

# Comparison Of The Effect Of Two-dose And One-dose Dexamethasone On Post-inflammatory Complications In Third Molar Surgery

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## ABSTRACT

**Objective:** This study aimed to compare the effects of administration of both preoperative and postoperative dexamethasone with that of only preoperative dexamethasone, and with that of a no dexamethasone (control) on reduction of pain, trismus and swelling following lower impacted 3<sup>rd</sup> molar surgery.

**Methods:** A prospective randomized controlled double blinded study at the dental clinic of Babcock University Teaching Hospital on 84 subjects that were divided into 3 groups. Group A had both preoperative and postoperative dexamethasone, while group B had only preoperative dexamethasone and group C was a 'no dexamethasone' group. Differential mean facial swelling, mouth opening and pain scores were compared within the three groups.

**Results:** The pattern of postoperative swelling, pain and trismus showed a general decrease from day 1 to 7, with group A showing the highest rate of decrease. On postoperative day 1, there was a difference between the swelling of groups A and C ( $p = 0.01$ ) and groups B and C ( $p = 0.02$ ) and also between the pain scores of group A and group C ( $p = 0.01$ ). On postoperative day 3, there was only a difference between the swelling of groups A and C ( $p = 0.02$ ), but not in pain and trismus and no difference was seen in all the measured variables on postoperative day 7.

**Conclusion:** Administration of a combination of both preoperative and postoperative dexamethasone to reduce the postoperative inflammatory sequelae that follows lower third molar surgery gave better results than administration of only a single preoperative dose.

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## 1. INTRODUCTION

Surgical removal of mandibular third molar is one of the most common surgical events in medical practice<sup>1</sup>. This is why, in spite of the diversified demands of practice, many dental surgeons will still need to face the problem of removal of impacted mandibular third molars.<sup>1,2</sup> This invariably involves trauma to hard and soft tissues. The greater the tissue injury is, the more extensive the amount of tissue response and inflammation in the surgical area.<sup>2</sup>

This inflammation is regarded as a protective reaction of vascular connective tissue to damaging stimuli and it is associated with vasodilatation, increased vascular permeability, recruitment of inflammatory cells and the release of inflammatory mediators from these cells.<sup>3</sup>

The most important of these mediators are the prostaglandins and the leukotrienes.<sup>2,3</sup> Ironically, this protective mechanism may bring discomfort to patients and affect their quality of life as a result of resultant pain, swelling and

trismus,<sup>4</sup> otherwise called post-operative complications.<sup>5,6</sup> The factors affecting these postoperative complications have been grouped into patients' factors, tooth related factors and operative factors.<sup>6</sup>

Pain is the most commonly encountered post-operative complication following mandibular 3<sup>rd</sup> molar surgery.<sup>5</sup> Pain sensation is subjective and can be influenced by different factors such as patient age, sex, anxiety and surgical difficulty.<sup>4</sup> In this sense, longer operations are typically associated with more pain, and the pain furthermore increases with the difficulty of the operation.<sup>7</sup> Similarly, swelling may be particularly significant when the duration of surgery is prolonged and manipulation of tissues is extensive.<sup>8</sup> Trismus is defined as a limitation in maximum oral aperture, and is caused by the swelling and pain attributed to surgical trauma.<sup>7</sup> It has been described to be more intense on the first day after surgery followed by gradual improvement and resolution

one week after the operation.<sup>9,10</sup>

The adverse effects of the mandibular third molar surgery on the quality of life have been reported to show a three-fold increase in patients who experience pain, swelling and trismus alone or in combination, compared to those who were asymptomatic.<sup>4</sup> Many clinicians have thus emphasized the necessity for better pain, swelling and trismus control in patients who undergo third molar surgery.<sup>6</sup> Several methods of controlling the immediate inflammatory response associated with the third molar surgery abound in the literature. These include different surgical closure techniques with or without incorporation of drains,<sup>5,6</sup> use of drugs such as analgesics,<sup>8</sup> corticosteroids,<sup>9,10</sup> and antibiotics.<sup>2</sup> Other reported modalities include physical therapeutic methods such as cryotherapy and laser application.<sup>5</sup>

