To Evaluate Opioid Sparing effect of Diclofenac Sodium when used as an Intraoperative Analgesic during Maxillofacial Surgeries: A Prospective, Randomized, Placebo-control Study

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ABSTRACT

Introduction: Addition of single dose of diclofenac at the time of induction would exert opioid sparing effect during intra-operative period and reduce surges in blood pressure and pulse rate during noxious stimuli. Study aim was to compare the difference in intraoperative opioid consumption between two groups.

Material and Methods: The patients included in the study were randomized prior to anaesthesia in two groups 1. Group D (diclofenac group) received diclofenac sodium 1 mg/kg in 100 cc normal saline IV before induction of anaesthesia.2. Group P (placebo group) received 100 cc normal saline before induction of anaesthesia. Both groups received continuous infusion of IV fentanyl 1 mcg/kg/h as the standard analgesic. During surgery BP and pulse rate above 20% of baseline values will consider as sign of inadequate analgesia and will treat with an additional bolus dose of IV fentanyl 1mcg/kg.

Result: cases were comparable according to age, sex and ASA criteria. Difference in Intraoperative fentanyl requirement between two group were statistically significant at time of incision (p – 0.041), at 30 min. after incision (p-0.032) and at 60 min after incision (p- 0.046) with the lower requirements were found in diclofenac group.significant difference were also found in pain score and sedation score.

Conclusion: The diclofenac group patients shows that there is less requirement of fentanyl boluses to maintain haemodynamic stability. On the contrary placebo group required more fentanyl boluses intraoperatively.

Patient in the placebo groups were more sedated till the 8 hr postoperatively and their VAS score was significantly high in comparison to diclofenac group.

Keywords: ASA- American Society of Anaesthesiologist, MPR- Mean Pulse Rate, MBP- Mean Blood Pressure, VAS- Visual Analog Score, SBP- Systolic Blood Pressure, DBP- Diastolic Blood Pressure.

INTRODUCTION

In present era Incidence of road traffic accidents are on increasing trends leading to multiorgan trauma specially various fractures including fractures of mandible, maxilla and other head and neck area fractures which requires immediate interventions. Manipulation and excision of mandible, maxilla and tongue are extremely noxious stimuli and severe hypertension and tachycardia during these procedures is not unusual. Management includes deepening the plane of anaesthesia by increasing the anaesthetic drugs doses and addition intravenous opioids. Traditionally, strong analgesics such as opioids have been used intra-operatively whereas non-steroidal anti-inflammatory drugs (NSAIDs) and paracetamol are most commonly given at the end of surgery as part of multimodal approach to post-operative analgesia.[1,2] NSAIDs are highly effective in controlling bone pain and have analgesic effects in various conditions especially where tissue inflammation contributes to pain.[3,4] Concerns regarding the deleterious effects of NSAIDs on platelet function and renal function in conditions of renal hypoperfusion are some of the reasons why NSAIDS are not preferred as intra-operative analgesics. We hypothesized that addition of single dose of diclofenac at the time of induction would exert opioid sparing effect during intra-operative period and reduce surges in blood pressure and pulse rate during noxious stimuli.Study primary aim was to compare the difference in intraoperative opioid consumption between two groups. Secondary aims was to compare pain score and sedation score in recovery between two groups and to compare haemodynamic variables between two groups intraoperatively and postoperatively.

MATERIAL AND METHODS

This study was conducted in Department of Anaesthesiology M.G.M.Medical college indore after getting permission from the college ethics committee written informed consent were obtained from all the patients. In the operation theatre after establishing an intravenous route, a ringer lactate solution started. All patients received intravenous glycopyrollate 0.2 mg, ondensatron 0.1 mg /kg. All patients received a standard general anaesthesia. Standard monitoring including electrocardiography (ECG), noninvasive blood pressure (NIBP), oxygen saturation (SaO2) was contineously performed. The patients included in the study were randomized prior to anaesthesia to either:1. Group D (diclofenac group) received diclofenac sodium 1 mg/kg in 100 cc normal saline IV after induction of anaesthesia2. Group P(placebo group) received 100 cc normal saline after

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induction of anaesthesia.

Patients were randomized in two groups using computer randomization technique and the patients were blind to their group assignment.

