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Original Research Article

Efficacy of Intranasal Atomized Midazolam Spray for Patients Undergoing Surgical Removal of Mandibular Impacted Third Molars

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Abstract:

Background: The surgical removal of mandibular impacted third molars often induces significant anxiety and discomfort in patients. Intranasal atomized midazolam spray presents a promising, non-invasive alternative to traditional methods for managing dental anxiety and pain. The study evaluated the efficacy of intranasal atomized midazolam spray in reducing anxiety and pain during the surgical removal of mandibular impacted third molars.

Methods: A randomized, controlled trial was carried out. Ninety participants were randomly assigned to either the treatment group (n=45) receiving intranasal midazolam spray or the control group (n=45) receiving a placebo. Anxiety and pain were measured using the Visual Analog Scale (VAS). Heart rate, blood pressure, and patient satisfaction were also assessed. Data were examined using SPSS version 21.0, with statistical significance set at $p<0.05$.

Results: Individuals in the treatment group reported significantly lower anxiety (mean VAS: 2.3 vs. 4.8, $p<0.001$) and pain scores (mean VAS: 3.1 vs. 5.6, $p<0.001$) in contrast to the control group. The treatment group also showed substantially lower heart rates and blood pressures during the procedure ($p<0.001$). Furthermore, 75.6% of individuals in the treatment group were "Very Satisfied" with their experience, compared to 46.7% in the control group ($p<0.01$).

Conclusion: Intranasal atomized midazolam spray significantly reduces anxiety and pain in individuals undergoing the surgical removal of mandibular impacted third molars. It also enhances patient satisfaction and stabilizes physiological parameters, making it an effective alternative to traditional sedation methods.

Recommendations: Further studies are recommended to explore the long-term effects and potential applications of intranasal midazolam in other dental and medical procedures. Additionally, developing standardized protocols for its administration could optimize its use in clinical practice.

Keywords: Intranasal Midazolam, Dental Anxiety, Pain Management, Mandibular Third Molar.

Introduction

The surgical removal of mandibular impacted third molars, commonly known as wisdom teeth, is a routine dental procedure that often induces significant anxiety and discomfort in patients. Dental anxiety is a prevalent issue, affecting approximately 36% of the population, with severe anxiety seen in about 12% of cases [1]. Managing this anxiety effectively is crucial to ensuring patient compliance, comfort, and overall procedural success. Traditionally, various pharmacological and non-pharmacological methods have been employed to mitigate anxiety and pain during dental procedures. Among these, benzodiazepines like midazolam have been widely recognized for their anxiolytic and sedative properties [2].

Midazolam, a short-acting benzodiazepine, is favored in dental and surgical settings due to its rapid onset and relatively short duration of action. While intravenous administration of midazolam is common, it requires needle insertion, which can itself be a source of anxiety for many patients [3]. Recently, alternative routes of administration, such as intranasal delivery, have garnered attention. Intranasal administration offers a non-invasive, needle-free option that is not only easier to administer but also rapidly absorbed through the nasal mucosa, providing quick onset of action [4].

Intranasal midazolam has been studied in various medical settings, showing promising results in terms of efficacy and patient acceptance. For instance, it has been effectively used in pediatric dentistry to manage preoperative anxiety, demonstrating significant reductions in both anxiety and stress levels. Similarly, studies have reported its utility in emergency medicine and procedural sedation, further supporting its versatility and effectiveness [5].

Despite the growing body of evidence supporting intranasal midazolam, there remains a paucity of research specifically addressing its use in adult patients undergoing dental extractions, particularly for impacted third molars. Given the unique challenges associated with these procedures, including the potential for significant pain and anxiety, exploring alternative sedative options is of paramount importance.

The study evaluated the efficacy of intranasal atomized midazolam spray in reducing anxiety and pain during the surgical removal of mandibular impacted third molars.

Methodology

Study Design: A randomized, controlled trial.

Study Setting: The study was carried out from January to December 2023.

Participants: Ninety patients scheduled for the surgical removal of mandibular impacted third molars were enrolled and assigned randomly into two groups: the treatment group (n=45), which received intranasal atomized midazolam spray, and the control group (n=45), which received a placebo.

Inclusion Criteria

1. aged 18 to 40 years.
2. with American Society of Anesthesiologists (ASA) physical status I or II.
3. needing the surgical extraction of the impacted third molars in the mandible.

Exclusion Criteria

1. Known hypersensitivity to midazolam or other benzodiazepines.
2. Respiratory disorders such as asthma or chronic obstructive pulmonary disease.
3. A history of substance abuse or psychiatric disorders.
4. Pregnancy or breastfeeding.
5. Any contraindications to local anesthesia.