Corticosteroids are known to reduce inflammation, fluid transudation and edema.<sup>2</sup> They induce the synthesis of endogenous proteins, which block the enzymatic activation of phospholipase A2.<sup>7</sup> Block exerted at this point in turn inhibits arachidonic acid release by the cell membrane components, with ulterior inhibition of the synthesis of prostaglandins, leukotrienes or substances related to thromboxane.<sup>7,8</sup> These effects with the resultant reduction in pain, swelling and trismus, constitute the basis of corticosteroid use in clinical practice.<sup>7</sup>

Though several studies have shown the efficacy of steroid in the reduction of post-operative swelling following third molar surgery, the selection of appropriate drug, its proper dosage and route of administration is still discussable.<sup>7,11,12,13</sup> There are also arguments and counter-arguments on the time at which the steroid drug is given, vis-à-vis preoperatively or postoperatively or both. The most widely used corticosteroids are dexamethasone and methylprednisolone administered via the intravenous, oral or intramuscular route.<sup>7</sup> A fluorinated steroid such as dexamethasone would appear to be preferable, because it is an excellent synthetic corticosteroid having very high anti-inflammatory activity, long duration of action, no mineralocorticoid potency and a long biological half-life.<sup>14,15</sup>

There is abundant literature on the use of dexamethasone in lower 3<sup>rd</sup> molar surgery,<sup>1,5,6,15</sup> but there appears to be no reported randomized control study that compares preoperative dexamethasone with that of combination of preoperative and postoperative dexamethasone in sub-Saharan Africa.

This study attempted to show the appropriate time at which dexamethasone a widely used steroid, can be given in lower third molar surgery to reduce or alleviate the postoperative swelling, pain and trismus.

This study was therefore, aimed at comparing the effects of administration of both preoperative and postoperative dexamethasone with that of only preoperative dexamethasone, and with that of a no dexamethasone (control) on reduction post-operative swelling, pain and trismus.

## 2. METHODOLOGY:

The study was a prospective randomized controlled double blinded study of effects of using combination of preoperative and postoperative dexamethasone or using of only preoperative dexamethasone on reduction of pain, trismus and swelling. It was carried out by the researchers at the dental clinic of Babcock University Teaching Hospital, Ilishan-Remo, Ogun State, Nigeria from October 2015 to September 2016. The clinic draws its clientele from the students and staff of the university, and also from referrals from outside the school. Approval for the study was obtained from the Health Research Ethics Committee of the Babcock University and written informed consent was also obtained from each subject before inclusion in the study.

Ninety-six subjects that presented for surgical extraction of impacted lower 3<sup>rd</sup> molar at the dental clinic of Babcock University Teaching hospital, within the study period were the target population of the study. The inclusion criteria were subjects with bony impaction of lower 3<sup>rd</sup> molar with 2 or more episodes of pericoronitis or subjects with soft tissue impaction of lower 3<sup>rd</sup> molar with failed operculectomy and subjects with at least 30mm of mouth opening. Subjects with history of hypertension, peptic ulcer disease, diabetes mellitus, thromboembolic events glaucoma, psychosis or that are pregnant were all excluded from the study.

The subjects were randomly allocated to three study groups through the use of balloting; a box containing sealed envelopes with folded pieces of paper on which either "A", "B" or "C" had been written. Group A was both preoperative and postoperative dexamethasone group, while Group B was only preoperative dexamethasone group. Group C was no dexamethasone (control) group. Intramuscular dexamethasone (Rosemont pharmaceutical), 8mg was administered by the

dental nurses to the subjects in groups A and B 30 minutes before the commencement of surgery. Subjects in group A also had, in addition, oral dexamethasone 4mg 8-hourly in three doses post-operatively. Subjects in group C were not asked to take any medication preoperatively, but were asked to take routine postoperative medications, the same with the subjects in other groups.

