Original Article

A Comparison of Dexmedetomidine and Midazolam for Sedation in Third Molar Surgery

Anindita Bhagawati[1]*, Mriganka Madhav Misra[2], S. C. Debnath[3]

[1]Department of Oral and Maxillofacial Surgery, GDCH, Dibrugarh, Assam, India.
[2]Department of Respiratory Medicine, AMCH, Dibrugarh, Assam, India.
[3]Department of Oral and Maxillofacial Surgery, RDC, Guwahati, Assam, India.

Abstract

Purpose: The study was conducted to compare the efficacy of dexmedetomidine and midazolam in third molar surgery. **Materials and Methods:** A total of 40 patients belonging to ASA grade I or II were included in the study. The baseline vitals of the patients were recorded, moreover the anxiety score, pain score, amnesia score, cooperative scale, Ramsey Sedation score, Modified Steward score recorded. **Results:** The study concludes that although widely midazolam is used for sedation, dexmedetomidine is a suitable alternative and in many ways better replacement for the former drug.

Keywords: Third molar surgery, Sedation, Midazolam, Dexmedetomidine.

Introduction

Conscious sedation has been defined as a minimally depressed level of consciousness that retains the patient's ability to independently and continuously maintain an airway and respond appropriately to physical stimulation and verbal command and that is produced by a pharmacological or non-pharmacological method or combination thereof.[1]

Extraction and surgical removal of impacted teeth being the most common procedure in oral and maxillofacial surgery; the removal of which is always associated with fear and anxiety and the management of it has always been an integral part.

Dental anxiety can be managed by psychotherapeutic interventions, pharmacological interventions, or a combination of both, depending on the dentist's expertise and experience, degree of dental anxiety, patient characteristics, and clinical situations. Psychotherapeutic interventions are either behaviorally or cognitively oriented, and recently, the use of cognitive behavior therapy has been shown to be highly successful in the management of extremely anxious and phobic individuals. Based on specific indications, these patients can be managed pharmacologically using either sedation or general anesthesia.[2]

The drugs most commonly used for IV sedation are the benzodiazepines. Midazolam being most commonly used as anxiolytic, hypnotic, anticonvulsant, and muscle relaxant. Benzodiazepines, particularly midazolam, are relatively free from cardiovascular and respiratory side effects at clinical doses. Whereas the arterial blood pressure (BP), cardiac output, and peripheral vascular resistance decrease only slightly, there may be an increase in heart rate with midazolam, which may cause slight changes in the systolic BP.[3] Midazolam has a long half-life and it may have prolonged sedation effects such as excessive sleepiness and psychomotor impairment.[4]

Dexmedetomidine on the other hand is a potent, highly selective alpha (2)-adrenoreceptor agonist suggested for intravenous sedation and postoperative analgesia.[5] Its use is usually associated with a decrease in heart rate and BP.[6]

The average protein binding of an intravenously administered dose of Dexmedetomidine is 94%, with distribution and elimination half-lives of 6 minutes and 2 h, respectively. It induces electroencephalographic activity similar to natural sleep. The drug reduces catecholamine secretion, thereby

Access this article online

Website:
www.jrad.co.in

DOI:
https://doi.org/10.53064/jrad.2022.14.5.385

Address for correspondence: Anindita Bhagawati,
AMCH, L Lane, APQ - 7, Barbari, Dibrugarh - 786 002, Assam, India.
Email: bhagawatijimli@gmail.com

Received: May 12, 2023; **Accepted:** Jun. 13, 2023; **Published:** Jul. 22, 2023

How to cite this article: Bhagawati A, Misra MM, Debnath SC. A Comparison of Dexmedetomidine and Midazolam for Sedation in Third Molar Surgery. J Res Adv Dent 2023;14(5):1-5.

reducing stress and leading into modest (10–20%) particularly beneficial in patients with cardiovascular disease.[7] It also produces analgesia,[8] which could alleviate pain.

Such photodynamic profile has advantage over midazolam for conscious sedation.

Hence, the present study aims to compare between Dexmetedomidine versus Midazolam for sedation in third molar surgery.

