Comparison of a Combination of Intranasal Midazolam and Nitrous Oxide Versus Intravenous Midazolam for Patients Undergoing Surgical Extraction of Impacted Teeth under conscious sedation: A Randomised Control Trial

Dr. Roohika Sharma[1], Dr. Ramsesh Manohar[2], Dr. Melvin George[3], Dr. K Murugesan[4]

[1]Post Graduate Resident, Department of Oral and Maxillofacial Surgery, Saveetha Dental College

[2]Anaesthetist, Saveetha Dental College

[3]Department of Oral and Maxillofacial Surgery, Saveetha Dental College

[4]Head of department, Department of Oral and Maxillofacial Surgery, Saveetha Dental College

ABSTRACT

Introduction: Effective sedation during surgical procedures is crucial for patient comfort and cooperation. This study focuses on comparing the onset of action, depth of sedation, recovery time, and adverse effects between a combination of intranasal midazolam and nitrous oxide (INM-NO) and intravenous midazolam (IVM) for conscious sedation during the surgical extraction of impacted teeth. **Aim**: To evaluate and compare the onset of action, depth of sedation, and recovery time between INM-NO and IVM, using standardized sedation scales, with adverse effects as secondary outcomes. **Methods**: This prospective, randomized clinical study included 20 patients requiring surgical extraction of impacted teeth. Patients were allocated to either Group A (INM-NO) or Group B (IVM). The primary outcomes evaluated include the onset of action; measured using a stopwatch from drug administration to the first observable sedative effect, the depth of sedation, which was assessed using the Modified Observer's Assessment of Alertness/Sedation (MOAA/S) scale, and the recovery time, which was evaluated by the Aldrete Recovery Score.

Adverse effects including desaturation and nausea were also noted. **Results**: Group A (INM-NO) demonstrated a significantly faster onset of action (mean time: X ± SD minutes) compared to Group B (IVM) (mean time: Y ± SD minutes, $p < 0.05$). The depth of sedation was comparable between the groups, with no significant differences in MOAA/S scores at peak sedation ($p > 0.05$). Recovery time was shorter in Group B (IVM) (mean: X ± SD minutes) compared to Group A (mean: Y ± SD minutes, $p < 0.05$). Adverse effects were minimal and did not differ significantly between groups ($p > 0.05$). **Conclusion**: Intranasal midazolam combined with nitrous oxide achieves a faster onset of action, while intravenous midazolam offers quicker recovery. Both techniques provide comparable depth of sedation, with minimal adverse effects. The choice of sedation protocol can be tailored to the clinical setting and patient preference.

Keywords: Intranasal midazolam, Nitrous oxide, Intravenous midazolam, Conscious sedation, Onset of action, Depth of sedation, Recovery time

INTRODUCTION

Conscious sedation is widely employed in dental procedures, particularly for surgical extractions of impacted teeth, to ensure patient comfort and cooperation while maintaining protective reflexes. Among the sedative agents available, midazolam and nitrous oxide (N_2O) have demonstrated efficacy and safety in various clinical scenarios.[1] Intravenous (IV) midazolam, a benzodiazepine with rapid onset and predictable sedation, is a common choice. However, alternative delivery methods, such as intranasal administration, have garnered attention for their non-invasive nature, especially in patients with difficult IV access. [2]

Intranasal midazolam, when combined with nitrous oxide, has shown promise in achieving effective sedation. Studies suggest that intranasal midazolam induces sedation within minutes, with clinical effects enhanced by the anxiolytic and analgesic properties of N_2O. [3] This combination has been explored in pediatric and dental settings, where it minimizes patient discomfort and reduces procedure times while maintaining safety profiles comparable to IV midazolam. [4] Several randomized controlled trials noted that intranasal midazolam

achieved satisfactory sedation with fewer adverse effects compared to other routes in children undergoing dental extractions. [5]

Despite these advantages, differences in onset of action, depth of sedation, and recovery time between these modalities remain under-researched in adults undergoing surgical extractions. Moreover, while both methods are generally well-tolerated, adverse effects such as nausea, dizziness, or respiratory depression vary by administration route and combination used

This study aims to compare intranasal midazolam combined with nitrous oxide versus intravenous midazolam for conscious sedation in adult patients undergoing surgical extraction of impacted teeth. The primary focus will be on onset of action, depth of sedation, and recovery time using standardized scales, with adverse effects analyzed as secondary outcomes. This comparison seeks to inform best practices in procedural sedation, optimizing patient care and clinical efficiency.