### 2.1 Data collection:

All subjects had a standard periapical radiograph showing the lower 2<sup>nd</sup> and 3<sup>rd</sup> molar, and the retro-molar bone. The difficulty index was calculated for all 3<sup>rd</sup> molars using the Pederson scale<sup>1</sup> as described above (type of impaction, class of impaction and position of impaction).

Preoperatively, patients with poor oral hygiene had scaling and polishing done, after which all subjects were given chlorhexidine mouthwash for a mouth rinse immediately before the surgical procedure. Age, sex, weight and height were measured and body mass index was calculated from these. The following anthropometry measurements were also taken according to Shaikh et.al.<sup>2</sup> (fig 1):

-Vertical heights, evaluated by measuring the distance from lateral canthus of the eye to the angle of the mandible with the help of a flexible measuring tape in centimeters (cm).

-Horizontal height, measured from the skin of the commissure of the mouth to the middle of the tragus of ear on the same side with the help of flexible measuring tape in cm. The facial dimension was considered the sum of the two values.

-Inter-incisor distances (the mesial edges of the upper and lower central incisors) were also measured with the aid of a Vernier caliper to record the difference in maximum mouth opening preoperatively.

### 2.2 Surgical procedure:

Surgical extractions were carried out under local anesthesia by a single operator. All procedures involved raising a buccal flap and bone removal performed using a fast hand piece (80,000–150,000 rpm) under continuous cool water jet spray throughout the surgery. In all procedures the total intervention time (TIT) was measured in minutes using a stopwatch. Closure of the flap was done following the extraction of the 3<sup>rd</sup> molar with 3/0 black silk suture, after which haemostasis was ensured.

Postoperatively, all the 3 groups had oral antibiotics; amoxicillin (Glaxosmithkline) 500mg 8-

hourly for 5 days, oral secnidazole 400mg stat and oral ketovail (swipha) 200mg daily for 3 days. The following anthropometry measurements were taken by the same person who took the measurements preoperatively:

Vertical and horizontal heights, and Inter-incisor distances as measured preoperatively, were evaluated after 24 hours (1<sup>st</sup> day), after 72 hours (3<sup>rd</sup> day), and on 7<sup>th</sup> day postoperative periods (Appendix II).

Pain was measured with the use of visual analogue scale (scale of 0 to 10) on the 1<sup>st</sup>, 3<sup>rd</sup> and 7<sup>th</sup> postoperative days. Zero indicated no pain while 10 stands for the most severe pain that the patient was experiencing. Subjects were asked to indicate which value corresponded to the pain that he/she had.

### 2.3 Data analysis:

Statistical analysis was done with the use of SPSS version 20. Mean and standard deviation was calculated for age. Mean and SD of facial swelling, pain and mouth opening were calculated before extraction, and on the 1<sup>st</sup>, 3<sup>rd</sup> and 7<sup>th</sup> post-operative days in the 3 groups and comparison made between the two test groups and the control using One way ANOVA.

## 3. RESULTS

A total of 84 subjects that completed the study were included in the analysis, attrition rate was 12.50%. The mean age of the subjects was  $20.71 \pm 4.10$  years (range 18 – 41 years; group A:  $21.29 \pm 5.30$  years; group B:  $20.57 \pm 3.28$  years; group C:  $20.29 \pm 3.53$  years). Seventy (83.3%) of the subjects were within the age group 18-22 years (table 1). 16 (19%) were males while 68 (81%) were females in the ratio of 1 to 4.25. Most, 40 (47.6%) of the teeth were in the category of “moderate” difficulty (using Pederson scale).

There is no significant difference between the mean ages and the difficulty index of all the 3 groups ( $p = 0.77$  and  $0.37$  respectively) (Table 1).