Anaesthesia induced with fentanyl 2mcg/kg followed by propofol 2 mg/kg. Muscle relaxation achieved with succinylcholine 2mg/kg and inj Atracurium 0.5 mg/kg. Anaesthesia maintained with oxygen and nitrous oxide (40:60) and Isoflurane 1.5% dialed concentration for first 15 min which will be reduced to 0.8% there after and Atracurium 0.1 mg/kg (if required). Both groups received continuous infusion of IV fentanyl 1 mcg/kg/h as the standard analgesic. During surgery BP and pulse rate above 20% of baseline value considered as sign of inadequate analgesia and was treated with an additional bolus dose of IV fentanyl 1mcg/kg. At the end of surgery fentanyl infusion stopped. The neuromuscular block reversed with IV neostigmine 0.05 mg /kg and IV glycopyrrolate .01 mg/kg. All patients received standard post-operative care. Primary outcome was difference in opioid consumption between two groups. Secondary end point was pain score and sedation score in recovery patients. Pain score using visual analog scale (VAS) and sedation score, using University of Michigan sedation scale[5,6] were measured as part of vital signs monitoring on arrival and every four hourly for next 12 hours.

Inclusion criteria

- ASA Grade I and II patients
- Adult patients aged between 18 years to 60 years
- Patients posted for maxillofacial surgery.

Exclusion criteria

- Known allergy or contraindication to any drug going to be use in study.
- Patient's refusal
- Patients already on treatment with NSAIDs opioids, anticoagulants, methotrexate, cyclosporin, lithium or phenytoin.
- Bleeding disorders, pregnancy, acid-peptic disorder, heart disease, liver and kidney disease ASA grade III IV and V patients.

STATISTICAL ANALYSIS

Unpaired T test, Z test and fisher's exact test were applied and SPSS software was used for analysis of data.

RESULTS

Our study showed statistically significant difference between two study groups in consumption of fentanyl boluses during intraoperative period. During the period of incision, 30 min after incision and 60 min after incision there were significant less fentanyl requirement in diclofenac groups. P value were 0.041, 0.032 and 0.046 at incision, at 30 min and at 60 min respectively.(p value is < 0.05). in all other time periods fentanyl requirement were comparable in two groups. There was also significant difference in pain score between two groups at 0 hour,4 hour and 8 hour postoperatively with more mean pain score were found in placebo group. P values at 0,4,8 hours were less than 0.05. In Sedation score there were significant difference between two groups. Mean sedation score were more in placebo group with statistically significant P values of less than0.05.

Fentanyl Requirement	Diclofenac sodium group	Placebo group	Z value	P value
At intubation	7 (14.0%)	13 (26.0%)	-1.52	0.129, NS
At incision	6 (12.0%)	14 (28.0%)	-2.04	0.041*
At 5 min after incision	3 (6.0%)	7 (14.0%)	-1.35	0.179, NS
At 10 min after incision	3 (6.0%)	6 (12.0%)	-1.05	0.292, NS
At 20 min after incision	3 (6.0%)	8 (16.0%)	-1.62	0.105, NS
At 30 min after incision	2 (4.0%)	8 (16.0%)	-2.04	0.032*
At 60 min after incision	1 (2.0%)	6 (12.0%)	-2.00	0.046*
At closure	0 (0.0%)	1 (2.0%)	-1.01	0.312, NS
Z test for two sample proportion applied. P value < 0.05 was taken as statistically significant				

Table-1: Comparison of intraoperative fentanyl boluses requirement between the two groups at different time intervals (N=100)

Time interval	Diclofenac Sodium Group [Mean ± SD]	Placebo Group [Mean ± SD]	't' value	P value
0 hours	0.94 ± 1.13	3.64 ± 1.58	-9.843, df=98	0.016*
4 hours	1.04 ± 1.21	2.96 ± 1.47	-7.126, df=98	0.020*
8 hours	1.22 ± 1.25	1.92 ± 1.81	-2.254, df=89	0.026*
12 hours	0.86 ± 1.01	1.12 ± 1.33	-1.098, df=98	0.275, NS

Table-2: Comparison of pain score between the two groups at different time intervals (N=100)

Time interval	Diclofenac Sodium Group [Mean ± SD]	Placebo Group [Mean ± SD]	't' value	P value
0 hours	0.70 ± 0.71	1.66 ± 0.92	-5.861, df=98	0.010*
4 hours	0.06 ± 0.31	0.56 ± 0.79	-4.175, df=98	0.009*
8 hours	0.00 ± 0.00	0.08 ± 0.39	-1.429, df=98	0.156, NS
12 hours	0.00 ± 0.00	0.00 ± 0.00	-	-
Unpaired 't' test applied. P value < 0.05 was taken as statistically significant				

