COMBINED DEXAMETHASONE AND DICLOFENAC VS SINGLE DICLOFENAC BASED ANALGESIC REGIMEN IN PATIENTS UNDERGOING MAXILLOFACIAL SURGERY: COMPARISON OF POST OPERATIVE ANALGESIA

Anaesthesiology

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ABSTRACT

Background: Pain Management is one of the most important aspects in maxillofacial surgery. This study was conducted to compare post-operative analgesic effect of combination of Dexamethasone and Diclofenac with Diclofenac only, in patients undergoing maxillofacial surgery under GA.

Materials and Method: Sixty adult patients of both genders of ASA physical status I and II undergoing maxillofacial surgery were randomly allocated in two groups. In Group C (n=30) patients received combination of injection dexamethasone (8 mg IV) and injection diclofenac sodium (75 mg) in 1st bottle of NS. In Group D (n=30) patients received injection diclofenac sodium (75 mg) in 1st bottle of NS and 2 ml NS IV (placebo). Intensity of post-operative pain was assessed by VAS score at 0,1,4,8,12,24 hours after surgery. Duration of analgesia was noted from time of 1st administration of rescue analgesic and total amount of rescue analgesic needed in 1st 24 hours was also calculated.

Results: Both the groups were comparable with respect to mean age, gender, body weight. VAS score of Group C was significantly lower than Group D with $p < 0.05$. Mean duration of analgesia in Group C was significantly higher than Group D with $p < 0.001$. Consumed dose of rescue analgesic (injection paracetamol) was higher in Group D than Group C with $p < 0.05$. Lesser Cumulative VAS scores were observed in Group C at 0,1,4,24 hours with p value < 0.05 .

Conclusion: Combination of injection diclofenac and dexamethasone is superior analgesic regimen than single diclofenac in maxillofacial surgery with lesser VAS score, prolonged duration of analgesia and lesser dose of rescue analgesic.

KEYWORDS

Maxillofacial Surgery, Diclofenac, Dexamethasone, VAS Score,

INTRODUCTION

Maxillofacial Surgery is a surgical specialty which involves the diagnosis, surgery and adjunctive treatment of diseases, injuries and defects of hard and soft tissues of oral and maxillofacial region. Postoperative pain is a major concern for this surgery. Among the various analgesic modalities diclofenac having both analgesic and anti-inflammatory effects found to be useful in controlling post-operative pain after maxillofacial surgical procedures. The administration of dexamethasone may synergize the anti-inflammatory effect of diclofenac and contribute to the reduction of inflammatory exudate as well as oedema and pain.¹

Most of the previous studies were done mainly on molar tooth extraction. Therefore this study was conducted to ascertain and compare the duration and intensity of analgesia measured by VAS score (primary outcome) in post maxillofacial surgery patient receiving either combined dexamethasone and diclofenac analgesic regimen or single diclofenac based analgesic regimen in first 24 hours of surgery. Mean duration of analgesia and total requirement of rescue analgesics (secondary outcome) were also observed in each group.

MATERIALS AND METHODS

After getting approval from the institutional ethics committee and obtaining consent from each patient, the study was conducted among sixty patients of ASA physical status I and II, aged between 18-60 years, who were undergoing maxillofacial surgery under general anaesthesia in plastic surgery operation theatre of R.G. Kar Medical College and Hospital between January 2016 and January 2017.

Exclusion criteria whereas –

1. ASA physical status $> II$
2. Contraindication or known allergy to diclofenac or dexamethasone
3. H/O of excessive bleeding
4. Chronic opioid therapy

Sample Size Calculation

Sample size (N) for each arm will be determined by the following formula:

$$N = [(Z\alpha + Z\beta)^2 \times (S1^2 + S2^2)] / d^2 \quad \text{Where,}$$

$$Z\alpha = 1.96 \text{ (Considering 95\% Confidence Interval)}$$

$$Z\beta = 0.84 \text{ (Considering 80\% Power of the test)}$$

$$S1 (2.1), S2 (2.9) = \text{Expected Standard Deviation of two groups from previous study conducted by Al-qudah et al in 2010.}^2$$

$$d = \text{Minimum clinically important difference of VAS Score between two groups (taken as 2)}$$

Now putting all the values, $N = [(1.96 + 0.84)^2 \times 2 \times (2.12 + 2.92)] / (2)^2 = 25.127 = 25$. As 20% of patients undergoing maxillofacial surgery need ventilatory support post-operatively they will be excluded from my study. So, sample size for each arm will be $= 25/0.8 = 31.25 = 31$. After rounding up, 30 samples have been taken in each group ($n=30$).

