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# Dexmedetomidine versus Midazolam for Monitored Anesthesia Care during Middle Ear Surgery

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***Abstract:*** ***Background****: Local anesthesia with sedation is a well established approach used for tympanoplasty. Dexmedetomidine is a new drug which acts on alpha-2 adrenergic receptors in the dorsal horn of spinal cord to produce analgesic effects.*
***Aims****: To study the efficacy and safety of dexmedetomidine in comparison to midazolam.*
***Setting and Design:*** *Randomised controlled trial.*
***Materials and Methods****: 50 patients were randomly allocated to receive either dexmedetomidine or midazolam as intravenous bolus followed by the same in infusion supplemented with local anesthesia for tympanoplasty.*
***Statistical analysis used:*** *Statistical package for social sciences version 15.0.*
***Results****: Dexmedetomidine and midazolam provide adequate sedation but the use of midazolam is associated with more requirements of rescue analgesia and poor patient and surgeon satisfaction.*
***Conclusion:*** *Dexmedetomidine appears to be a better drug than midazolam for monitored anaesthesia care in middle ear surgery. It produces a highly satisfactory sedation with additional analgesic effect, without any serious respiratory or cardiovascular side effects.*
***Key Word****: Dexmedetomidine, Midazolam, Sedation, Surgery*

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## I. Introduction

Tympanoplasty as a procedure can be done under either local or general anaesthesia. Some surgeons prefer to do it under local anaesthesia because it allows faster recovery, less bleeding and ability to test hearing during the procedure. However, local anesthesia alone is known to cause anxiety, dizziness, claustrophobia and earache [(1, 2)]. To minimise these side effects, it is appropriate to use intravenous sedation along with local anesthesia. Various drugs have been used for sedation including propofol, benzodiazepines and opioids [(3, 4)]. But each drug has its own advantages and disadvantages. Propofol, which is the most widely used drug for Monitored Anesthesia Care (MAC) can cause oversedation and disorientation [(5)].

Midazolam, a short acting benzodiazepine, is a very good agent for MAC. It causes anxiolysis, sedation and antegrade amnesia. Its hypnotic-sedative effects can be rapidly reversed with flumazenil [(6)]. Hence it is a very well established agent for MAC [(7)].

Dexmedetomidine on the other hand is a centrally acting alpha-2 adrenoreceptor agonist with both sedative and analgesic properties without causing respiratory depression. It is also known to maintain good hemodynamic stability owing to its sympatholytic effects [(8, 9)]. Also it has a relatively shorter half life of 2 hours, in contrast to 3-4 hours of midazolam. All these properties make dexmedetomidine an attractive agent for sedation.

A review of literature showed several clinical trials done to study sedation in middle ear surgery, but none involved comparison between midazolam and Dexmedetomidine [(10)]. Thus this randomised double blind clinical study was undertaken to compare effects of dexmedetomidine sedation with that of midazolam sedation.

## II. Material And Methods

After obtaining approval from the Institutional Ethics Committee, 50 American Society of Anesthesiologist (ASA) grade 1-2 patients, aged between 18-60 years who were posted for elective middle ear surgery under local anesthesia at Goa Medical College were included in the study. An informed consent was obtained from all the patients. The duration of the study was from January 2019 to August 2019. Type of study planned was randomised double blind clinical study. Exclusion criteria included patients with cardiac, respiratory, CNS, endocrine disorders, patients with active upper respiratory tract infections, alcoholics,

pregnant/lactating females and patients with Obstructive Sleep Apnoea (OSA) and Body Mass Index (BMI) more than 30 $kg/m^2$ .

Patients were randomly allocated into 2 groups. Group M which receives midazolam for sedation and Group D which receives dexmedetomidine.
Group M :- Midazolam was used in the concentration of 1mg/ml.
Loading dose – 0.05 mg/kg
Maintainence dose – 0.02 mg/kg/hour.

Group D :- Dexmeditomidine 200 mcg ( per ampoule) was diluted in 0.9% Normal Saline in 50cc syringe to achieve a concentration of 4 mcg/ml.
Loading dose – 1 mcg/kg over 10 mins ( via infusion )
Maintainenec dose – 0.4 mcg/kg/hour.

