ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 8, Issue, 05, pp.31894-31899, May, 2016

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

EFFECT OF SINGLE PREOPERATIVE DOSE OF INTRAVENOUS AND INTRAMUSCULAR DEXAMETHASONE ON SURGICAL REMOVAL OF THIRD MOLAR

Rashmi Patwa, *Sonal Shah, Pallavi Sarve, Pushkar Waknis, Lakshmi Shetty and Pratik Suthar

Department of Oral and Maxillofacial Surgery, Dr. D. Y. Patil Vidyapeeth; Dr. D. Y. Patil Dental College and Hospital, Pimpri, Pune

ARTICLE INFO

Article History:
Received 20th February, 2016
Received in revised form
21st March, 2016
Accepted 14th April, 2016
Published online 31st May, 2016

Key words:

Dexamethasone,
Intramuscular,
Intravenous,
Swelling,
Pain,
Trismus.

ABSTRACT

Purpose: The surgical extraction of lower third molars is the most frequent intervention in oral surgery. Swelling, trismus and pain are normal phenomena induced after surgical removal of impacted mandibular third molar. The use of corticosteroids has gained wide acceptance to reduce postoperative complications. Many studies have used dexamethsone in dentoalveolar surgery to reduce facial swelling, pain and trismus but the comparative study on half an hour preoperative intramuscular and intravenous injection of dexamethasone has not been undertaken for studying its effect on postoperative sequlae of surgical removal of mandibular third molar which has been done in the present study.

Methodology: Study was conducted on 15 patients with bilaterally impacted mandibular third molars with similar difficulty index. The patients were given single preoperative dose of 8mg intravenous and intramuscular dexamethasone for surgical removal of impacted mandibular third molar with a minimum interval of 1 month between two surgeries. Pre operative and first, third and seventh postoperative day's inter-incisal distance, facial swelling & pain was assessed based on VAS. The data was subjected for statistical analysis.

Results: The significant lower values of pain score on VAS scale were noted with the intravenous route of administration of dexamethasone.

Conclusion: This study reveals that the half an hour preoperative intravenous route of administration of dexamethasone is preferable over the intramuscular route to reduce the incidence of post operative pain on surgical removal of impacted mandibular third molar.

Citation: Rashmi Patwa, Sonal Shah, Pallavi Sarve, Pushkar Waknis, Lakshmi Shetty and Pratik Suthar, 2016. "Effect of single preoperative dose of intravenous and intramuscular Dexamethasone on surgical removal of third molar", *International Journal of Current Research*, 8, (05), 31894-31899.

INTRODUCTION

"The surgical extraction of lower third molars is the most frequent intervention in oral surgery" (Warraich *et al*., 2013). Inflammatory edema and pain is normal phenomena induced after any surgical procedure including surgical removal of impacted mandibular third molar (Arakeri *et al*., 2013). The patient's qualities of life get affected as a result of the postoperative inflammatory response is often associated with swelling, pain and trismus (Majid and Mahmood, 2011). Inflammatory process is designed to protect and promote healing of injured tissues (Becker, 2013) "Post operative inflammation is characterized by increased vascular permeability, migration of leucocytes into the inflamed area, the release of chemical meadiators of inflammation from leucocytes and interaction of these mediators with the other mediators, such as kinin and complement" (Arakeri *et al*., 2013). To solve these problems different drugs like steroids, non-steroidal anti-inflammatory drugs, antihistamins, long acting local anesthetics and antibiotics have been tried with the varying degree of success (Arakeri *et al*., 2013). The use of corticosteroids has gained wide acceptance to reduce postoperative complications (Majid and Mahmood, 2011). In 1949 the first discovery of anti-inflammatory action of corticosteroids given by Hench and co-workers in the treatment of Rheumatoid arthritis. During the 1950s several researchers demonstrated that hydrocortisone may prevent inflammation following oral surgery (Stewart and Ross., 1958) (Balakrishnan and Ebenezer, 2014). The first published article in oral surgery with the use of hydrocortisone given in dates back to 1952 (Ata-Ali *et al*., 2011). Due to the powerful anti-inflammatory effects Corticosteroids these are well known adjuncts to surgery (Bortoluzzi *et al*., 2013). "The administration of corticosteroids is thought to inhibit mast cell production and secretion of cytokine, kinin and histamine which promotes an inhibition of thromboxane and bradykinin,