Table-3: Comparison of sedation score between the two groups at different time intervals postoperatively (N=100)

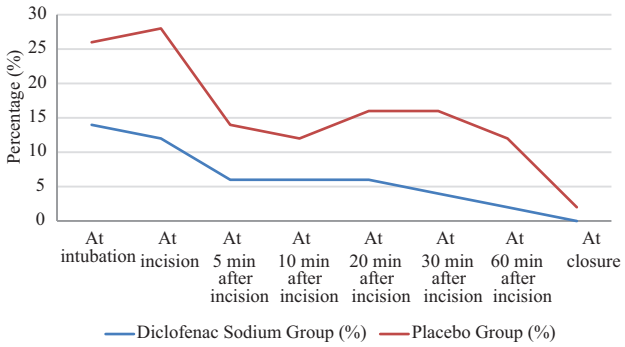

Figure-1: Line diagram showing percentage fentanyl requirement in both the groups

DISCUSSION

In our study primary end point was to compare fentanyl bolus requirement during intraoperative period at different time intervals between two groups. Results of our study showed that patients in the study group consumed significantly more I/V fentanyl boluses intraoperatively than diclofenac group. This increased consumption were mainly noted during the phase of incision (28% patients in placebo group vs. 12% patients in diclofenac group, $p< 0.05$), at the time of 30 minutes after incision (16% patients in Placebo group vs. 4% patients in diclofenac group, $p< 0.05$) and at 60 minutes interval after incision (12% patients in placebo group vs. 2% patients in diclofenac group, $p<0.05$). These values of fentanyl consumption between two groups in above mentioned time intervals were statistically significant.

Our study showed that diclofenac administered at the beginning of surgery reduced opioid required to control the haemodynamic response to surgical stimulation. During balanced anaesthesia, optimum analgesia reduces the dose of anaesthetic agents and muscle relaxants resulting in a better post-operative recovery. Better analgesia also helps to maintain cardiovascular Stability. NSAIDs are highly effective in conditions especially where tissue inflammation contributes to pain while lacking most of the side effects of opioids. They have been used as part of pre-emptive analgesia and shown to have an opioid sparing effect in many studies in post-operative pain management.[10-12]

The second end point in our study was to compare sedation score and pain score in two groups in postoperative period at 0 hr, 4 hr, 8 hr and 12 hr.

.In our study sedation score on arrival in recovery room were 0.70 ±0.71 and 1.66±0.79 respectively in diclofenac and placebo group ($p<0.01$) at 0 hr and sedation score 0.06±0.31 vs. 0.56±0.79 at 4 hr ($p<0.01$) showed that the patients in diclofenac group were less sedated in comparison to placebo group.

There was no statistically significant difference in sedation score between two groups at 8 hr and 12 hr interval.

On comparison of pain score the mean pain intensity at rest which was measured on VAS at arrival was 3.64±1.58 in placebo group compared to 0.94±1.13 in diclofenac group which was statistically significant ($p<0.01$). At 4 hrs postoperative period VAS in placebo group was 2.96±1.47 vs. 1.04±1.21 in diclofenac group which was statistically significant ($p<0.01$).There was also significant difference in VAS score between two groups at 8 hr postoperatively. ($p<0.05$) At 12 hours pain score were comparable in both groups ($p>0.05$).

CONCLUSION

This prospective and randomized comparative study shows that Diclofenac when given as an intra-operative analgesic reduced fentanyl consumption in the intra-operative period with extension of analgesia into the early post-operative period. Patients receiving diclofenac were significantly less sedated than those in the placebo. The diclofenac group patients shows that there is less requirement of fentanyl boluses to maintain haemodynamic stability in terms of mean blood pressure and mean heart rate in range of 20% of preoperative values. On the contrary placebo group required more fentanyl boluses intraoperatively. Both groups did not required any other drugs for controlling MBP and heart rate. Patient in the placebo groups were more sedated till the 8 hr postoperatively and their mean VAS scores were significantly high in comparison to diclofenac group.

Mean blood pressure were also increased significantly on various events such as incision and till closure to postoperatively 12 hrs in placebo group showed more haemodynamic stable trend in diclofenac group patients.

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