



## Research Article

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# Diazepam and Its Effects on Postoperative Sequelae of Surgically Extracted Impacted Mandibular Third Molars

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## Abstract

**Objective:** This study evaluates the role of oral sedation, using 5 mg diazepam, on the postoperative sequelae (Pain, trismus and swelling) following impacted mandibular third molar surgery.

**Materials and methods:** This is a randomised control study involving 100 patients whose anxiety levels were assessed with the Modified Dental Anxiety Scale (MDAS) just before drug administration and thirty minutes after administering either Diazepam or placebo. The facial dimensions and maximum interincisal distance were measured and recorded preoperatively. After that, the surgical extraction of the impacted mandibular third molar was done. The Visual Analogue Scale was used to assess pain immediately after the procedure. The assessment of pain, facial dimensions, and interincisal distance were carried out at 24 hours, third and seventh days postoperatively. The Statistical Package for Social Sciences, 23.0 (International Business Machine [IBM]) version, was used to analyse the data ( $p > 0.005$ ).

**Results:** The median pain score is lower in the test (preoperative Diazepam) group compared with the control group immediately after the procedure (1.50 and 2.0 respectively) and 24 hours after the procedure (4.00 and 5.00 respectively). However, the median pain score was only statistically significant immediately after the procedure ( $p = 0.018$ ). No statistically significant difference was obtained in the values for trismus and swelling postoperatively in the two groups on the assessment days.

**Conclusion:** Preoperative administration of 5 mg diazepam orally is associated with a significant reduction in pain only immediately after the surgical extraction of the impacted mandibular third molar but not afterwards. It had no significant effect on trismus and swelling postoperatively in subjects undergoing surgical extraction of the impacted mandibular third molar.

## Keywords

Dental anxiety, Diazepam, Anxiolytic, Impacted third molar surgery

## Introduction

Fear is an emotional, physiological and behavioural response to a recognised external threat [1]. On the other hand, anxiety is an unpleasant emotional state, the causes of which are less clear. It is often accompanied by physiological changes and behaviours similar to those caused by fear [2]. There has always been an inextricable linkage between dentistry and anxiety [3,4].

Removal of impacted mandibular third molars through surgical extraction is often associated with considerable postoperative discomfort or sequela. This discomfort includes trismus, swelling and pain. They are common, expected postoperative events that depend on several factors: The difficulty of the surgical procedure, the surgical technique employed, and the severity of the impaction [5]. There can

also be complications such as haemorrhage, infection, alveolar osteitis, dentoalveolar fracture, paraesthesia of the inferior alveolar nerve and the lingual nerve, temporomandibular joint injury and mandibular fracture [6]. The complication

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rates are documented to vary between 2.6 and 30.9% and are influenced by different factors, such as age, the health condition of the patient, gender, severity of tooth impaction, surgeon's experience, smoking, intake of contraceptives, quality of oral hygiene [7] and the patient's physiological and psychological context [5].

Excessive stress and fear initiated before and during dental procedures can affect a patient's physiology and cause psychosomatic illnesses, which may influence the occurrence of postoperative complications [8].

Dental anxiety can be assessed successfully with either self-reported or observer-reported scales. Validated scales used in dentistry to assess anxiety, as reported by Newton, et al. [9] include Corah's Dental Anxiety Scale, Modified Dental Anxiety Scale, Klein Knecht's Dental Fear Survey and Dental Anxiety Question. Corah's Dental Anxiety Scale (CDAS) is widely used in adults and has high internal consistency and test-retest reliability. It has, however, been modified to the Modified Dental Anxiety Scale (MDAS) to increase the number of possible responses and thus improve its effectiveness in clinical studies [10].

Many studies [2,11,12] have adopted different scales to estimate perioperative anxiety associated with third molar surgeries across different socio-demographic variables and their effects on the duration of surgical extraction [13]. Scott, et al. [14] and Vallerand, et al. [15] have suggested that the anxiety level accurately predicts postoperative pain and recovery in oral surgery. However, these studies did not specifically investigate its correlation with other sequelae of third molar surgery.

There is a paucity of data on dental anxiety in Nigeria [16], particularly in third molar surgeries. Therefore, this study aims to evaluate the anxiolytic effect of preoperative oral Diazepam on postoperative sequelae in patients undergoing surgical extraction of impacted mandibular third molars. The result of this study will influence the decision to use anxiolytics for indicated patients undergoing surgical extraction of impacted mandibular third molars.