Corresponding author: Sonal Shah,
Dr. D. Y. Patil Dental College and Hospital, Pimpri, Pune, India.

resulting in less blood vessel dilatation and less permeability (Huffman 1997; Schaberg 1984). (Montgomery and Hogg J P, 1990) described that a single pre-operative or postoperative dose of corticosteroids given intramuscular gives a good plasma concentration of the drug and prolonged anti-inflammatory action" (Balakrishnan and Ebenezer, 2014). Dexamethasone which is a synthetic analog of prednisolone is the most commonly used forms of corticosteroids in dentoalveolar surgery, and may help reducing pain, edema and trismus (Bortoluzzi *et al*., 2013). Dexamethasone is 25-50 times more potent than hydrocortisone and is up to sixteen times as potent as prednisolone (Allen, 2007). The forms of corticosteroids in dentoalveolar surgery which include dexamethasone (oral), dexamethasone sodium phosphate (IM or IV) and dexamethasone acetate (IM), methylprednisolone (oral), methylprednisolone sodium succinate (IV or IM) (Arakeri *et al*., 2013). The steroid should have few mineralocorticoid effects and good biological activity. Dexamethasone has no mineralocorticoid activity with the half life of 36-72 hours and it is 25 times more potent than hydrocortisone. It also has least depressing effect on leucocyte chemotaxi (Mushtaq *et al*., 2011).

Many studies have used dexamethsone in dentoalveolar surgery to reduce facial swelling, pain and trismus (Klongnoi *et al*., 2012). Many types, dosages and times of administration have been studied for dexamethasone but a comparative study on half an hour preoperative intramuscular and intravenous injection of dexamethasone has not been undertaken for studying its effect on postoperative sequlae of surgical removal of mandibular third molar.

MATERIALS AND METHODS

Source of data

It is an in-vivo, randomised, split-mouth study whereby the data analyzer was blind conducted on 15 patients with clinical and radiological confirmation undergoing surgical extraction of bilateral impacted mandibular third molars with similar degree of difficulty attending the Department of Oral and Maxillofacial Surgery over a period of one and a half years. Institutional ethics committee clearance was obtained prior to commencement of the study.

Inclusion criteria

a. Medically fit patients requiring surgical removal of bilateral mandibular third molars.
b. Patients willing to participate in study.

Exclusion criteria

The following diseases are aggravated by corticosteroids hence any patient giving history of any of these will be excluded from the study:

- Peptic ulcer
- Diabetes mellitus
- Hypertension
- Viral and fungal infections
- Tuberculosis
- Epilepsy
- CHF
- Renal failure

METHODOLOGY

15 patients requiring surgical extraction of bilateral impacted mandibular third molars fulfilling the above mentioned inclusion criteria had undergone clinical and radiological confirmations, followed by routine haematological examination. The details of the procedure and the possible complications had been explained to the patient and written informed valid consent had obtained. Detailed case history was taken. All patients undergoing surgical removal of impacted mandibular third molar on one side had been given a single dose of injection dexamethasone 8mg (Figure 1) intravenously half an hour prior to surgery. Pre operative inter-incisal distance, facial swelling & pain was assessed based on VISUAL ANALOGUE SCALE. The length of their faces had been measured using the reference points:

Fig.1. Injection Dexamethasone 8mg

Fig.2. Inferior border of earlobe to corner of mouth

Fig.3. Inferior border of earlobe to soft tissue pogonion

Fig.4. Lateral corner of eye to angle of the mandible

Fig. 5. Normal interincisal distance

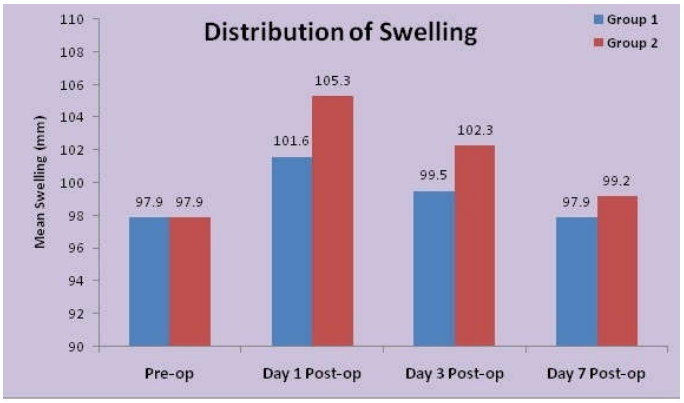

Fig.6. Distribution of Facial swelling

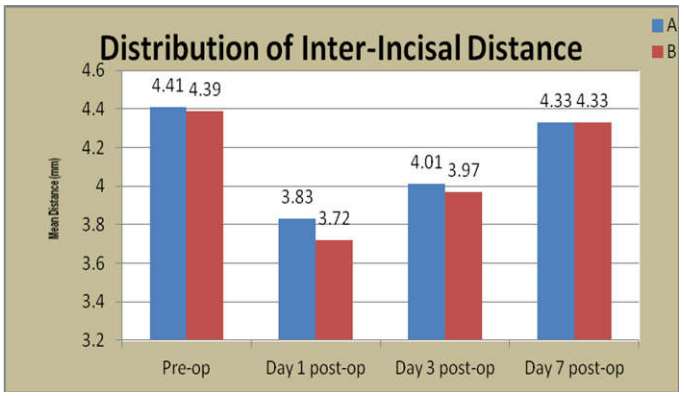

Fig. 7. Distribution of Interincisal distance

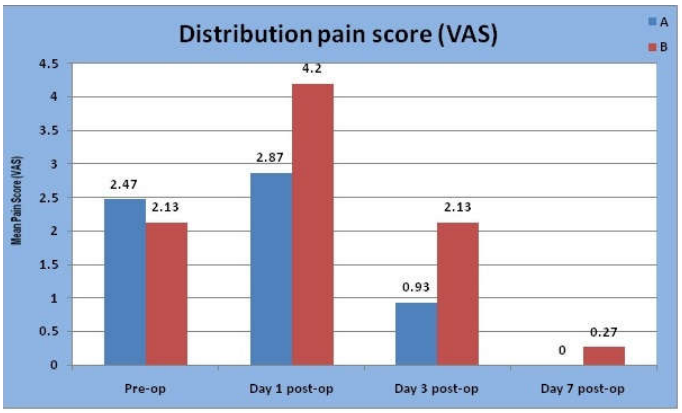

Fig.8. Distribution of Pain Score

- Inferior border of earlobe to corner of mouth (Figure 2)
- Inferior border of earlobe to soft tissue pogonion and (Figure 3)
- Lateral corner of eye to angle of the mandible (Figure 4)

Normal interincisal distance was measured and recorded with the help of metallic scale (Figure 5). Surgical procedure of removal of impactsssed mandibular third molar was carried out. Patient had been recalled for first, third and seventh post operative days and evaluated for pain, trismus and facial swelling. After an interval of one month same patient had been given a single dose of injection dexamethasone 8mg intramuscularly at deltoid muscle half an hour prior to surgery for surgical removal of third on the other side and similar procedures were repeated. Similarly patient had been recalled

for first, third and seventh post operative days and evaluated for the pain, swelling and trismus. The data obtained was tabulated and sent for statistical analysis. The methods of statistical analysis employed were Wilcoxon ranked test for intergroup comparison and Sign ranked test for intragroup comparison.