Methods

Patient selection

A prospective study was performed on patients visiting Department Of Oral and Maxillofacial Surgery, Dental College and Hospital. The study protocol was approved by the Institutional Ethical Committee, and informed consent was obtained from all selected patients under the Helsinki Declaration. A total of 40 patients were including in the study belonging to American Society of Anaesthesiologists (ASA) Grade I and Grade II category after obtaining written consent of both the patient and the attendant. Patients were randomly selected irrespective of gender and ethnic differences who visited the department for surgical procedure of removal of impacted third molar.

Inclusion criteria

ASA Grade I or II, patients of either sex within age group 18–50 years, patients needing third molar extractions, and willing to cooperate in the study with informed consent (Helsinki) were included in the study.

Exclusion criteria

Patient suffering from severe systemic disease, congenital disorders, history of psychiatric illness, history of allergy to drugs used in the study, pregnant or lactating females, patients with poor visible superficial veins, ASA Grade III or IV patients, and patients who are chronic alcoholics with compromised airway were excluded from the study.

Pre-operative preparation of the patient

Pre-operatively, a detailed case history of the patients was recorded. Patients were randomly selected after they agreed for a written consent. Based on the inclusion and exclusion criteria; patients were divided into two groups. Before surgery preoperatively, patients were advised not to have any solid food 6 h prior and liquid food 2 h prior on the day of surgery. They were advised to accompany with a responsible attendant to take them safely home. Preoperatively baseline vitals, oxygen saturation (S_pO_2), systolic BP (SBP), diastolic BP (DBP), pulse rate (PR), and respiratory rate (RR) along with body weight were taken.

Group I comprised of 20 patients with impacted mandibular third molar where the surgery was performed under the influence of midazolam.

Group II comprised of 20 patients with impacted mandibular third molar where the surgery was performed under the influence of dexmedetomidine.

Procedure

The patient after the preparation was made to sit on the dental chair, a 20-gauge IV cannula was inserted. Demographic and surgical data, including age, weight, gender, difficulty index, and duration of surgery were recorded. (Pedersons difficulty index).[9] Anxiety of patients was recorded based on visual analog scale of anxiety.[10]

The base line vitals were recorded. The patients of midazolam group received bolus/loading dose-0.08 mg/kg weight. Maintainence dose of 0.05 mg/kg was given till the end of procedure. On the other hand, patients of dexmedetomidine group received bolus/loading dose-1 μg/kg weight. Maintenance dose of 0.5 μg/kg was given till the end of procedure.

Patient was positioned in supine position and monitored. PR, SPO_2, RR, and BP was recorded by a blinded resident doctor at 5-min interval for 30 min and at 45 min after doses have been administered and procedure started. After the administration of dexmedetomidine or midazolam, operator assessed Ramsey sedation score.[11] About 2% lignocaine with 1:80,000 adrenaline was used for inferior alveolar and long buccal nerve blocks. Any pain reaction during administration was recorded. Efficacy of local anesthesia was confirmed by verbal contact and by gentle probing the buccal gingiva and lingual gingiva. Duration of surgery was recorded as period between the incision and the last suture.

Three different pictures of easily recognizable objects were shown to the patients before the incision, at 15 and 30 min, respectively. Inability to recall the objects was assessed as amnesia.

Post-operative management

The patient was accompanied to the recovery room where blinded resident doctor collected the post-operative data and operator assigned the cooperation score.[12] The overall pain encountered during the procedure was recorded on a 10 unit Visual Analog Scale. Modified Steward Recovery Scale[13] and amnesia score[14] was recorded by blinded resident doctor. Analgesics if needed were given. Over all pain assessment was done by visual analog scale 1–10 by Wong-Baker FACES pain rating scale.[15] All patients were discharged after ascertaining that they were in state of being fully awake without any complications. Verbal and written post-sedation instructions were given to the patients along with emergency phone numbers. Alcohol and driving were advised to be avoided postoperatively.

Statistical analysis

Statistical tools and techniques

The collected data were tabulated in a spreadsheet using Microsoft Excel 2019 and then statistical analysis was carried out using the GraphPad Prism for Windows, Version 9.0 (GraphPad Software, La Jolla California USA). A Shapiro–Wilks test and a visual inspection of the histograms, normal Q-Q plots, and box plots showed that the collected data were approximately normally distributed for both the groups.

Independent samples t-test and Chi-square test were employed to test the quantitative and categorical background variables, respectively. Mixed model analysis was employed to compare the cardiorespiratory data between the study groups. $P \leq 0.05$ was considered as the level of significance.