Procedure and Data Collection

Patients were randomly allocated in Group C and Group D using Sealed envelope technique. Airway preparation for awake intubation was done with nebulization with 4% lignocaine. Injection glycopyrrolate 0.2 mg IM and injection, ondansetron 0.4 mg IV was administered half an hour before induction. Fiber optic bronchoscope was prepared, and awake intubation was done. Induction was done with injection midazolam (0.5 mg/Kg), injection fentanyl (2 micro gram/Kg), injection propofol (2 mg/Kg) IV. Muscle relaxation was achieved with injection vecuronium bromide (0.1 mg/Kg of body weight). Injection diclofenac sodium – 75 mg IV was given in 1st running bottle of normal saline to both the group. Injection dexamethasone 8 mg IV was administered to Group C and normal saline 2 ml was administered to Group D patients. Maintenance of anaesthesia was achieved with nitrous Oxide (66%), oxygen (33%) and isoflurane (1%) and incremental dose of vecuronium bromide (0.2 mg/kg of body weight) and injection fentanyl (1 micro gram/kg /hour) IV. Two patients who needed to be kept on ventilator were excluded from my study. Duration and intensity of analgesia was assessed in post-operative period after 1 hour, 4 hours, 8 hours, 12 hours, 24 hours by VAS score (consist of 10 cm horizontal or vertical line with two end points zero – no pain, 10 – worst ever pain). If the patient pain score as assessed by VAS was more than 4, then rescue analgesia – injection paracetamol (1 gm infusion IV) was administered. Maximum

permitted dose of paracetamol was 4gm IV infusion per day. Time of first administration of first dose of rescue analgesia was noted and total amount of rescue analgesic needed in 1st 24 hours was also noted. Mean values of rescue medication for each of the regimen were calculated.

RESULTS AND ANALYSIS

Data was analyzed by SPSS 20 software. A 'P' value of $\leq 0.05\%$ was considered as significant. In this study, 29 patients were finally followed up of whom Group C had **44.83%** male population and **55.17%** female population whereas group D had **62.07%** male and **37.93%** female population. Mean age of Group C and Group D were **48.2 $\pm$ 7.9** and **47.5 $\pm$ 7.1** respectively. Mean body weight of Group C and D were **61.8 $\pm$ 7.8** and **65.8 $\pm$ 8.9** Kg respectively. ASA grade I patients were **58.62%** in group C compared to **51.72%** in group D and ASA grade II patients were **41.38%** in group C compared to **48.28%** in group D. The difference was not statistically significant. So both the groups were comparable in terms of demographic profile.

Mean VAS Score of both the groups were compared at different point of time at post-operative period (Table 1, Fig 1) by using independent-t test. Mean difference was significant after 0-hour, 1 hour, 4 hour and 24 hours with the p value of 0.0000001, 0.00005, 0.000007 and 0.025. Mean difference was not significant after 12 hours and 24 hours.

Table 1 - Comparison Of Post Operative Visual Analogue Scale (vas) Score

VAS (Hours)	Group C (Mean)	Group D (Mean)	P value	Significance
VAS (0 Hr)	1.3 $\pm$ 0.72	2.6 $\pm$ 0.50	0.0000001	YES
VAS (1 Hr)	1.8 $\pm$ 1.01	2.9 $\pm$ 0.68	0.00005	YES
VAS (4 Hr)	2.6 $\pm$ 0.72	3.9 $\pm$ 0.81	0.000007	YES
VAS (8 Hr)	3.8 $\pm$ 0.60	3.7 $\pm$ 0.76	0.45	NO
VAS (12 Hr)	2.9 $\pm$ 0.75	3 $\pm$ 0.75	0.52	NO
VAS (24 Hr)	2.1 $\pm$ 1.46	2.5 $\pm$ 1.58	0.025	YES

Fig. 1 - Comparison of VAS Score at different point of time

Mean of Cumulative VAS Score of both the groups were compared (Fig 2), by using independent-t test. Mean difference was significant (Gr C = 2.4 $\pm$ 1.55 vs Gr D 3.1 $\pm$ 1.76) with the p value of 0.044.