## Objectives

This study evaluates the role of oral sedation, using 5 mg diazepam, on the postoperative sequelae (Pain, trismus and swelling) following impacted mandibular third molar surgery.

## Materials and Methods

This study was a double-blinded randomised control study conducted from July 2019 to January 2020 at the Department of Oral and Maxillofacial Surgery, Lagos State University Teaching Hospital (LASUTH), Ikeja, Lagos, Nigeria. All patients aged 18 years and above were included however patients with routine contraceptives, debilitating medical conditions, alcohol abuse, and tobacco use were excluded from the study. Other exclusion criteria include pregnant or lactating patients, use of anxiolytics, acute pericoronitis, allergy to lignocaine or Diazepam, a score of < 10 on the MDAS and recent history of a stressful life event occurring within two weeks from the date of surgical extraction.

Patients' socio-demographic information and other relevant medical, social and family history, indication for extraction and type of tooth impaction were also recorded. Also data on preoperative facial dimensions, inter-incisal distance (mm) and duration of the surgical procedure in minutes were noted. Data also included a Modified Dental Anxiety Scale (MDAS). MDAS is a short, self-complete questionnaire comprising five questions combined to give a total score ranging from 5 to 25 [17]. Only Subjects with a minimum score of 10 on the MDAS were recruited for the study.

Patients were allocated randomly into test and control groups. The test group were patients who received 5 mg oral diazepam 30 minutes before surgical extraction of the mandibular third molar, while the control group were subjects who received a placebo which resembles diazepam tablets closely (Prepared by the Pharmacy department of the hospital).

Preoperative measurements of the maximum interincisal distance and facial dimensions were recorded before surgery. The pain was assessed using the Visual Analogue Scale (VAS). The Visual Analogue Scale (VAS) consists of a 10 cm (100 mm) line where subjects indicate their current pain intensity. Facial swelling was evaluated using the method described by Schultze-Mosgau, et al. [18]. And trismus was measured as the maximal interincisal opening in millimetres. All patients were recalled on postoperative days 1, 3 and 7 for clinical review and measurement of pain, trismus and swelling. Statistical analysis was done using the Statistical Package for Social Sciences (IBM) 23.0 version. The significant level was set at a p-value of 0.05 at a 95% confidence interval.

## Result

One hundred patients who met the inclusion criteria participated in the study. There were fifty subjects each in the test and control groups. The mean anxiety score for the test group was  $13.28 \pm 2.6$ , while that for the control group was  $13.76 \pm 2.7$ . There was no significant statistical difference between the two groups (p-value: 0.382).

Table 1 shows the mean anxiety scores at different intervals in both groups. MDAS recorded thirty minutes after the administration of 5 mg diazepam for subjects in group A was  $12.87 \pm 2.9$ , depicting a decrease from the value of  $13.28 \pm 2.6$  obtained just before drug administration. For group B, the anxiety level, as shown by the score on the MDAS, thirty minutes after the placebo administration, increased from

**Table 1:** Comparison of Mean Anxiety scores (using MDAS) at different Intervals in groups A and B.

	Group A (Mean $\pm$ SD)	Group B (Mean $\pm$ SD)
Just before drug administration	13.28 $\pm$ 2.6	13.76 $\pm$ 2.7
Thirty minutes post medication	12.87 $\pm$ 2.9	13.84 $\pm$ 2.5
t-value	-0.879	-0734
p-value	0.782	0.683

**Table 2:** Comparison of Median pain scores in both groups.

	Group A	Group B	U-value	p-value
<b>Just after surgery (Zero hours)</b>	1.50 (1.0-2.0)	2.0 (1.0-5.0)	-2.368	<b>0.018*</b>
<b>1<sup>st</sup> day</b>	4.00 (3.0-7.0)	5.00 (3.0-7.0)	-0.517	0.605
<b>3<sup>rd</sup> day</b>	4.00 (3.0-5.0)	4.00 (2.0-5.0)	-1.020	0.308
<b>7<sup>th</sup> day</b>	1.00 (1.0-1.0)	1.00 (1.0-2.0)	-0.160	0.873

**Table 3:** Comparison of mean maximal inter-incisal distance (mm) in the two groups.

	Group A (Mean ± SD)	Group B (Mean ± SD)	t-value	p-value
<b>Before surgery</b>	43.10 ± 2.6	43.36 ± 2.0	-0.539	0.591
<b>1<sup>st</sup> day</b>	29.70 ± 4.9	29.35 ± 5.2	0.346	0.730
<b>3<sup>rd</sup> day</b>	36.16 ± 3.7	35.31 ± 4.3	1.047	0.298
<b>7<sup>th</sup> day</b>	42.69 ± 3.7	42.88 ± 2.2	-0.312	0.756