Results

Table 1 depicts the characteristics of the background variables. No statistically significant differences were noted between the mean age, distribution of gender, mean weight, and the mean scores for the difficulty index of the study participants of both the groups ($P > 0.05$); hence, the study participants were matched for the background variables, thus eliminating the possible effect of confounding.

For the cardiopulmonary data at the end of 40 min, it was found that patients in the Dexmedetomidine groups had lesser SBP, DBP and PR than the Midazolam group, whilst the oxygen saturation levels and the RRs were comparatively higher in the patients administered with Dexmedetomidine. However, the findings were not statistically significant [Figures 1-4].

Concerning the other outcome variables, it was found that patients in the Dexmedetomidine group (1.45 ± 1.572) were more cooperative than the patients in the Midazolam group (3.1 ± 1.553) with a statistically significant difference in the cooperation scores ($P = 0.002$). The VAS scores for pain were also found to be significantly higher in the Midazolam group (3.3 ± 1.418) than the Dexmedetomidine group (2.4 ± 0.883) ($P = 0.021$) [Table 2].

It was also found that duration of the procedure and the Ramsey sedation scores in the patients administered with Dexmedetomidine was less than the patients administered with Midazolam. However, the Anxiety scores and the Modified Steward Scale scores were higher in the patients of the Dexmedetomidine group than the Midazolam group. However, the above-mentioned indicators were not found to be statistically significant ($P > 0.05$) [Table 2].

Table 1: Characteristics of the patient's background variables

Variables	Study groups		*P*-value
	Midazolam (*n*=20)	Dexmedetomidine (*n*=20)	
Age (in years)[a]	29.75±7.677	28.3±7.116	0.539 ns
Gender[b]			
Males	12 (60%)	12 (60%)	1 ns
Females	8 (40%)	8 (40%)	
Weight (in kgs)[a]	54.45±8.438	52.9±10.228	0.06 ns
Difficulty Index	4.75±1.251	4.05±1.099	0.068 ns

Age and weight denoted in terms of Mean±Standard deviation; gender is denoted in terms of frequencies (percentage). n: Subjects per group, [a]Analyzed by Independent samples *t*-test, [b]Analyzed by χ^2 test, ns: Not statistically significant (P>0.05)

Discussion

Midazolam had been the drug of choice in cases of intravenous sedation uses in oral surgery since long. Drawbacks like lack of analgesic properties led to the advent of new agents or

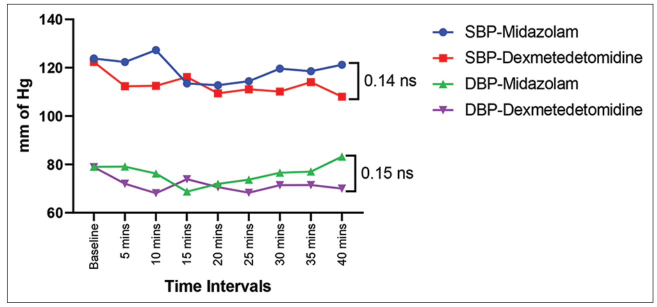

Figure 1: Mean alternations in the systolic blood pressure and the diastolic blood pressure