MATERIALS AND METHODS

A prospective, randomized clinical trial was conducted to compare the efficacy of intranasal midazolam combined with nitrous oxide (INM-NO) versus intravenous midazolam (IVM) for conscious sedation in adult patients undergoing surgical extraction of impacted teeth.

The study included 40 patients, aged 18–40 years, randomly allocated into two equal groups (20 patients each): Patients in Group A (INM-NO) Patients received intranasal midazolam combined with nitrous oxide. Patients in group B received intravenous midazolam.

Inclusion Criteria:

- Patients requiring surgical extraction of impacted mandibular third molars.
- ASA I or II classification.
- Aged 18–40 years.
- No known allergies to midazolam or nitrous oxide.

Exclusion Criteria:

- Severe nasal obstruction or nasal deformities.
- History of respiratory disorders or adverse reactions to sedative agents.
- Pregnancy or lactation.
- Use of psychotropic medications within 24 hours before the procedure.

Patients were randomized using a computer-generated sequence. The surgeon performing the procedure was blinded to the sedation protocol to minimize bias.

Group A (INM-NO):

For patients in group A, intranasal midazolam (0.4 mg/kg, maximum dose 10 mg) was administered using a mucosal atomization device. Nitrous oxide was delivered via inhalation at a concentration of 50%.

Group B (IVM):

Patients in Group B received intravenous midazolam (0.05–0.1 mg/kg) which was administered through a pre-inserted venous catheter.

Outcome Measures:

Primary outcomes measured included

- Onset of Action: this was measured as the time from drug administration to the first observable sedative effect, measured using a stopwatch.
- Depth of Sedation: This was assessed using the Modified Observer's Assessment of Alertness/Sedation (MOAA/S) scale.
- Recovery Time: This was evaluated using the Aldrete Recovery Score (score ≥9 indicating readiness for discharge).

Secondary Outcomes outcomes measured included adverse effects (e.g., nausea, vomiting, respiratory depression) were recorded during and after the procedure.

All patients were administered local anesthesia- bilateral inferior alveolar nerve blocks before sedation administration. Vital signs, including heart rate, oxygen saturation, and blood pressure, were monitored continuously during the procedure..

Data were analyzed using SPSS version 23 software. Descriptive statistics (mean ± SD) were used for continuous variables. The independent t-test was applied to compare onset of action, depth of sedation, and recovery time between groups. Chi-square tests were used for categorical variables (e.g., adverse effects). A p-value <0.05 was considered statistically significant.

Ethical Considerations:

The study was approved by the institutional ethics committee. Written informed consent was obtained from all participants. The study adhered to the principles of the Declaration of Helsinki.

RESULTS

Table 1: Demographic and Baseline Characteristics of Patients

Table 1

Parameter	Group A (INM-NO) (n = 20)	Group B (IVM) (n = 20)	p-value
Age (years)	28.2 ±6.3	29.1 ±5.8	0.62
Gender (M/F)	12/8	11/9	0.78
ASA Classification	18 ASA / 2 ASA II	I7 ASA/ 3 ASA 2	0.65
Procedure Duration (min)	42.5 ±8.2	43.1 ±9.1	0.71

Table 2: Primary Outcomes

Table 2

Outcome	Group A (INM-NO)	Group B (IVM)	p-value
Onset of Action (min)	5.3 ±1.2	2.4 ±0.8	<0.001

Table 2

Outcome	Group A (INM-NO)	Group B (IVM)	p-value
Depth of Sedation (MOAA/S Score at Peak Sedation)	2.1 ±0.5	2.0 ±0.4	0.45
Recovery Time (min)	25.6 ±5.1	18.9 ±4.7	<0.001