All patients received premedication with injection glycopyrollate 0.2 mg and injection fentanyl 1 mcg/kg.Intraoperative monitoring for vitals was done using Electrocardiogram (ECG), pulse oximeter and non invasive blood pressure cuff. All patients received oxygen at 2 L/min via nasal prongs.
Intraoperatively sedation was assessed using the Ramsay sedation score (RSS) and analgesia level recorded using the 10 point Visual Analogue Scale ( VAS).

After achieving Ramsay sedation score of 3, local anesthesia was infiltrated using lignocaine 2% and 1/100000 epinephrine (2:1 v/v). The tympanic branch of auriculotemporal nerve, branches of the great auricular nerve and the auricular branches of vagus were blocked by this local infiltration. After this, surgery was started.

**Table 1 : Ramsay sedation score**

| Score | Response |
|---|---|
| **1** | Anxious or restless or both |
| **2** | Cooperative, oriented and tranquil |
| **3** | Responding to commands |
| **4** | Brisk response to stimulus |
| **5** | Sluggish response to stimulus |
| **6** | No response to stimulus |

During the surgery, all vital parameters like blood pressure, pulse, $S_pO_2$ and respiratory rate were recorded at 5 minutes interval for the first 15 minutes and then every 15 minutes till the end of surgery. The sedation and analgesia scores were also recorded these intervals.
Throughout the surgery, the rate of infusion of the study drug was titrated to maintain Ramsay sedation score of 3 and normal cardiovascular and respiratory variables.

All adverse effects were recorded. At any point if respiratory rate was <12/minute and $S_pO_2$ was < 94%, then the sedation was stopped and manual ventilation was applied. Rescue injection of fentanyl 1 mcg/kg was used if patient complained of pain. If more than 2 rescue doses used, then that patient was excluded from the study. Regarding blood pressure, if Mean Arterial Pressure (MAP) was < 60 mmHg then initial fluid challenge was given. If failed to increase blood pressure, then inj.ephedrine 6 mg was given and the rate of infusion was reduced to half. Heart rate of < 50/minute was treated with inj.atropine 0.6 mg.

At the end of surgery the infusion was stopped and patients were shifted to recovery room. Patients were monitored for 1 hour in the recovery room. Vitals were recorded every 5 minutes for the first 15 minutes and then every 15 minutes. The Ramsay sedation score and the pain scores were assessed every 15 minutes in the recovery room. Patients were asked to rate their level of satisfaction with sedation on a 7 – point Likert like verbal rating scale. Also the surgeon satisfaction was also recorded using the same 7 – point Likert like verbal rating scale.

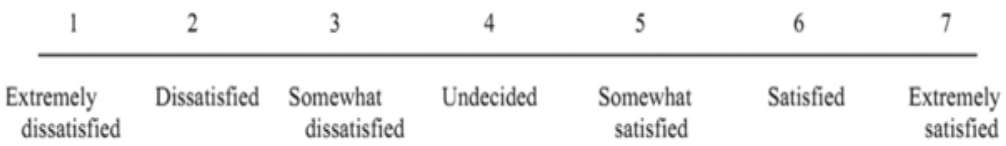



**Figure 1 :** Seven point Likert like verbal rating scale for patient or surgeon satisfaction

**Statistical analysis**

Data was analysed using the Statistical Package for Social Sciences (SPSS) version 15.0 (Themis and Neon). Independent sample's t-test was used to compare parametric data, while Chi-square test was used for categorical data. Confidence level of the study was kept at 95% and hence P<0.05 indicated a statistically significant association.

## III. Results

All the patients in both the groups tolerated the medications well and no serious side effects were observed. No patient was excluded from the study.

Both the groups were matched in terms of baseline characteristics such as age, sex, BMI and ASA grade (Table 2). Also, the preoperative vitals such as pulse, blood pressure and respiratory rate were similar in both the groups (Table 3). There was no statistically significant difference in duration of surgery in both the groups.

**Table 2 : Patients demographic profile**

| | Group D | Group M | P value |
|---|---|---|---|
| **Age ( in years)** | 33 ± 13.67 | 32.28 ± 9.783 | 0.831 |
| **Sex (Male : Female)** | 10 : 15 | 16 : 9 | 0.89 |
| **ASA 1:2** | 19 : 6 | 17 : 8 | 0.529 |
| **BMI** | 24.20 ± 3.28 | 24.880 ± 3.18 | 0.503 |
| **Duration of Surgery** | 95.60 ± 7.14 | 93.72 ± 7.260 | 0.361 |

The time to achieve adequate Ramsay sedation score (RSS) was 14.52 ± 1.418 mins in group D and 3.44 ± 0.82 mins in group M, thus showing a significant difference between the two groups (P<0.0001).