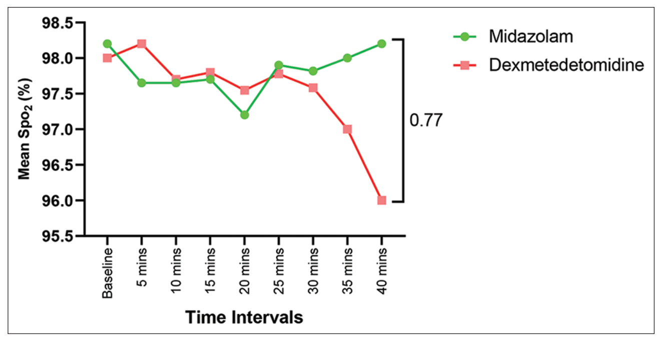

Figure 2: Mean alternations in the Oxygen Saturation Levels

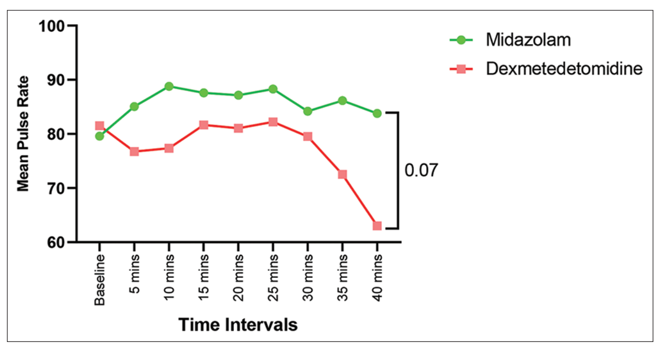

Figure 3: Mean alternations in the pulse rate

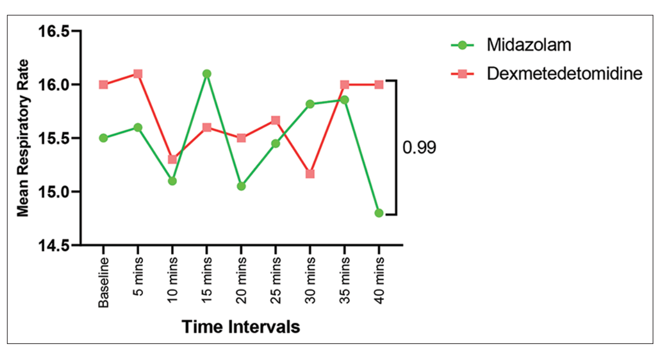

Figure 4: Mean alternations in the respiratory rate

Table 2: Characteristics of the patients' operative data

Indicators	Study groups		*P*-value
	Midazolam (*n*=20)	Dexmedetomidine (*n*=20)	
Duration (in mins)	31.75±6.129	28.5±4.617	0.066 ns
Anxiety Score	5.25±0.55	5.6±0.754	0.102 ns
Ramsey Sedation	2.85±0.489	2.7±0.47	0.329 ns
Cooperation Score	3.1±1.553	1.45±1.572	0.002**
Modified Steward Scale	3.45±0.686	3.55±0.759	0.665 ns
Visual Analog Scale for Pain	3.3±1.418	2.4±0.883	0.021*
Amnesia	4±0.725	3.6±0.754	0.095 ns

All the variables are denoted in terms of Mean±standard deviation and analyzed by the Independent samples *t*-test. n: Subjects per group, ns: Not statistically significant ($P>0.05$), *: Statistically significant ($P<0.05$), **: Highly statistically significant ($P<0.01$)

drug combinations. Dexmedetomidine is used as an adjuvant for premedication, especially in patients susceptible to pre-operative and perioperative stress because of its sedative, anxiolytic, analgesic, sympatholytic, and stable hemodynamic profile. Its use in Daycare surgery also would prove to be effective.

The present study compares if dexmedetomidine can be a comparable alternative to midazolam for third molar surgery. The study comprised of 40 patients 20 in each group; of ASA I and II physical status. They belonged to age group of 18–50 years; 60% were male and 40% female in both the groups. The patients of midazolam group received bolus/loading dose-0.08 mg/kg weight. Maintenance dose of 0.05 mg/kg was given till the end of procedure. On the other hand, patients of dexmedetomidine group received bolus/loading dose – 1 µg/kg weight. Maintenance dose of 0.5 µg/kg was given till the end of procedure. The doses used in this study were comparable to the doses used in study by Cheung *et al*. (2007).[16]

Ustun *et al*. (2006)[17] reported mean Ramsey Sedation Score in their study after the drug infusion was 2.9 ± 1.21 for Group M and 2.90 ± 1.19 for the Group D and found that it was comparable for the two groups. Mishra *et al*. (2016)[14] in their study found RSS scores to be comparable between the two groups. In our study, the mean Ramsey sedation score in case of the Midazolam cases was 2.85 ± 0.49 and that in case of the Dexmedetomidine cases was 2.7 ± 0.47, that is, a difference of 0.15 which was statistically not significant. Hence, the study indicated similar results to the above studies.