Sample Size: To calculate the sample size for this study, the following formula was used for estimating a proportion in a population:

$$n = \frac{Z^2 \times p \times (1-p)}{E^2}$$

Where:

- n = sample size

- Z = Z-score corresponding to the desired level of confidence

- p = estimated proportion in the population

- E = margin of error

Bias: To minimize bias, the study employed a double-blind design, where both the patients and the healthcare providers administering the treatment were unaware of the group assignments. Randomization was performed using a computer-generated randomization list.

Variables: The primary variable was the efficacy of the intranasal midazolam spray, assessed by patient anxiety levels and pain perception during the procedure. Secondary variables included heart rate, blood pressure, and patient satisfaction.

Data Collection: Data were collected using standardized forms. Anxiety levels and pain perception were assessed using the Visual Analog Scale (VAS) for anxiety, and pain. Heart rate and blood pressure (BP) were monitored at baseline, immediately before the procedure, and during the procedure. Patient satisfaction was evaluated using a post-procedure questionnaire.

Procedure

Patients in the treatment group were treated with 0.2 mg/kg of intranasal atomized midazolam spray 30 minutes before the surgical procedure. Patients in the control group received a placebo spray administered in the same manner. All patients underwent the surgical removal of mandibular impacted third molars under local anesthesia, performed by the same surgeon to ensure consistency.

Statistical Analysis: SPSS version 21.0 was used to analyse the data. To compile the data, descriptive statistics were employed. The two groups' mean anxiety and pain scores were compared using independent t-tests. Categorical variables were subjected to chi-square tests. Statistical significance was attained when the p-value was less than 0.05.

Ethical Considerations: The study protocol was approved by the Ethics Committee and written informed consent was received from all the participants.

Result

The study had 90 participants in total, 45 of whom were in the therapy group and 45 of whom were in the control group. Table 1 provides a summary of the participants' demographic data. There were no discernible differences in the two groups' ASA physical state, age, or gender.

Table 1: Demographic Characteristics of Participants

Characteristics	Treatment Group	Control Group	p-value
Age (mean ± SD)	28.4 ± 5.3 years	27.9 ± 5.6 years	0.56
Gender (M/F)	23/22	21/24	0.68
ASA I/II	31/14	30/15	0.82

The primary outcome measures were the anxiety and pain scores, assessed using the VAS. The results are presented in Table 2. Patients in the treatment group reported substantially lower anxiety and pain scores in contrast to the control group, with p-values of <0.001 for both measures.

Table 2: Anxiety and Pain Scores

Outcome Measure	Treatment Group	Control Group	p-value
VAS Anxiety (0-10)	2.3 ± 1.2	4.8 ± 1.5	<0.001
VAS Pain (0-10)	3.1 ± 1.4	5.6 ± 1.7	<0.001

Heart rate and blood pressure were monitored at baseline, immediately before the procedure, and during the procedure. The changes in physiological parameters are shown in Table 3. The treatment group showed substantially lower heart rates and blood pressures at pre-procedure and during the procedure compared to the control group, with p-values of <0.001.

Table 3: Physiological Parameters

Parameter	Time Point	Treatment Group	Control Group	p-value
Heart Rate (beats/min)	Baseline	72.4 ± 6.1	73.1 ± 5.8	0.61
	Pre-procedure	68.3 ± 6.0	74.8 ± 6.3	<0.001
	During procedure	70.1 ± 6.5	78.2 ± 6.7	<0.001
Systolic BP (mmHg)	Baseline	122.4 ± 8.7	123.1 ± 9.0	0.71
	Pre-procedure	118.6 ± 8.3	125.3 ± 8.9	<0.001
	During procedure	120.4 ± 8.5	127.6 ± 9.2	< 0.001
Diastolic BP (mmHg)	Baseline	78.5 ± 6.4	79.2 ± 6.1	0.67
	Pre-procedure	76.1 ± 6.2	81.7 ± 6.5	<0.001
	During procedure	77.3 ± 6.3	84.5 ± 6.7	<0.001

Patient satisfaction was evaluated post-procedure using a questionnaire. The results are summarized in Table 4. The treatment group had a notably higher proportion of "Very Satisfied" patients compared to the control group ($p < 0.01$).