RESULTS

Facial swelling (Figure 6, Table 1)

1) Inter-group comparison: The average pre-op swelling did not statistically differ between side A**(intravenous group)** and side B **(intramuscular group)** for all the parameters of facial measurements. (P value > 0.05 for all) The average day 1 post op swelling did not statistically differ between side A and side B for all the parameters of facial measurements.(P value > 0.05 for all) The average day 3 post op swelling did not statistically differ between side A and side B for all the parameters of facial measurements. (P value > 0.05 for all) The average day 7 post op swelling did not statistically differ between side A and side B for all the parameters of facial measurements. (P value > 0.05 for all)

2)Intra- group comparison: There was statistically significant difference between Pre- op and day 1 Post op for all the measurements in both side A and side B. There was statistically significant difference between pre-op and day 3 post –op for facial measurement related to corner of mouth to inferior border of ear lobe in side A. There was statistically significant difference between Pre- op and day 3 Post op for all the measurements in side B. There was statistically non-significant difference between Pre- op and day 7 Post op for all the measurements in both side A and side B.

Interincisal distance (Figure 7, Table 2)

1) Inter-group comparison: The average pre-op interincisal distance did not differ statistically between side A and side B.(P value > 0.05)The average day 1 post op interincisal distance did not differ statistically between side A and side B.(P value > 0.05) The average day 3 post op interincisal distance did not differ statistically between side A and side B.(P value > 0.05) The average day 7 post op interincisal distance did not differ statistically between side A and side B.(P value > 0.05)

2) Intra- group comparison: There was statistically significant difference between Pre- op and day 1, day 3 Post op for side A i.e. in intravenous group for the interincisal distance. (P- Value < 0.05) There was no statistically significant difference between pre-op and day 7 post op for side A i.e. in intravenous group for the interincisal distance. (P value > 0.05) There was statistically significant difference between Pre- op and day 1, day 3, day 7 Post op for side B i.e. in intramuscular group for the interincisal distance.(P- Value < 0.05)

Pain (Figure 8, Table 3)

1) Inter-group comparison: The average pre-op pain score did not differ statistically between side A and side B.(P value > 0.05) The average day 1 post op pain score differ statistically between side A and side B. (P value < 0.05) The average day 3 post op pain score differ statistically between side A and side B. (P value < 0.05)The average day 7 post op pain score did not differ statistically between side A and side B. (P value > 0.05)

Table 1* The inter and intra group comparison of swelling

Swelling Score	Line	Side A (n=15) (IV injection Dexamethasone)	Side B (n=15) (IM injection Dexamethasone)	Inter-Group P-values (Side A v Side B)
Pre-operative	(1)Corner of the mouth to inferior border ear lobe	11.22±1.29	11.39±1.28	0.6890 **(NS)**
	(2)Lateral canthus of the eye to angle of mandible	9.50±0.77	9.60±0.67	0.6582 **(NS)**
	(3)Inferior border of ear lobe to soft tissue pogonion.	13.27±0.74	13.35±0.77	0.6873 **(NS)**
	Above combined	11.33±1.82	11.45±1.80	
Day 1 Post-op	(1)Corner of the mouth to inferior border ear lobe	11.65±1.21	12.03±1.04	0.3938 **(NS)**
	(2)Lateral canthus of the eye to angle of mandible	9.67±0.86	10.22±0.85	0.1224 **(NS)**
	(3)Inferior border of ear lobe to soft tissue pogonion.	13.45±0.66	13.67±0.69	0.4055 **(NS)**
	Above combined	11.59±1.8	11.97±1.66	
Day 3 Post-op	(1)Corner of the mouth to inferior border ear lobe	11.47±1.19	11.82±1.09	0.4296 **(NS)**
	(2)Lateral canthus of the eye to angle of mandible	9.55±0.86	9.99±0.72	0.2281 **(NS)**
	(3)Inferior border of ear lobe to soft tissue pogonion.	13.34±0.69	13.49±0.67	0.5572 **(NS)**
	Above combined	11.45±1.81	11.77±1.67	
Day 7 Post-op	(1)Corner of the mouth to inferior border ear lobe	11.23±1.28	11.39±1.26	0.7043 **(NS)**
	(2)Lateral canthus of the eye to angle of mandible	9.49±0.79	9.94±1.41	0.4400 **(NS)**
	(3)Inferior border of ear lobe to soft tissue pogonion.	13.23±0.79	13.34±0.76	0.5994 **(NS)**
	Above combined	11.32±1.82	11.56±1.82	
Intra-Group Comparisons	P-values			
Pre-op v/s Day 1 Post-op	(1)Corner of the mouth to inferior border ear lobe	0.0001 **(S)**	<.0001 **(S)**	
	(2)Lateral canthus of the eye to angle of mandible	0.0081**(S)**	<.0001 **(S)**	
	(3)Inferior border of ear lobe to soft tissue pogonion.	0.0039 **(S)**	0.0002 **(S)**	
Pre-op v/s Day 3 Post-op	(1)Corner of the mouth to inferior border ear lobe	0.0010 **(S)**	0.0002 **(S)**	
	(2)Lateral canthus of the eye to angle of mandible	0.1797 **(NS)**	0.0001 **(S)**	
	(3)Inferior border of ear lobe to soft tissue pogonion.	0.0625 **(NS)**	0.0156 **(S)**	
Pre-op v/s Day 7 Post-op	(1)Corner of the mouth to inferior border ear lobe	1.0000 **(NS)**	0.8750 **(NS)**	
	(2)Lateral canthus of the eye to angle of mandible	0.7500 **(NS)**	0.3125 **(NS)**	
	(3)Inferior border of ear lobe to soft tissue pogonion.	0.5000 **(NS)**	1.0000 **(NS)**	