Fig2 - Comparison of Mean of Cumulative VAS Score

Mean duration of analgesia (Fig :3) of two groups were compared by independent t-test. The difference is significant (Gr C : 7.1 $\pm$ 3.10 hrs vs Gr D : 4.07 $\pm$ 2.18 hrs) with the p value of 0.0008.

Fig. 3 - Comparison of mean Duration of Analgesia (Hours) in Two Groups

Total dose of rescue analgesic (mean) consumed by two groups within 24 hours of surgery, were compared (Table:2) by independent t-test. The difference is significant with the p value of 0.009.

Table 2- Comparison Of Requirement Of Total Dose Of Rescue Analgesic Within 24 Hours

Variable	Group C (Mean)	Group D (Mean)	P value	Significance
Total Dose of Rescue Analgesics (gm)	1.24 $\pm$ 0.51	1.68 $\pm$ 0.54	0.009	YES

DISCUSSION

Maxillofacial surgery deals with diagnosis and management of benign and malignant pathology of oral and maxillofacial region and reconstruction of the defects. Postoperative pain is one of the main concerns of this surgery. It is usually managed by multimodal approach. Diclofenac acts as a good analgesic due to its great penetration into inflamed tissues and synovial fluid. On the other hand, local reactions like redness, swelling and tenderness are suppressed by cortisol and its synthetic analogue.³ Jose Leonardo Simone et al, in 2013 concluded that both steroidal and non-steroidal analgesic drugs act by inhibiting the same chain reactions that degrade phospholipids of injured cell membranes, responsible for the allergic and inflammatory response. Preemptive administration of the above medication contributes to lowering the concentration of these mediators in tissue.⁴ Dexamethasone prevents hyperalgesia through phospholipase A2 and inducible cyclooxygenase inhibition. Diclofenac acts directly on ongoing inflammatory hypersensitization. These analgesics restore the nociceptor by stimulating the arginine/NO/cGMP/K(ATP) channel pathway.⁵ Clinical trials in oral surgery have also supported the hypothesis that preemptive NSAIDs and corticosteroids are effective in delaying and preventing many postoperative events.⁶ The apparent interactions between the mechanisms of action of nonsteroidal anti-inflammatory drugs (NSAIDs) and steroids suggests that co-therapy may provide beneficial anti-inflammatory effect and pain relief in the absence of side effects. Considering all these data, the present prospective comparative study was done at plastic surgery of R.G. Kar Medical College & Hospital.

Patients of the two groups were comparable in respect to the demographic profile and baseline vital parameters. Statistically significant difference in VAS scores between two groups were observed immediately after surgery, after 1 hour, 4 hours and 24 hours of surgery ($p < 0.05$). Lesser VAS scores were seen in Group C. There was no significant difference in VAS Scores between the groups after 8 and 12 hours of surgery.

Onset of action of Diclofenac is within 15 minutes when given in IV fluid. Tmax for Diclofenac is 1 hour. Mean half-life of Dexamethasone is around 200 minutes and onset is within 30 minutes. So, immediately after surgery and after 1 hour, blood levels of both Diclofenac and Dexamethasone are at its maximum level. So, Group C who received combination regime, showed significantly lower mean VAS score than the Group D. After 4 hours, blood level of Diclofenac starts to decrease gradually, but Dexamethasone still has its pharmacological effect upto 7 hours. So, VAS scores were comparable after 8 and 12 hours of surgery. As, after 4 hours, most of the patients received rescue analgesics, there was no significant difference in VAS scores after 8 hours and 12 hours of surgery with the p value 0.45 and 0.52