**Table 3 : Patients preoperative vitals**

| | Group D | Group M | P value |
|---|---|---|---|
| **Pulse** | 66.80 ± 8.426 | 63.60 ± 4.967 | 0.108 |
| **Mean arterial pressure** | 87.420 ± 11.03 | 86.476 ± 8.98 | 0.742 |
| **Respiratory rate** | 18.52 ± 2.725 | 18 ± 2.449 | 0.481 |

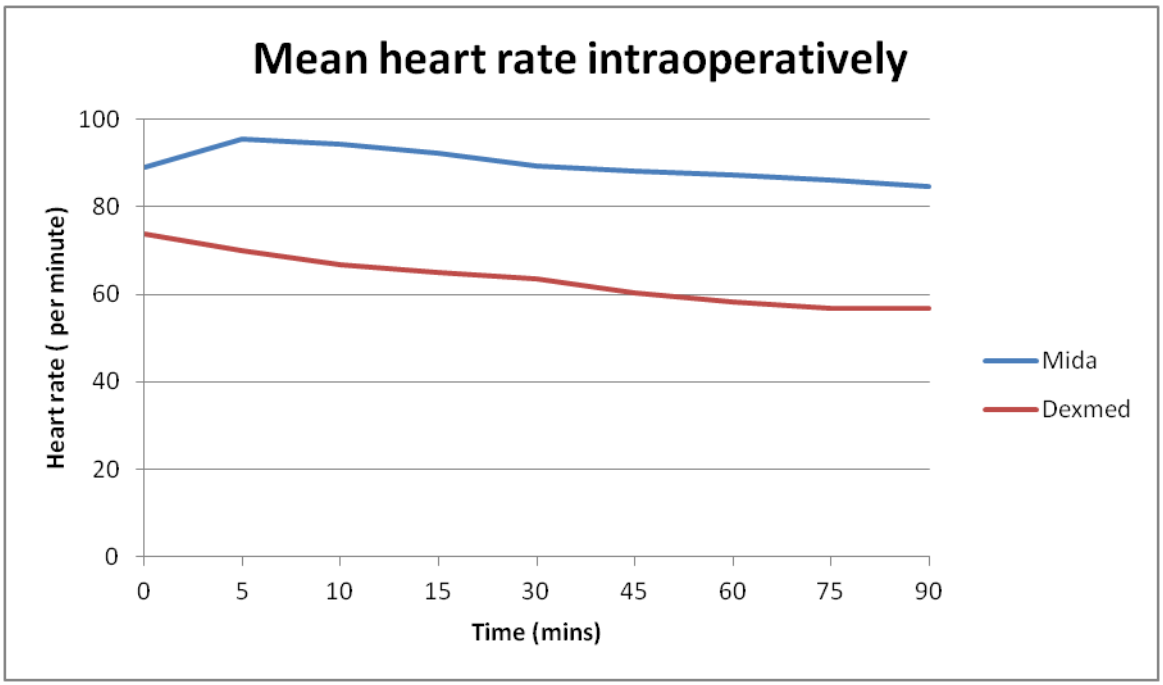
Patients in group D had a significantly lower incidence of local anaesthesia injection pain compared to group M (P=0.004). A total of 9 patients in group M could not be sedated using specified protocol and they had to be supplemented with injection fentanyl as they kept complaining of pain. However, in group D, only 3 patients required rescue analgesia, thus showing a significant difference between the two groups (P=0.046). Also, the timing of rescue analgesia requirement was delayed in group D (93.33 ± 10.40 mins) compared to group M (47.44 ± 8.14 mins), the difference being statistically significant (P<0.0001).