Table 2* The inter and intra group comparison of Inter-incisal distance (mm)

Inter-Incisal (mm)	Side A (n=15) (IV injection Dexamethasone)	Side B (n=15) (IM injection Dexamethasone)	Inter-Group P-values (Side A v Side B)
Pre-operative	4.41±0.61	4.39±0.56	0.8120 (NS)
Day 1 Post-op	3.83±0.76	3.72±0.68	0.7508 (NS)
Day 3 Post-op	4.01±0.80	3.97±0.70	0.6891 (NS)
Day 7 Post-op	4.33±0.64	4.33±0.61	0.8278 (NS)
Intra-Group Comparisons			
Pre-op v/s Day 1 Post-op	0.0002 (S)	<.0001(S)	
Pre-op v/s Day 3 Post-op	0.0005 (S)	0.0001 (S)	
Pre-op v/s Day 7 Post-op	0.0625 (NS)	<.0001 (S)	

Table 3* The inter and intra group comparison of pain score (VAS)

Pain Score (VAS)	Side A (n=15) (IV injection Dexamethasone)	Side B (n=15) (IM injection Dexamethasone)	Inter-Group P-values (Side A v Side B)
Pre-operative	2.47±2.23	2.13±1.60	0.8802 **(NS)**
Day 1 Post-op	2.87±1.68	4.2±1.08	0.0198 **(S)**
Day 3 Post-op	0.93±1.03	2.13±1.60	0.0180 **(S)**
Day 7 Post-op	0±0	0.27±0.59	0.2241 **(NS)**
Intra-Group Comparisons			
Pre op v/s Day 1 Post-op	0.2573 **(NS)**	0.0004 **(S)**	
Pre op v/s Day 3 Post-op	0.0273 **(S)**	1.0000 **(NS)**	
Pre op v/s Day 7 Post op	0.0010 **(S)**	0.0010 **(S)**	

*Values are Mean ± standard deviation. P-values for intergroup comparison are obtained from Wilcoxon ranked test and intragroup comparison are obtained from Sign ranked test.
P - Value < 0.05 is considered to be statistically significant.
S: Statistically Significant; NS: statistically non significant

2) Intra- group comparison: There was statistically no significant difference between Pre- op and day 1 post op for side A i.e. in intravenous group for pain score. There was statistically significant difference between Pre- op and day 3, day 7 post op for side A i.e. in intravenous group for pain score. There was statistically significant difference between Pre- op and day 1, day 7 post op for side B i.e. in intramuscular group for pain score. There was statistically no significant difference between Pre- op and day 3 post op for side B i.e. in intramuscular group for pain score.

