ± 5.687 years (Table: 2) diagnosed with chronic periodontitis and indicated for periodontal surgery were included in this split mouth crossover study. All the participants were prescribed both the drugs one after first surgery other after a cross-over period of 3 weeks for the second surgery. Patients were asked to note Numerical Rating Scale (NRS) at different intervals in their pain diary.

Results of the present study show that NRS value was 6 for 68% for test group and was 7 for 60 % for controls at an interval of 2 hours on first day after periodontal surgery. NRS value was 5 for 44% for intervention group and NRS value was 7 for 44 % of controls at an interval of 5 hours on first day after periodontal surgery. NRS value was 5 for 40% for cases and NRS value was 6 for 52% for controls at an interval of 8 hours on first day after periodontal surgery. (Table 3-5)

NRS value on second day at night was 5 for 44% cases and 6 for 76% controls. NRS value on third day at night was 2 for 40% for cases and 4 for 36% controls. (Table 6 and 7)

IV. DISCUSSION

Caffeine is combined with different NSAIDs to enhance pain control after various dental treatments like after tooth extraction and endodontic treatment. There are only few studies proving efficacy of this combination for pain control after periodontal flap surgery. So, this study was conducted with an aim of comparing efficacy of Ibuprofen 400 mg to combination of Ibuprofen 400 mg, paracetamol 325 mg and caffeine 25mg in pain management after periodontal surgeries.

Results of present study shows that NRS values are significantly low for test group for 2, 5, 8 hours on first day and at night for second and third day after periodontal surgery (P=0.000). No serious adverse effects were noted for any drug in any patients. Thus, the results of the present study indicate that Ibuprofen, Paracetamol and Caffeine combination is more potent for pain control after periodontal flap surgery as compared to Ibuprofen alone.

Similar results were observed in a cross over pilot study done by **Rashwan A. et al** [2] in 2009. They concluded by the study that Acetaminophen 500 mg, with caffeine 30 mg can be used efficiently in controlling postoperative pain as compared to ibuprofen 400 mg alone after open flap debridement.

In a systematic review conducted by **Nguyen L et al** [3] in 2011 to determine effectiveness of caffeine as an analgesic adjuvant to acetaminophen, ibuprofen and aspirin for postoperative dental pain appear to be weakly positive and they also suggested that caffeine potentiates the analgesic effects of some analgesics.

Derry C et al [4] in 2012 concluded by a systematic review that Caffeine is an effective analgesic adjuvant in acute pain after third molar extraction and it confers about 5-10% of extra pain relief. Use of caffeine as an analgesic adjuvant is very limited for pain control after periodontal surgery. Hence, as per results of the present study it can be said that caffeine in combination with NSAIDs is very effective in pain control after periodontal flap surgery without any significant adverse effects and can be used routinely for pain control after periodontal surgery.

Use of caffeine as an analgesic adjuvant for pain control is very common in medicine. According to a literature review by **Zhang W. et al** [5] in 1996, caffeine has been used for management of episiotomy pain, postpartum uterine cramp, cluster headache and a miscellaneous group of postoperative pain. **Diamond S. et al** [6] in 2000 performed a randomized; double masked, parallel, single-dose, placebo and active-controlled study in which 301 subjects were diagnosed with tension-type headache and were treated with Ibuprofen and caffeine, ibuprofen alone, caffeine alone, or placebo. Pain intensity was recorded using the VRS-4. The results of the study showed that administration of Ibuprofen and Caffeine combination showed significant improvement in tension-type headache over shorter time span as compared to Ibuprofen alone, caffeine alone or placebo. A study with high level of evidence with larger sample size should be carried out to prove the analgesic efficacy of caffeine.

V. CONCLUSION:

The data in the present study showed that caffeine with limited dose when combined with paracetamol and ibuprofen potentiates the analgesic effect. This combination is an efficient replacement for routinely used analgesics in the management of post-surgical pain. Based on the findings it may be suggested that the use of combination of ibuprofen, paracetamol and caffeine may be more valuable and effective protocol for post operative pain control in patients undergoing periodontal flap surgery.

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