In the present study, cooperation by the patients during the procedure was analyzed based on cooperation scale. The operator gave the score based on three set of questions where minimum score was 0 and maximum score was 9. The mean cooperation score in case of the Midazolam cases was 3.10 ± 1.55 and that in case of the Dexmedetomidine cases was 1.45 ± 1.57, that is, p value of.002, which was statistically significant. Hence, dexmedetomidine group proving to be more cooperative than midazolam. Ustun *et al*. (2006)[17] in their study obtained mean cooperation score for Group M as 1.75 ± 2.19 and for Group D as 0.6 ± 1.4, showing similar results like the present study.

Consciousness score was measured using Modified Steward Recovery Scale, where 1 denoted no response and 5 was fully awake, eyes open, conversing. The mean Modified Steward Scale score in case of the Dexmedetomidine cases was 3.55 ± 0.76 and that in case of the Midazolam cases was 3.45 ± 0.69, denoting no significant difference between the two groups. The present study was comparable to that obtained by Ustun *et al*. (2006)[17] where he too obtained no statistical significance between the two groups.

Overall pain was measured using VAS score. Pain is stressful during dental treatment. Dexmedetomidine group in our study sample had mean Visual Analog Pain Scale score of 2.40 ± 0.88 which was lower than the Midazolam group which was 3.30 ± 1.42; proving dexmedetomidine to have analgesic property. Mishra *et al*. (2016)[14] in their study although obtained values for overall pain scores lower for dexmedetomidine group, it was statistically not significant. Cheung *et al*. (2007)[16] also mentioned in their study that dexmedetomidine did not exhibit additional analgesic benefit compared to midazolam. VAS scores of pain obtained from study by Ustun *et al*. (2006)[17] was 0.5 ± 0.76 for dexmedetomidine group and 1.35 ± 2.3 for midazolam group. Although dexmedetomidine group had lower scores, it was not statistically significant.

Midazolam is known to have potent anterograde amnesic effect. Hall *et al*. (2000)[8] in his study has also mentioned dexmedetomidine infusion also results in impairment of memory and psychomotor performance. Ustun *et al*. (2006)[17] in their study that the difference in the number of patients recalling the shown objects during the procedure was statistically significant between the two groups ($P < 0.001$). About 90% of people of midazolam group could not recall the objects whereas all the subjects in dexmedetomidine group could easily recall the objects shown to them. Cheung *et al*. (2007)[16] also in their study found midazolam to have anterograde amnesic effects. They also concluded that amnesic effects diminished with time and by the end of the procedure the amnesic properties became comparable. In our study, mean Amnesia score in case of the Dexmedetomidine cases is 3.6 ± 0.75 and that in case of the Midazolam cases is 4 ± 0.72, that is, a difference of 0.45 which was statistically not significant although midazolam group showed more amnesia compared to dexmedetomidine.

Jaakola (1994)[18] reported a 16–20% decrease in BP and heart rate when 1 µg/kg of dexmedetomidine was given intravenously in 10 min. Bhana *et al*. (2000)[19] mentioned that dexmedetomidine has biphasic changes in BP. There is an initial increase in mean arterial pressure followed by decrease. This increase is due to direct effects of α_2-adrenoceptor stimulation of vascular smooth muscle. After the transient increase in BP, the decrease may be presumably caused by an inhibition of sympathetic outflow that overrode the direct effects of dexmedetomidine on the vasculature. Whereas Ustun *et al*. (2006)[17] in their study did not obtained such biphasic changes; they found lower values for dexmedetomidine group which was also statistically significant. Similar were in the studies of Cheung *et al*. (2007)[16] and Fan *et al*. (2013).[7] In the present study, the SBP and DBP for dexmedetomidine group were less at all instances. However, the mean SBP and DBP of the two groups were statistically significant during the 5th and 10th minute time interval. The results obtained from our study were comparable to the above studies.

Oxygen saturation in the present study was comparable among the two groups. At no intervals, statistically significant difference was found between the two groups. The mean minimum SPO2 observed in either of the groups was 96% which was similar to study by Ustun *et al*. (2006).[17] He mentioned in his study as favorable S_pO_2 for a healthy individual is within 98–99%, dexmedetomidine and midazolam have minimum respiratory effects with the doses used in the study. Similarly, Hall *et al*. (2000),[8] Bhana *et al*. (2000)[19] stated that dexmedetomidine sedation preserves the SpO_2 throughout operation and recovery periods. Whereas Cheung *et al*. (2007)[16] in his study found that SPO_2 was lower for midazolam group during drug infusion, lower in dexmedetomidine group during surgery, and was similar between two groups during recovery period.