DISCUSSION

Impacted lower third molar surgery is one of the common procedures used in oral surgery which can lead to postoperative complication such as facial swelling, severe pain and trismus. Many studies about reducing postoperative swelling, pain and trismus after dentoalveolar or lower third molar have used dexamethasone (Boonsiriseth *et al*., 2012). The steroid elected should have few mineralocorticoid effects and good biological activity. Dexamethasone is 25 times more potent than hydrocortisone and it also seems to have the least depressing effect on leukocyte chemotaxis (Mushtaq *et al*., 2011). All the patients chosen for the study were healthy and no discernible side effects, including infection or complications in wound healing were observed. In this study we used intramuscular and intravenous injections of 8mg dexamethasone, half an hour prior to surgery because of the onset of the drug. Dexamethasone act immediately after the traumatic effect of mandibular third molar removal (Klongnoi *et al*., 2012). This study also showed no side effects from 8mg dexamethasone intramuscular or intravenous injections. "After single dose of corticosteroids there was suppression of the pituitary adrenal hypophysis axis. Cortisol levels return to normal value within 5 to 10 days" (Williamson *et al*., 1980; Zora *et al*., 1986; Novak *et al*., 1970). Therefore we selected a gap of 1 month between the two surgeries providing the patients sufficient time to recover from the effects of the earlier surgery. This study showed no significant difference in the surgical times between the groups because the difficulty index of the impacted mandibular third molar was similar. In this study we found no significant difference between facial swelling in the intravenous and intramuscular dexamethasone groups on first, third and seventh post operative days. This result is concurrent with the study of Mushtaq *et al*. in which they studied the effect of 8 mg IM dexamethasone in third molar surgeries and they found significant reduction in swelling when compared with the control group (Mushtaq *et al*., 2011). According to the another study conducted by Arakeri *et al*. the use of dexamethasone IV when removing impacted third molar has been shown to have objective and subjective benefits (Arakeri *et al*., 2013).

In our study, the mean facial measurements on first, third and seventh post operative days in intravenous group were 11.59 ±1.81, 11.45 ± 1.81 and 11.32 ±1.82 respectively and in intramuscular group were 11.97 ± 1.66,11.77±1.67 and 11.56 ± 1.82 respectively. There was less swelling with the intravenous group but this result is not statistically significant. This result is concurrent with the study conducted by the Majid O W and Mahmood W K which concluded that as long as swelling is considered, intravenous route gave the best improvement, followed by the intramuscular route (Majid and Mahmood, 2013).

Study conducted by Majeed and Mahmood and also study conducted by Klongnoi *et al* showed that IM route of dexamethasone had no significant effect on the trismus as compared with the control group (Majid and Mahmood, 2011; Klongnoi *et al*., 2012). In our study we compared the effect of

intravenous and intramuscular dexamethasone on the interincisal distance which showed no significant difference on first, third and seventh post op days. In this study, significant difference was found with the pain score measured by VAS scale in the two groups on first and third postoperative days, with less pain being experienced by the patient in the intravenous group. Clasmen *et al*. studied the analgesic effect of IV Ketorolac and Dexamethasone following surgical removal of third molar, and they found that the pain score was significantly lower than the control group (Claseman *et al*., 1998). Majeed and Mahmood also studied the pain score on VAS scale after the administration of 4 mg dexamethasone intravenous and intramuscular postoperatively and found that intravenous dexamethasone showed less pain when compared with the other routes of administration of dexamethasone (Majid and Mahmood, 2011).

In conclusion, in our study intravenous and intramuscular routes of administration of dexamethasone half an hour preoperatively showed no significant difference with respect to the facial swelling and interincisal distance postoperatively but significant lower values of pain score on VAS scale were noted with the intravenous route of administration of dexamethasone. Hence the half an hour preoperative intravenous route of administration of dexamethasone is preferable over the intramuscular route to reduce the incidence of post operative pain on surgical removal of impacted mandibular third molar.

Conclusion

In conclusion, the result of this study shows that the single preoperative injection of 8 mg of dexamethasone intravenously and intramuscularly clinically reduces postoperative swelling and interincisal distance but it was not statistically significant difference was noted postoperatively but significant lower values of pain score on VAS scale were noted with the intravenous route of administration of dexamethasone. Hence the half an hour preoperative intravenous route of administration of dexamethasone is preferable over the intramuscular route to reduce the incidence of post operative pain on surgical removal of impacted mandibular third molar. Whether given intravenous or intramuscular dexamethasone preoperatively for surgical removal of impacted mandibular third molar, there is reduction of swelling, trismus and pain which helps the patients return to work early and improves their quality of life.