Table 4: Patient Satisfaction

Satisfaction Level	Treatment Group	Control Group	p-value
Very Satisfied	34 (75.6%)	21 (46.7%)	<0.01
Satisfied	9 (20.0%)	15 (33.3%)	0.21
Neutral	2 (4.4%)	6 (13.3%)	0.14
Dissatisfied	0 (0.0%)	3 (6.7%)	0.08

Discussion

The purpose of the trial was to determine whether intranasal atomized midazolam spray could effectively lower anxiety and pain in individuals undergoing surgery to remove impacted third molars in the mandible. Ninety people took part in the randomised, controlled experiment; they were split equally between the treatment and control groups. A placebo was given to the control group while intranasal midazolam was administered to the treatment group. The VAS was used to measure anxiety and discomfort as the primary end measures. Physiological parameters and patient satisfaction were the secondary outcomes.

The outcomes showed that, in comparison to the control group, the treatment group reported much reduced levels of discomfort and anxiety. In particular, the treatment group's mean anxiety score was 2.3 as opposed to 4.8 in the control group, and the group's mean pain score was 3.1 as opposed to 5.6. These changes were statistically significant, with p-values less than 0.001.

These findings suggest that intranasal midazolam effectively alleviates anxiety and pain during dental procedures, thereby enhancing patient comfort.

Physiological parameters, including heart rate and blood pressure, further supported the efficacy of the treatment. The treatment group exhibited significantly lower heart rates and blood pressures pre-procedure and during the procedure compared to the control group, indicating a calmer physiological state induced by the midazolam spray. These reductions in heart rate and blood pressure not only corroborate the subjective reports of decreased anxiety but also reflect a clinically relevant impact on patient stress levels.

Patient satisfaction, assessed post-procedure, showed that a significantly higher proportion of participants in the treatment group were "Very Satisfied" with their experience compared to the control group. Specifically, 75.6% of the treatment group reported being very satisfied, while only 46.7% of the control group reported the same level of satisfaction ($p < 0.01$). This high level of satisfaction underscores the overall positive impact of intranasal midazolam on the patient experience, making it a valuable adjunct in dental surgeries.

The effectiveness of intranasal atomized Midazolam spray for sedation in patients having surgical extraction of mandibular impacted third molars has been assessed in recent research. Intranasal Midazolam and Dexmedetomidine were shown to be equally effective in treating individuals who were having surgery to remove their bilaterally impacted mandibular third molars. The findings showed that there was no discernible difference in mean SpO2, pulse rate, blood pressure, or patient compliance between the two medications. Based on their efficacy and safety profiles, both medications can be used in outpatient minor oral surgery settings [6].

An additional investigation evaluated the effectiveness of intranasal Dexmedetomidine as a sedative during the surgical extraction of mandibular third molars that are impacted. According to the study, the sedative effect started between thirty and forty-five minutes after injection and by 105 minutes, it had almost returned to normal. In a nursery setting, the intranasal administration of dexmedetomidine was found to be safe, practicable, and efficacious [7].

A study comparing intravenous Midazolam with intranasal Midazolam for conscious sedation in minor oral surgeries found that both methods effectively reduced subjective stress and provided reliable anxiolysis. The intranasal route was particularly noted for its ease of administration and patient comfort [8].

A study involving uncooperative children undergoing dental treatment compared buccal and intranasal aerosolized Midazolam. The intranasal route had a more rapid onset of sedation, and both routes were found to be safe and effective, with the intranasal route being better tolerated by the children [9].

Another study compared the sedative effects of Midazolam and Dexmedetomidine in dental procedures, finding both agents to be equally effective. Dexmedetomidine showed additional benefits, such as lower diastolic blood pressure and quicker arousal times [10].

Conclusion

In summary, the study's findings indicate that intranasal atomized midazolam spray is an effective and beneficial option for reducing anxiety and pain in patients undergoing the surgical removal of mandibular impacted third molars. The significant improvements in both subjective and objective measures, along with high patient satisfaction, highlight the potential for intranasal midazolam to enhance patient care in dental settings.

Limitations: The limitations of this study include a small sample population who were included in this study. Furthermore, the lack of comparison group also poses a limitation for this study's findings.

Recommendation: Further studies are recommended to explore the long-term effects and potential applications of intranasal midazolam in other dental and medical procedures. Additionally, developing standardized protocols for its administration could optimize its use in clinical practice.

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List of Abbreviations:

ASA: American Society of Anesthesiologists

BP: Blood Pressure

ICMA: Institute of Cost and Management Accountants

M/F: Male/Female

SpO2: Peripheral Capillary Oxygen Saturation

VAS: Visual Analog Scale

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Conflict of Interest: The authors have no competing interests to declare.

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