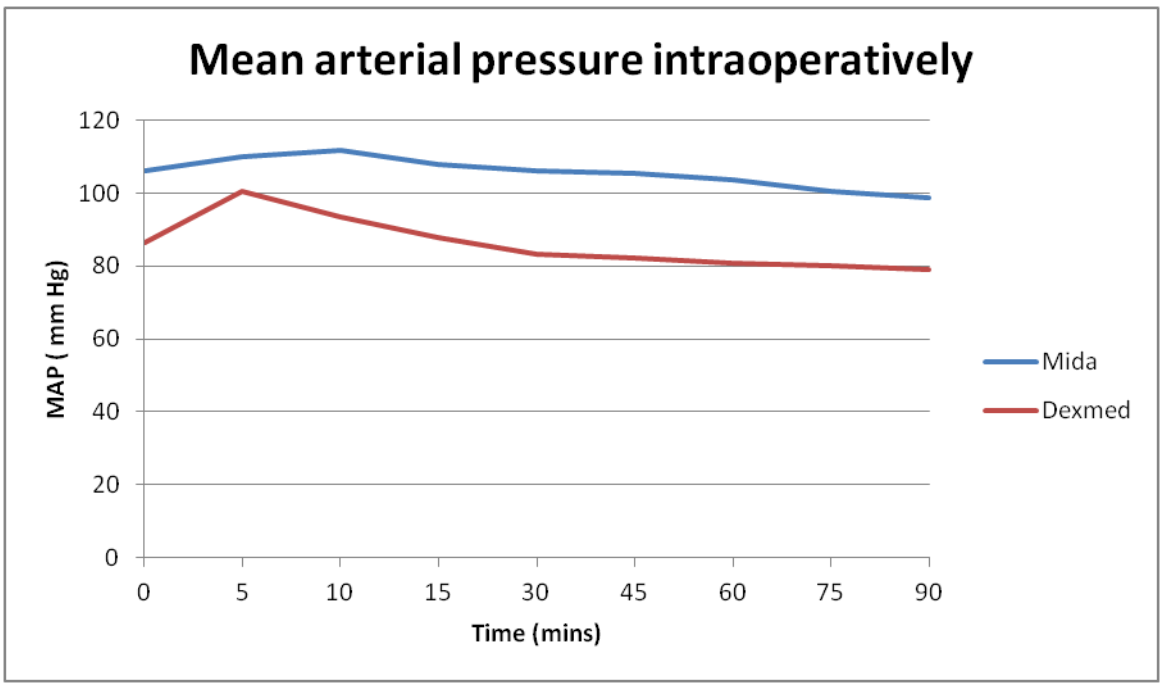
The degree of patient satisfaction and surgeon satisfaction were observed to be higher in group D compared to group M (P<0.0001).

**Table 4 : Intraoperative clinical data and measured particular times**

| | Group D | Group M | P value |
|---|---|---|---|
| **Degree of patient satisfaction ( Likert scale)** | 6 ± 0.5 | 4.92 ± 0.702 | < 0.0001 |
| **Degree of surgeon satisfaction ( Likert scale)** | 5.12 ± 0.526 | 4.24 ± 0.663 | < 0.0001 |
| **Time to rescue analgesic (min)** | 93.33 ± 10.40 | 47.44 ± 8.14 | < 0.0001 |
| **Need for rescue analgesia** | 3 (6) | 9 (6) | 0.046 |
| **Time to achieve RSS – 3 (min)** | 14.52 ± 1.418 | 3.44 ± 0.82 | < 0.0001 |
| **Local anaesthetic injection pain incidence** | 8 (13) | 18 (13) | 0.004 |