**Table 1: Socio-demographic characteristics and anthropometrics of the participants**

Variables	Group A	Group B	Group C	Total
<b>Age</b>				
18-22	22(26.2)	23(27.4)	25(29.7)	70(83.3)
23-27	3(3.6)	3(3.6)	1(1.2)	7(8.3)
28-32	1(1.2)	2(2.4)	1(1.2)	4(4.8)
33-37	1(1.2)	0(0)	1(1.2)	2(2.4)
38-42	1(1.2)	0(0)	0(0)	1(1.2)
<b>Total</b>	28(33.3)	28(33.3)	28(33.3)	84(100)
<b>Tooth side</b>				
Right	11(13.1)	11(13.1)	18(21.4)	40(47.6)
Left	17(20.2)	17(20.2)	10(12.0)	44(52.4)
<b>Total</b>	28(33.3)	28(33.3)	28(33.3)	84(100)
<b>Sex</b>				
Male	1(1.2)	7(8.3)	8(9.5)	16(19.0)
Female	27(32.1)	21(25.0)	20(24.0)	68(81.0)
<b>Total</b>	28(33.3)	28(33.3)	28(33.3)	84(100)
<b>Difficulty index</b>				
Easy	7(8.3)	10(12.0)	12(14.3)	29(34.5)
Moderate	15(17.9)	11(13.1)	14(16.6)	40(47.6)
Difficult	6(7.1)	7(8.3)	2(2.4)	15(17.9)
<b>Total</b>	28(33.3)	28(33.3)	28(33.3)	84(100)

On the first post-operative day, the mean differential swelling of subjects in group 'A' ( $0.21 \pm 0.26\text{cm}$ ) was the least, while those in group C ( $0.67 \pm 0.52\text{cm}$ ) was the highest. The comparison showed that there was a difference between groups 'A' and 'C' ( $p = 0.01$ ) and between groups 'B' and 'C' ( $p = 0.02$ ). The pattern of mean pain values of the groups was similar to that of mean differential swelling as shown in the table II, but the comparison only showed that there was a difference between that of group 'A' and group 'C' ( $p = 0.01$ ). For trismus, although the mean trismus (decrease in inter-incisal distance) of the subjects in group A was lowest ( $1.95 \pm 1.29\text{cm}$ ) while those of group C ( $2.51 \pm 0.83\text{cm}$ ) was the largest, there was no significant difference between the three groups (Table 2).

**Table 2: Comparison of combination of preoperative and postoperative dexamethasone**

Xctkdrgu	Mean	S.D	Comparison
<b>Swelling</b>			
Grp A	0.21	0.26	Grp A and B = 0.72
Grp B	0.29	0.36	Grp A and C = *0.01
Grp C	0.67	0.53	Grp B and C = *0.02
<b>Pain</b>			
Grp A	4.00	2.26	Grp A and B = 0.54
Grp B	4.60	2.11	Grp A and C = *0.05
Grp C	5.35	2.04	Grp B and C = 0.39
<b>Trismus</b>			
Grp A	1.95	1.29	Grp A and B = 0.57
Grp B	2.25	1.21	Grp A and C = 0.15
Grp C	2.51	0.83	Grp B and C = 0.67

On the 3rd postoperative day, the pattern of the mean differential swelling, mean pain and trismus was similar to that of the first day, with values lowest in group A, and highest in group C. The difference was only significant for swelling between group A and C ( $p = 0.02$ ), but not for pain and trismus (Table 3).