**Table 4:** Comparison of the mean daily facial size (cm) at different intervals in both groups.

	Group A (Mean ± SD)	Group B (Mean ± SD)	t-value	p-value
<b>Before surgery</b>	38.08 ± 2.4	37.90 ± 2.4	0.379	0.706
<b>1<sup>st</sup> day</b>	39.96 ± 2.9	39.46 ± 2.6	0.911	0.365
<b>3<sup>rd</sup> day</b>	39.70 ± 2.6	39.01 ± 2.4	1.368	0.174
<b>7<sup>th</sup> day</b>	38.08 ± 2.1	37.80 ± 2.3	0.645	0.520

13.76 ± 2.7 to 13.84 ± 2.5. It is worthy of note that there is no significant statistical difference between the values of anxiety scores in both groups.

Table 2 shows that the median pain scores experienced by patients in both groups were comparable. It increased steadily in the days following the procedure, peaked, and then reduced gradually towards the seventh day. There was a statistically significant difference in the median pain between the two groups ( $p = 0.018$ ) only immediately after the surgery.

Table 3 shows the mean Inter-incisal distance between groups A and B during the study period. The mean inter incisal distance was least on the day following surgery in both groups, 29.70 ± 4.9 mm in group A and 29.35 ± 5.2 mm in group B. By the seventh postoperative day, it had increased significantly to 42.69 ± 3.7 mm and 42.88 ± 2.2 mm in both groups respectively. There was no statistically significant difference in the mean inter-incisal distance in both groups during the study period.

Postoperative swelling on each assessment day was taken as the sum of all measurements on each of these days (Daily facial size). The daily facial size denoting postoperative oedema increased gradually after surgery, only to reduce towards the seventh day, almost equal to the baseline value. This is as depicted in Table 4.

## Discussion

The Surgical extraction of the impacted mandibular third molar is associated with considerable postoperative discomfort with the potential for adverse effects on the

patients' quality of life [6,19]. Various agents have been documented as influencing the occurrence of these sequelae in different ways [19-22], but the effect of anxiolytics on the postoperative sequelae remains sparsely reported [23]. Therefore, this study contributes to the body of knowledge in this regard as it investigates the anxiolytic effect of preoperative oral Diazepam on postoperative pain, trismus, and swelling following mandibular third molar surgery.

The mean anxiety scores of 13.28 ± 2.6 and 13.76 ± 2.7 in the test group and control group, respectively, on the Modified Dental Anxiety Scale are similar to the finding by Xu, et al. [24], who reported a mean score of 12.8 ± 4.01 on the same scale in a study to determine the influence of dental anxiety on postoperative pain in subjects undergoing impacted mandibular third molar surgery. However, White, et al. [25] reported a lower mean score of 10.19 ± 4.7 in a study to determine the prevalence of dental anxiety in dental practice settings. The lower value by White, et al. [25] may be due to the higher mean age (51.55 ± 14.7 years) of their participants, as dental anxiety has been reported to reduce with increasing age [16]. The mean anxiety score was reduced in the test group thirty minutes after administration of 5 mg diazepam orally but increased slightly in the control group. The difference between the values was not statistically significant ( $p > 0.05$ ). This is contrary to the observation of Chen, et al. [3], De Morais, et al. [26], Moares, et al. [27] and Baker, et al. [28], where Diazepam was reported to cause a significant reduction in anxiety levels in patients undergoing mandibular third molar surgery. However, the use of multiple anxiety measuring questionnaires or measurements of vital

signs like blood pressure may be more sensitive to detect significant changes in anxiety levels.

Postoperative pain following surgical extraction of impacted mandibular third molars in this study increased gradually, attaining a peak on the third day and decreased gradually to close to pre-surgery level by the seventh day. This finding is supported by reports that postoperative oral surgical pain results from the release of an array of chemical mediators such as prostaglandins  $E_2$ (PGE<sub>2</sub>) and bradykinin which stimulates the terminal nerve endings of A-delta and C-fibers of the trigeminal nerve resulting in hyperalgesia that may last for a few days after the surgery [29]. A similar finding was made by White, et al. [30] and Akinleye, et al. [31]. In contrast, Ibikunle, et al. [19] reported the highest pain scores about 24 hours after surgical extraction of impacted mandibular third molars.