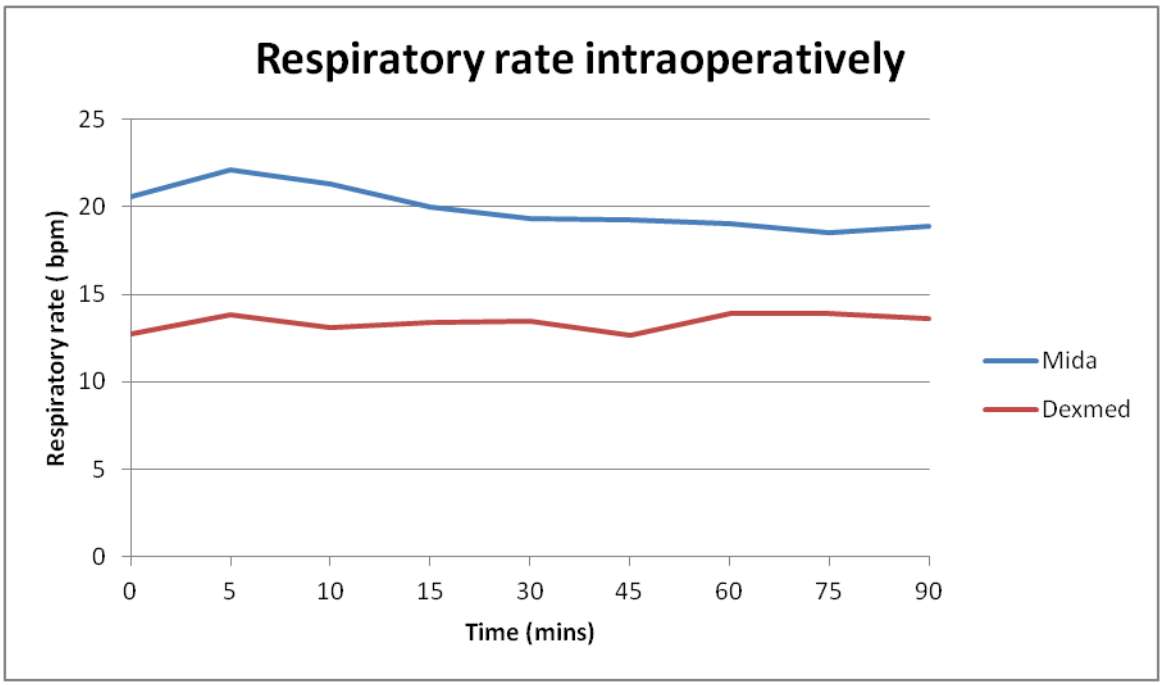
Intraoperatively, the heart rate and mean arterial pressure (MAP) were observed to be significantly lower in group D compared to group M (P<0.0001). In contrast, there was a trend of higher respiratory rate and lower $SpO_2$ levels over time among patients who received midazolam.

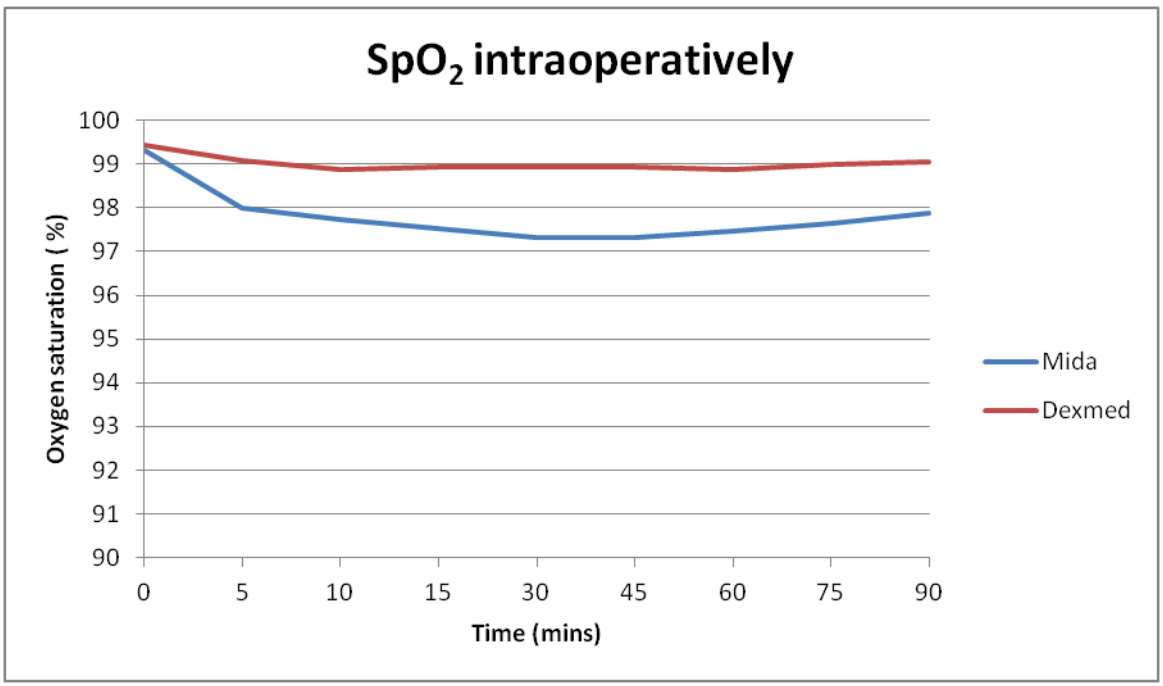



There was a statistically significant difference in VAS scores over time among both groups, with group D showing lower VAS scores of pain (P<0.0001).

