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RESEARCH ARTICLE

COMPARATIVE STUDY OF DEXMEDETOMIDINE VERSUS MIDAZOLAM FOR MONITORED ANAESTHESIA CARE IN MIDDLE EAR SURGERIES

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ABSTRACT

Background: Monitored anaesthesia care (MAC) involves administration of local anaesthesia in combination with intravenous sedatives, anxiolytic and/or analgesics, which is a common practice during ENT procedures that are superficial, less invasive and can be done under local anesthesia in well counseled patients. Midazolam has been in use for MAC because of a number of beneficial effects. Recent studies suggest that α_2 agonists provide adequate sedation and analgesia and also improve surgical field visibility. Dexmedetomidine, a highly selective α_2 agonist is emerging as a preferred choice for MAC.

Aim: To compare the efficacy of Inj. Dexmedetomidine and Inj. Midazolam for Middle ear surgeries under Local Anaesthesia with Monitored Anaesthesia Care in terms of sedation, analgesia and hemodynamic stability in the perioperative period.

Methods: 96 patients of either sex, aged between 18-60 years of ASA grade I & II undergoing Middle ear surgeries under local anaesthesia with Monitored Anaesthesia Care were divided into two groups of 48 patients each to receive either Inj. Dexmedetomidine (Group D) 1 µg/kg IV bolus over 10 minutes followed by continuous infusion at the rate of 0.5 µg/kg/hr. or Inj. Midazolam (Group M) 40 µg/kg IV bolus over 10 minutes followed by continuous infusion at the rate of 20 µ/kg/hr for sedation during surgery. Sedation as titrated to Ramsay sedation score of 3. Vital parameters like Heart rate, Blood pressure, SpO_2, Respiratory rate were recorded every 5 minutes for up to 120 minutes in the intraoperative period and for 120 minutes in post operative period. The need for rescue sedation (Inj. Propofol), rescue analgesic (Inj. Fentanyl) and surgeon satisfaction scores were assessed.

Results: Analgesic effect of Dexmedetomidine was better than Midazolam ($p<0.001$). Sedation was comparable in both groups ($p>0.05$). Fall in Heart Rate was significantly more in Group D compared to baseline value and compared to Group M. Blood Pressure was maintained within normal limits in both the groups but the fall in SBP, DBP and MAP from baseline value was significantly more in Group D than in Group M ($p < 0.05$). Surgeon satisfaction scores were significantly higher with Dexmedetomidine compared to Midazolam.

Conclusion: Dexmedetomidine is a safe and attractive agent for sedation in patients undergoing middle ear surgeries under local anaesthesia with monitored anaesthesia care as it provides a calm patient, causes better analgesia and rapid recovery.

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INTRODUCTION

Monitored anaesthesia care (MAC) involves administration of local anaesthesia in combination with intravenous sedatives, anxiolytic and/or analgesics, which is a common practice during ENT procedures that are superficial, less invasive and can be done under local anesthesia in well counseled patients. "American society of Anaesthesiologists (ASA) defines monitored anaesthesia care as instances in which an anaesthesiologist has been requested to provide specific anaesthesia services to a particular patient undergoing a planned procedure, in connection with which a patient receives local anaesthesia or in some cases no anaesthesia at all" (Ronald D. Miller, 2009). Primary objective in providing monitored anaesthesia care is to ensure patient comfort, safety and satisfaction during surgery. (American Society of Anesthesiologists: Position on monitored anesthesia care, 1997) Monitored anaesthesia care can be used for middle ear surgeries and has many advantages like less bleeding, ability to test hearing intra operatively, post operative analgesia, cost effectiveness and rapid recovery. Middle ear surgeries like