Table 3: Secondary Outcomes - Adverse Effects

Table 3

Adverse Effect	Group A (INM-NO) (n = 20)	Group B (IVM) (n = 20)	p-value
Nausea (%)	2 (10%)	1 (5%)	0.55
Dizziness (%)	3 (15%)	2 (10%)	0.64
Respiratory Depression (%)	0 (0%)	0 (0%)	—
Total Adverse Events (%)	5 (25%)	3 (15%)	0.44

Table 4: Patient and Surgeon Satisfaction

Table 4

Satisfaction Score (1–10)	Group A (INM-NO)	Group B (IVM)	p-value
Patient Satisfaction	8.9 ±0.8	9.2 ±0.7	0.24
Surgeon Satisfaction	8.7 ±0.9	8.8 ±0.6	0.81

Group B (IVM) had a significantly faster onset of action compared to Group A (INM-NO) ($p < 0.001$).
Both groups achieved a similar depth of sedation ($p > 0.05$).
Recovery time was significantly shorter in Group B (IVM) ($p < 0.001$).
Adverse effects were minimal and comparable between the two groups ($p > 0.05$).
Both patients and surgeons reported high satisfaction levels, with no significant difference between groups.

DISCUSSION

This study compared intranasal midazolam combined with nitrous oxide (INM-NO) to intravenous midazolam (IVM) for conscious sedation in patients undergoing surgical extraction of impacted teeth. The findings revealed significant differences in onset of action and recovery time, while the depth of sedation and incidence of adverse effects were similar. The onset of sedation in the IVM group (2.4 ± 0.8 minutes) was significantly faster than in the INM-NO group (5.3 ± 1.2 minutes, $p < 0.001$). These results align with studies that highlight intravenous midazolam's rapid action due to direct bloodstream absorption, compared to the slightly slower onset of intranasal midazolam, which undergoes mucosal absorption. However, intranasal midazolam offers a practical, non-invasive alternative, especially in patients with difficult venous access or needle phobia. Both groups achieved similar sedation depths, as indicated by comparable MOAA/S scores ($p = 0.45$), consistent with evidence that both methods provide effective conscious sedation while maintaining patient responsiveness. [6, 7] Recovery time was significantly faster in the IVM group (18.9 ± 4.7 minutes) than in the INM-NO group (25.6 ± 5.1 minutes, $p < 0.001$), likely reflecting the faster clearance of intravenous midazolam compared to the combined effects of intranasal administration and nitrous oxide. Adverse effects were minimal in both groups, with minor symptoms such as nausea and dizziness reported, and no significant respiratory depression observed. These results reinforce the safety of both sedation protocols, corroborating prior studies. While intravenous midazolam offers the advantage of faster onset and recovery, the combination of intranasal midazolam and nitrous oxide provides a non-invasive alternative with adequate sedation depth, making it suitable for patients with specific needs. [8, 9] However, its slightly prolonged recovery may limit its utility in cases requiring rapid discharge. The small sample size is a limitation, and further studies with larger populations are recommended to explore additional outcomes such as cost-effectiveness and patient satisfaction. Overall, this study highlights the efficacy and safety of both methods, emphasizing the importance of tailoring sedation strategies to individual patient needs and clinical contexts.

CONCLUSION

This study demonstrates that both intranasal midazolam combined with nitrous oxide (INM-NO) and intravenous midazolam (IVM) are effective and safe for conscious sedation in patients undergoing surgical extraction of impacted teeth. While IVM offers faster onset and recovery times, INM-NO provides a viable non-invasive alternative with comparable sedation depth and minimal adverse effects. These findings suggest that INM-NO may be particularly useful in patients with challenging venous access or those who prefer needle-free procedures, despite its slightly prolonged recovery time. Future research with larger sample sizes and additional parameters, such as cost-effectiveness and patient satisfaction, is warranted to further refine sedation strategies. Ultimately, the choice of sedation method should be guided by patient needs, clinical scenarios, and provider expertise.

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