**Table 3: Comparison of combination of preoperative and postoperative dexamethasone with only preoperative dexamethasone and with no dexamethasone**

Xctkdrgu	Mean	S.D	Comparison
<b>Swelling</b>			
Grp A	0.08	0.15	Grp A and B = 0.26
Grp B	0.25	0.53	Grp A and C = *0.02
Grp C	0.37	0.43	Grp B and C = 0.50
<b>Pain</b>			
Grp A	1.64	1.83	Grp A and B = 0.27
Grp B	2.44	2.08	Grp A and C = 0.15
Grp C	2.60	1.81	Grp B and C = 0.94
<b>Trismus</b>			
Grp A	1.32	1.13	Grp A and B = 0.51
Grp B	1.61	1.03	Grp A and C = 0.42
Grp C	1.65	0.69	Grp B and C = 0.98

On the 7th postoperative day, the pattern of mean differential swelling, pain and trismus remain the same again, with values lowest in group A, and highest in group C. The facial dimension had returned to the preoperative values in group A, and nearly almost in groups B and C. Mouth opening was nearly to the preoperative values and pain had reduced to less than 1. The differences were however, not significant for either swelling, pain or trismus between all the 3 groups (Table 4).

**Table 4: Comparison of combination of preoperative and postoperative dexamethasone with only preoperative dexamethasone and with no dexamethasone**

Xctkdrgu	Mean	S.D	Comparison
<b>Swelling</b>			
Grp A	-0.01	0.03	Grp A and B = 0.16
Grp B	0.06	0.20	Grp A and C = 0.22
Grp C	0.06	0.15	Grp B and C = 0.98
<b>Pain</b>			
Grp A	0.61	1.64	Grp A and B = 0.76
Grp B	0.88	1.66	Grp A and C = 0.93
Grp C	0.90	1.10	Grp B and C = 0.94
<b>Trismus</b>			
Grp A	0.21	0.95	Grp A and B = 0.90
Grp B	0.24	0.93	Grp A and C = 0.97
Grp C	0.26	0.33	Grp B and C = 0.93

## 1. DISCUSSION

The extraction of the impacted mandibular third molar is often attended by complications, which are distressing to patients.<sup>15</sup> Pain, trismus and swelling are common complications reported,<sup>16</sup> and they are thought to arise from inflammatory response which is a direct and immediate consequence of the surgical procedure.<sup>17</sup>

The methods of managing the postoperative pain, swelling and trismus are directed to controlling the immediate inflammatory response associated with the third molar surgery.<sup>15</sup> Dexamethasone is one of the most widely used pharmacological methods of controlling these complications,<sup>7</sup> but in spite of this, time of administration, its proper dosage and route of administration is still discussable.<sup>7,11,12,13</sup>

This study assessed the effects of only preoperative administration of dexamethasone, and combination of preoperative and postoperative administration of dexamethasone on reduction of pain, swelling and trismus, compared with those of controls, who had none.

Regardless of the modality used, the postoperative sequelae has been reported to subside gradually from the postoperative day 1 or 2, and resolves almost completely after one week.<sup>2,3,8</sup> Our results are in agreement with this observation and also with various studies<sup>2,7,8,11,14,18,19</sup> that have assessed and reported the role of steroid in reduction of postoperative swelling, pain and trismus following lower 3<sup>rd</sup> molar surgery.

On the first post-operative day, the group that had 2 doses of dexamethasone (combination of pre-operative and post-operative) had much less swelling and pain, and better mouth opening than the single dose, which in turn had less swelling and pain than the control group.

The study is in consonant with the reports by Sheikh *et al.*<sup>2</sup> and Zia and Fida<sup>20</sup> that administration of 2 doses of dexamethasone gives a much better reduction of swelling, and better reduction of pain and trismus following lower 3<sup>rd</sup> molar surgery.<sup>2</sup> It is, however, in contrast to the finding by Zia and Fida<sup>20</sup> in that there was a difference between the postoperative swelling experienced by the single dose and the two-dose groups in our study. The difference might be because the multi-dose group in Zia and Fida<sup>20</sup> had

4- and 2-mg dexamethasone on the postoperative day 1 and 2 respectively. This might not be enough to produce a clinical difference between the 2 groups. The result of this study is also contrary to that of Akinleye *et al.*<sup>21</sup> and Filho *et al.*<sup>22</sup> which did not find any difference in steroid group and the control in the 1<sup>st</sup> postoperative day. These two studies however, used just one preoperative dose of dexamethasone and did not follow it with postoperative doses.