Conclusion

The results conclude that the baseline vitals and other scores make both the drugs comparable to each other. Thus dexmedetomidine is a suitable alternative for midazolam for sedation in third molar surgery.

References

1. Malamed SF. Sedation: A Guide to Patient Management. 4th ed. Missouri: Mosby Inc.; 2003. P. 9-12.
2. Appukuttan DP. Strategies to manage patients with dental anxiety and dental phobia: Literature review. Clin Cosmet Investig Dent 2016;8:35-50.
3. Garip H, Gürkan Y, Toker K, Göker K. A comparison of midazolam and midazolam with remifentanil for patient-controlled sedation during operations on third molars. Br J Oral Maxillofac Surg 2007;45:212-6.
4. Gan TJ. Pharmacokinetic and pharmacodynamics characteristics of medications used for moderate sedation. Clin Pharmacokinet 2006;45:855-69.
5. Arain SR, Ruehlow RM, Uhrich TD, Ebert TJ. The efficacy of dexmedetomidine versus morphine for postoperative analgesia after major inpatient surgery. Anesth Analg 2004;98:153-8.
6. Venn RM, Grounds RM. Comparison between dexmedetomidine and propofol for sedation in the intensive care unit: Patient and clinician perceptions. Br J Anaesth 2001;87:684-90.
7. Cortinez LI, Hsu YW, Sum-Ping ST, Young C, Keifer JC, Macleod D, *et al*. Dexmedetomidine pharmacodynamics: Part II. Crossover comparison of the analgesic effect of dexmedetomidine and remifentanil in healthy volunteers. Anesthesiology 2004;101:1077-83.
8. Hall JE, Uhrich TD, Barney JA, Arian SR, Ebert TJ. Sedative, amnestic, and analgesic properties of small-dose dexmedetomidine infusions. Anesth Analg 2000;90:699-705.
9. Peterson LJ. Principles of management of impacted teeth. In: Peterson LJ, Ellis E 3rd, Hupp JR, Tucker MR, editors. Contemporary Oral and Maxillofacial Surgery. 3rd ed. St Louis, MO: Mosby-Year Book Inc.; 1998. p. 215-48.
10. Okitsu H, Sawamura J, Nishimura K, Sato Y, Ishigooka J. A comparison of a patient-rated visual analogue scale with the Liebowitz Social Anxiety scale for social anxiety disorder: A cross-sectional study. Open J Psychiatry 2014;4:68-74.
11. Salmon FF, Mets B, James MF, Murray AD. Intravenous sedation for ocular surgery under local anaesthesia. Br J Ophthalmol 1992;76:598-601.
12. Parworth LP, Frost DE, Zuniga JR, Bennett T. Propofol and fentanyl compared with midazolam and fentanyl during third molar surgery. J Oral Maxillofac Surg 1998;56:447-447-53, discussion 453-4.
13. Jensen AG, Møller JT, Lybecker H, Hansen PA. A random trial comparing recovery after midazolam-alfentanil anesthesia with and without reversal with flumazenil, and standardized neurolept anesthesia for major gynecologic surgery. J Clin Anesth 1995;7:63-70.
14. Mishra N, Birmiwal KG, Pani N, Raut S, Sharma G, Rath KC. Sedation in oral and maxillofacial day care surgery: A comparative study between intravenous dexmedetomidine and midazolam. Natl J Maxillofac Surg 2016;7:178-85.
15. Loretz L. Primary Care Tool for Clinicians. USA: Elsevier Health Sciences; 2005. p. 378-82.
16. Cheung CW, Ying LA, Wong GT, Irwin MG. A comparison of dexmedetomidine and midazolam for sedation in third molar surgery. Anaesthesia 2007;62:1132-8.
17. Ustün Y, Gündüz M, Erdoğan O, Benlidayi ME. Dexmedetomidine versus midazolam in outpatient third molar surgery. J Oral Maxillofac Surg 2006;64:1353-8.
18. Jaakola ML. Dexmedetomidine premedication before intravenous regional anesthesia in minor outpatient hand surgery. J Clin Anesth 1994;6:204-11.
19. Bhana N, Goa KL, McClellan KJ. Dexmedetomidine. Drugs 2000;59:263-8, discussion 269-70.