In this study, the median pain scores were lower in the test group than in the control group, immediately after the procedure and on the first day postoperatively. However, the median pain scores were the same on the third and seventh days postoperatively, and they are also only statistically significant immediately after the procedure. These findings can be explained because the anxiolytic used in this study, Diazepam, reaches its peak bioavailability at about 1-2 hours after oral use and has a half-life of about 20-40 hours [32]. Kaufman, et al. [33] reported a significantly increased pain threshold in response to electric pulp stimulation following the administration of Diazepam. Therefore, Diazepam does not exert an analgesic effect but may make the patients calmer, thus raising the pain threshold.

The finding corroborated reports by George, et al. [34], Wang, et al. [35] and Xu, et al. [24] that subjects with high dental anxiety levels have more postoperative pain immediately after third molar surgery. It also agrees with other reports [36,37] where the preoperative use of anxiolytics is associated with less postoperative pain after the surgical extraction of impacted mandibular third molar surgery.

It is worthy of note that Lago-Mendez, et al. [13] reported increased pain perception in more anxious third molar surgery patients lasting up to six days after the procedure. Onwuka, et al. [38], on the other hand, reported that preoperative dental anxiety has no significant effect on postoperative pain throughout the first one-week following impacted mandibular third molar surgery. However, the pain perception was not assessed in the immediate postoperative period.

Trismus measured as a limitation in mouth opening for both groups is most profound 24 hours after the procedure. The trismus then reduced gradually and was almost resolved by the end of the first week. This observation aligns with reports by Alexander and Thronson [39] and Maurette, et al. [40]. It may be due to the presence of inflammatory mediators that are responsible for pain in the first few days after surgery. Moreover, postoperative pain has been one of the principal reasons for the limitation in mouth opening following surgery of impacted mandibular third molars [20].

Although the reduction in mouth opening was lower in the test group (13.40 mm) than in the control group (14.01

mm) on the first postoperative day, probably due to the lower median pain scores in the test group, there was no significant statistical difference between the two groups in the values for trismus throughout the study period. This agrees with the reports by Eriksson and Tegelberg [37], who found no significant difference in the degree of mouth opening following lower third molar surgery in both subjects who were given midazolam preoperatively and the control group.

The mean percentage of facial swelling in both groups was highest on postoperative day 1 and then reduced gradually to the minimum by the end of the first week. This is congruent with multiple previous reports [19,21,22,41,42].

This study showed no positive correlation between preoperative dental anxiety and postoperative swelling following surgical extraction of the impacted mandibular third molar. This is evident as no statistically significant difference between the values obtained for the percentage of facial swelling in the two groups on the different assessment days. However, the facial swelling is less in the preoperative diazepam group when compared with the control group. The finding is consistent with the report by Eriksson and Tegelberg [37], who observed no difference in the degree of postoperative swelling following impacted mandibular third molar surgery in subjects given midazolam preoperatively and in the control group.

It is also in agreement with reports by Lago-Mendez L, et al. [13], who observed that preoperative anxiety has no significant effect on postoperative swelling following surgery of impacted mandibular third molars. However, Lago-Mendez L, et al. [13] only used validated questionnaires to grade anxiety levels in their subjects rather than use Diazepam, an anxiolytic, to modulate anxiety.

Reports by O'Donovan, et al. [43], Maes M, et al. [44], and Padgett DA, et al. [45] are contrary to the finding of this study. They suggested that anxious individuals have higher pro-inflammatory cytokines, like Interleukin-6 (IL-6) and Tumour necrosis factor-A (TNF-A), which are crucial mediators of inflammation that may cause more postoperative swelling. The apparent lack of significant impact of anxiety levels on postoperative swelling in this study may be because the same level of bone drilling still has to be done in each case, whatever the degree of anxiety in the subjects.

## Conclusion

Preoperative anxiety is common in patients scheduled for surgical extraction of impacted mandibular third molars. The use of 5 mg diazepam thirty minutes before the surgery causes a detectable reduction in the anxiety level, unlike subjects who received a placebo preoperatively that had increased anxiety levels compared with baseline. However, the changes in anxiety levels did not exhibit any statistically significant difference.

Furthermore, this study has also shown that using 5 mg oral diazepam thirty minutes before mandibular third molar surgery causes a significant reduction in pain immediately after the surgery lasting up to about 24 hours. However, 5 mg diazepam per oral preoperatively had no significant effect

on trismus and postoperative swelling following mandibular third molar surgery.

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