Chukwuenke and Onyejiaka<sup>23</sup> concluded in their review that corticosteroid could be used to minimize swelling, pain and trismus following 3<sup>rd</sup> molar surgery. They also opined that an initial intravenous/intramuscular dose of corticosteroid at the time of surgery had a major effect on swelling and trismus but if this is not followed up by additional doses of steroid, the early advantage disappears by the 2<sup>nd</sup> postoperative day.<sup>23</sup>

In line with this assertion, the study showed that there was a difference between the two steroid groups and the control 1<sup>st</sup> postoperative day, but on the 3<sup>rd</sup> postoperative day, there was only a difference between the 2-dose group and the control. Many earlier studies<sup>9,20,21,22</sup> however, revealed contrary results.

They concluded that the use of both preoperative and postoperative dexamethasone is of no significant advantage to the patient and that a single preoperative dose is enough to minimize the postoperative inflammatory sequelae following 3<sup>rd</sup> molar surgery. While this may be so, especially for early postoperative days, the latter postoperative days require that corticosteroid be given for at least 24 hours after the lower 3<sup>rd</sup> molar surgery as shown on the 3<sup>rd</sup> postoperative day in this study.

This study showed better pain and mouth opening control with steroid groups than with the non-steroid control group, even though these effects were not significant (significant only for pain on 1<sup>st</sup> day; between 2-dose and control). The study is in agreement with similar studies<sup>11,14,24,25</sup> which also reported improvement in mouth opening but otherwise insignificant difference between the steroid and non-steroid groups.

This is, however, contrary to some studies that reported that there is a significant difference between the steroid and non-steroid groups in term of pain and trismus.<sup>26,27</sup>

By the 7<sup>th</sup> postoperative day, the swelling in the 2-dose steroid group had completely resolved even though the mouth opening and pain values were similar in all the 3 groups. The findings in this study were also echoed by other studies that assessed the effect of steroid on postoperative inflammatory sequelae following lower 3<sup>rd</sup> molar.<sup>2,7,9,10,11,13,15,21</sup>

While corticosteroids have been shown to be effective in controlling acute and chronic inflammation,<sup>2,7,9,10,11</sup> as they interfere with multiple signaling pathways in inflammatory response phenomena (phospholipase A2, COX-2, etc.) their effects on trismus, and to a larger extent on postoperative pain, have been subject to controversy.<sup>7</sup>

Although many studies have reported statistically significant analgesic action with corticosteroid use,<sup>9,21,27</sup> others have found the analgesic efficacy of corticosteroids to be insignificant.<sup>28-30</sup> Trismus is associated with postoperative pain, and is more intense on the first day after surgery – with a mean reduction in oral aperture of 24.1%.<sup>7</sup>

In general, as postoperative swelling decreases, the postoperative pain also decreases, and so is trismus. This was evident in this study, and the group that had the highest rate of decrease in swelling also had the highest rates of decrease in postoperative pain and trismus.

While it may be argued that without steroid administration in lower 3<sup>rd</sup> molar surgery, the patients' morbidity eventually diminishes at day 7, the use of steroids, however, decrease the severity of postoperative sequelae in many patients and therefore decrease morbidity after lower 3<sup>rd</sup> molar surgery as shown in this study and other studies on lower 3<sup>rd</sup> molar surgery as stated above. : Measuring a 3-dimensional facial swelling with a flexible tape rule which is 2-dimensional was a significant but acceptable draw back for this study.

We believe a more accurate study would be possible with more sophisticated instrument.

## 2. CONCLUSION:

Combination of preoperative and postoperative administration of dexamethasone to reduce the postoperative inflammatory sequelae gave better results than administration of only a single preoperative dose in lower third molar surgery.

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**Fig 1: Schematic diagram showing the horizontal and vertical heights**