Both the medications were tolerated well in both groups and there were very few side effects. The most frequent side effect in group M was desaturation (12%) and restlessness (12%). Two patients in group D had bradycardia which was managed by injection atropine 0.6 mg intravenous.




## IV. Discussion

Anxiety is an inevitable component of middle ear surgery. Midazolam has long been used for intravenous sedation during middle ear surgery as it provides profound antegrade amnesia and satisfactory sedation, and has minimal effect on cardiovascular and respiratory system. Although local anaesthesia does provide adequate analgesia, patients usually do suffer from discomfort. Lack of analgesic properties of midazolam has lead some researchers to search for newer agents with additional analgesic property.

Dexmedetomidine has been used mainly in the ICU for its sedative, anxiolytic and analgesic properties. [11] Recently there have been many reports of successful use of dexmedetomidine as primary sedative agent for orthopaedic, ophthalmic, dental and plastic surgery and for diagnostic procedures. Dexmedetomidine is increasingly being used as a sedative for monitored anaesthesia care (MAC). [12, 13]

In our study we compared dexmedetomidine with midazolam because midazolam is the drug that has been used commonly in the past for MAC. Also no such studies have been published in literature regarding the comparison of these two agents in middle ear surgery.

No serious side effects were observed in our study. The total surgery time and the demographic profile of the patients did not differ between the two groups verifying the reliability of this study.

The time to achieve the target Ramsay Sedation Score (RSS) of 3 was faster in the group M compared to group D, but 72% of patients showed pain on local anaesthesia injection in group M, while only 20% patients reacted to local anaesthesia pain in group D. Hence, dexmedetomidine causes a significant decrease in pain associated with local anaesthesia injections. These findings were consistent with those seen by Ustun et al .[12]

Patients in group D also had a significantly reduced requirement of rescue analgesia with fentanyl. Similar findings were observed by Verma et al [14] and Arain and Ebert et al [15].

The mean heart rate and mean arterial blood pressures (MAP) were significantly lower in group D. This may be due to the inhibition of central sympathetic outflow and inhibition of norepinephrine release by dexmedetomidine by virtue of its stimulation of alpha-2 adrenoceptor.[16] Similar findings were seen by Jaakola et al [17] who reported a 16% to 20% decrease in blood pressure and heart rate when 1mcg of dexmedetomidine was given intravenous over 10 minutes. Bhana et al [11] also reported that dexmedetomidine produces a dose dependent reduction in heart rate and blood pressure.

One interesting finding seen in our study was the biphasic changes in blood pressures in group D, where in there was an initial increase in MAP and decrease in heart rate followed by decrease in both. Similar biphasic changes were observed by Dyck et al [18]. The initial increase can be attributed to the direct effects of alpha-2 adrenoceptor stimulation of vascular smooth muscles. After the transient increase in blood pressure, the following decrease is probably due to the inhibition of sympathetic outflow which overrides the direct effect of dexmedetomidine on vasculature.

Another interesting observation seen in our study was the trend towards high respiratory rate and lower $SpO_2$ in group M. This can be explained because of the decrease in tidal volume by midazolam and the compensatory increase in respiratory rate to maintain minute ventilation by the patient. Similar findings of low $SpO_2$ readings were observed by Fredman et al [19] and Oei-Lim et al [20]. Such effects were not seen by dexmedetomidine.

Although both drugs were effective in providing adequate intraoperative sedation, patients in group D showed a significantly higher patient satisfaction score. This can be explained due to the additional analgesic properties of dexmedetomidine. Surgeon satisfaction scores were also higher in group D. Similar findings were seen by Verma et al [14], Alhashemi et al [13] and Ustun et al [12].

In our study, one point of criticism is the use of Ramsay Sedation Score as an end point for administering study drugs as opposed to bispectral index. This was done because bispectral index is not a standard monitor during monitored anaesthesia care and is not readily available in all institutions. One could also argue that the doses of the study drugs were not comparable, however, as both drugs were titrated to a predefined endpoint (Ramsay Score of 3), it is unlikely that this was an issue as far as study outcomes were concerned.

## V. Conclusion

On the basis of the findings of our study, dexmedetomidine appears to be a better drug than midazolam for monitored anaesthesia care in middle ear surgery. It produces a highly satisfactory sedation with additional analgesic effect, without any serious respiratory or cardiovascular side effects.

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