REFERENCES

Allen K. 2007. Dexamethasone: An All Purpose Agent? Australian Anaesthesia, 65-70.

Arakeri G, Rai KK, Shivakumar HR, Jayade B.A. 2013. Randomized clinical trial to compare the efficacy of submucosal aprotinin injection and intravenous dexamethasone in reducing pain and swelling after third molar surgery:a prospective study. *J Maxillofac Oral Surg*., 12(1):73-9.

Ata-Ali J, Ata-Ali F, Oltra DP, Peñarrocha M. 2011. Corticosteroids use in controlling pain, swelling and trismus after lower third molar surgery. *J Clin Exp Dent*, 3(5):e469-75.

Balakrishnan R, Ebenezer V. 2014. Steroids - An Effective Drug in Pre Operative and Post Operative Maxillofacial Surgeries. *Biosci Biotechnol Res Asia*, 11(2): 947-951.

Becker DE. 2013. Basic and clinical pharmacology of glucocorticosteroids. *Anesth Prog*., 60(1):25-31.

Boonsiriseth K, Klongnoi B, Sirintawat N, Saengsirinavin C, Wongsirichat N. 2012. Comparative study of the effect of dexamethasone injection and consumption in Lower third molar surgery. *Int J Oral Maxillofac Surg*., 41: 244–247.

Bortoluzzi MC, Capella DL, Barbieri T, Pagliarini M, Cavalieri T, Manfro R.A. 2013. Single dose of amoxicillin and dexamethasone for prevention of postoperative complications in third molar surgery: a randomized, double-blind, placebo controlled clinical trial. *J Clin Med Res*., 5(1):26-33.

Claseman TS, Foley WL, Davis RD, Morrison JW, Palmore CA, 1998. Murchison DF.A clinical evaluation of the analgesic efficacy of preoperative administration of ketorolac and dexamethasone following surgical removal ofthird molars. Anesth Prog., 45:110-116.

Klongnoi B, Kaewpradub P, Boonsiriseth K, Wongsirichat N. 2012. Effect of single dose preoperative intramuscular dexamethasone injection on lower impacted third molar surgery. *Int J Oral Maxillofac Surg*., 41(3):376-9.

Majid OW, Mahmood WK. 2011. Effect of submucosal and intramuscular dexamethasone on postoperative sequelae after third molar surgery: comparative study. *Br J Oral Maxillofac Surg*., Dec;49(8):647-52.

Majid OW, Mahmood WK. 2013. Use of dexamethasone to minimise post-operative sequelae after third molar surgery: comparison of five different routes administration. O*ral Surg*., 6:200–208.

Mushtaq M, Khan AH, Hussain A. 2011. Effect of dexamethasone on swelling, pain and trismus following third molar surgery. *Gomal J Med Sci*., 9(1):74-77.

Novak E, Stubbs SS, Sedman CE, *et al*. 1970. Effects of single large intravenous dose of Methylprednisolone sodium succinate. *Clin Pharm Ther*., 11:711- 717.

Warraich R, Faisal M, Rana M, Shaheen A, Gellrich NC, Rana M. 2013. Evaluation of postoperative discomfort following third molar surgery using submucosal dexamethasone - A randomized observer blind prospective study. *Oral Surg Oral Med Oral Pathol Oral Radiol*., 116(1):16-22.

Williamson LW, Lorsan EL, Osborn DB. 1980. Hypothalamus pituitary adrenal suppression after short term Dexamethasone therapy for oral surgical procedures. *J Oral Surg*., 38;20-28

Zora JA, Zimmerman D, Carey TL, *et al*. 1986. Hypothalamic pituitary adrenal suppression after short term high dose glucocorticoids therapy in children with asthma. *J Allergy Clin Immunol*., 77:9-13.

****