respectively. So, in the present study, mean of cumulative VAS Score was also calculated and it was higher in Group D than Group C with the p value 0.044. In present study, it was found that in the group C mean duration of analgesia was 7.14 ± 3.1 hours with maximum duration of 12 hours and minimum duration of 1 hour. In the other group D mean duration of analgesia was 4.07 ± 2.1 hours with maximum duration of 8 hours and minimum duration of 1 hour. In 2005, Babatunde et al conducted a study in 100 patients undergoing oral surgery.⁷ The patients were randomly allocated to two treatment groups of dexamethasone (prophylactic 8 mg and postoperative 4 mg IV) and diclofenac (50 mg Oral before and after surgery), and diclofenac alone (as with first group). The overall analgesic efficacy of the drug combination was assessed postoperatively by determination of pain intensity using a category rating scale. Co-administration of dexamethasone and diclofenac was significantly superior to diclofenac alone as measured by pain intensity score ($P < 0.05$). Lin TC et al, in their study, showed that nonsteroidal anti-inflammatory drugs (NSAIDs) and steroid can effectively reduce the postoperative sequelae after impacted third molar removal.⁸ They concluded that combination of diclofenac and prednisolone has a better analgesic and anti-inflammatory effect. Present study corroborated with the above study findings.

Buyukkurt MC et al conducted a study in 2006 in forty-five patients undergoing surgical removal of lower third molars and they compared the effect of a single intramuscular dose of prednisolone and the prednisolone-diclofenac combination on postoperative pain, trismus, and edema after the removal of third molars.⁹ Statistical analysis of the data indicated that the prednisolone-diclofenac combination suppressed pain intensity in comparison with control ($P < .05$) at the 6-hour observation. Both the prednisolone and prednisolone-diclofenac combinations suppressed pain at the seventh postoperative hour in comparison with the control ($P < .05$). Prashar DV et al. in 2016, conducted a study to evaluate the effect of methylprednisolone with diclofenac sodium (group A) as compared with diclofenac sodium and placebo (group B) on three variables: Pain, swelling and trismus, after third molar surgery. Mean difference in pain experienced between the two groups was statistically significant at 24 h and 72 h and on the seventh day ($P = 0.005$). They concluded that the combination of oral dose of methylprednisolone (a corticosteroid) diclofenac sodium (a non-steroidal anti-inflammatory drug) was found to be more effective than diclofenac sodium alone on the sequelae of surgical removal of impacted mandibular third molar.¹⁰

The total amount of rescue medication (TARM) ingested (paracetamol) was another variable of this study. TARM required by group C was 1.24 ± 0.51 gms and by group D was 1.69 ± 0.54 gms. The difference was significant with p value of 0.009. Similar study was conducted by Dipashri Bhattacharya et al in 2005 in the group of patients undergoing tonsillectomy surgery and they found that mean duration of analgesia in the group who received both dexamethasone and diclofenac was (8 ± 2) hours and in the other group who received only diclofenac was (5 ± 1.5) hours with the P value $< .05$. The need for rescue analgesic was significantly lower in the dexamethasone + diclofenac group than only diclofenac.¹¹ De Oliveira GS Jr et al conducted a study and found that dexamethasone at doses more than 0.1mg/kg is an effective adjunct in multimodal strategies to reduce postoperative pain and opioid consumption after surgery.¹² Another study result may be mentioned here that Sisk et al. evaluated methylprednisolone and flurbiprofen for the inhibition of the postoperative inflammatory response and found that a combination of these two drugs was necessary to control postoperative pain effectively.¹³

There was no significant complication noted among both the groups. None of the patients showed any allergic reactions and wound related complications in post-operative period.

In a meta-analysis,¹⁴ it was concluded that perioperative administration of high-dose methylprednisolone (30–35 mg/kg), a dose equivalent to 50 times the dose of dexamethasone (8 mg), was not associated with significant side effects. Also, a recent meta-analysis of postoperative nausea and vomiting indicated that a single dose of dexamethasone did not increase infectious or other complications.¹⁵

CONCLUSION

It can be concluded from this study results that combination of diclofenac and dexamethasone can be used as superior analgesic for

maxillofacial surgery than diclofenac only without increasing side effects. There is no conflict of interest.

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