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Tympanoplasty and Mastoidectomy that address pathology of tympanic membrane and middle ear respectively can be performed under local anesthesia without sedation. Local anesthesia is cost effective but better pre operative counselling is needed. However local anaesthesia alone has been reported to be associated with anxiety, dizziness, claustrophobia etc (Caner *et al*., 2005; Yung, 1996). Patients may be uncomfortable and move due to pain, noise of suction, manipulation of instruments and position of head and neck. Pain during surgery may lead to sympathetic stimulation and a restless patient may have tachycardia and hypertension, leading to increased bleeding in surgical field. Therefore MAC is an attractive option as it causes less pharmacological disturbance, allows more rapid recovery than General anesthesia and is cost effective. Several drugs have been used for sedation under monitored anaesthesia care like Benzodiazepines, Opioids and Propofol. Midazolam is the most frequently used sedative and has been reported to be well tolerated in monitored anaesthesia care. Despite having a number of beneficial effects like quick onset, limited duration of action, it is far from being an ideal agent due to untoward effects like prolonged sedation after repeated administration, restlessness, cognitive impairment, respiratory depression. (Bergendahl *et al*., 2005) Recently α-2 adrenoreceptor agonists like Clonidine and Dexmedetomidine have been in use for their sedative, analgesic, anxiolytic, sympatholytic and cardiovascular stabilising effects. (Alhashemi, 2006) Dexmedetomidine, a selective α-2 adrenoreceptor agonist, is being used as a single agent in many painful procedures like awake intubation, shockwave lithotripsy, endoscopic examinations etc. It decreases sympathetic outflow and has been reported to reduce bleeding significantly in ENT surgeries. It provides excellent sedation and analgesia with minimal respiratory depression and can be safely and effectively used for surgeries under MAC. (Alhashemi, 2006) This study was undertaken to evaluate and compare the efficacy of Inj. Dexmedetomidine with Inj. Midazolam in terms of sedation, analgesia and hemodynamic stability in patients undergoing middle ear surgeries under local anaesthesia with monitored anaesthesia care.

MATERIALS AND METHODS

This randomised study was carried out in the Department of Anaesthesiology, B.L.D.E.U's Shri B.M Patil Medical College, Hospital and Research centre, Vijayapur from December 2015 to June 2017 in patients undergoing Middle ear surgeries under local anaesthesia with Monitored Anaesthesia Care. Study was approved by the institutional medical ethics committee and written informed consent was obtained from all patients participating in the study. 96 patients were selected based on inclusion criteria and were randomly divided into two groups-

Group D: Inj. Dexmedetomidine 1 µg/kg IV loading dose over 10 minutes followed by continuous infusion at the rate of 0.5 µg/kg/hr.

Group M: Inj. Midazolam 40 µg/kg IV loading dose over 10 minutes followed by continuous infusion at the rate of 20 µg/kg/hr.

Inclusion criteria

- Age 18-60 years
- Patient of either sex
- ASA Grade I and II
- Patients undergoing Middle ear surgeries under local anesthesia with MAC
- Patients consenting for the procedure

Exclusion criteria

- Pregnancy and Lactating women
- Patients with Bronchial Asthma
- Patients on Beta Blocker drugs
- MI in last 6 months, AF, Heart blocks
- Deranged renal profile
- Advanced liver disease (liver enzymes twice the normal range or higher)
- History of chronic use of sedatives, narcotics and alcohol
- Known sensitivity to Lignocaine or allergy to study drugs.

Pre anesthetic evaluation was done on the day before surgery and required investigations were advised. Patients were explained in detail about LA, operative procedure and sedation. Visual Analogue Scale was explained to patient during pre-operative visit (0-10, where 0 indicates no pain while 10 corresponds to maximum pain). Patients meeting above criteria were asked to participate in study and informed consent was taken and they were instructed to be nil by mouth for 6-8 hours. All the resuscitation and monitoring equipment like bag-valve-mask system, laryngoscope, endotracheal tubes and emergency drugs were kept ready in the operating room for management of any adverse events. On the day of surgery, patients were taken to Operating room. Intravenous access with a 20 gauge I.V cannula was secured on the dorsum of contralateral upper limb under aseptic precautions. ECG, non invasive BP and Pulse oximetry were attached and baseline vitals were recorded. Inj. Glycopyrrolate 0.01-0.02 mg/kg and Inj. Ondansetron 0.15 mg/kg IV were given and IV Ringer Lactate was started at 2 ml/kg/hr. O_2 was administered via nasal prongs at 2 lit/min. Loading doses of both the drugs were calculated and diluted to 20 ml with 0.9% Normal saline and kept at constant rate of 120 ml/hr given over 10 minutes. After the loading dose of the drug, Ramsay Sedation Score was assessed and sedation titrated to target sedation of RSS 3. Infusion was stopped when RSS of 3 was achieved or full 20 ml bolus had been given, whichever was earlier. If the RSS < 3 at the end of 10 min of loading dose, patients were given Inj. Propofol 100-300 mcg/kg IV bolus as a rescue sedative. The protocol of upto a maximum of 2 rescue doses was set. RSS was assessed throughout the duration of surgery and in postoperative period every 15 minutes up to 120 minutes. Once RSS was 3, Lidocaine 2% with adrenaline 1:200,000, 6-7 ml was given by the surgeon. Intraoperative pain intensity was assessed with VAS (0-10). If VAS >3 or whenever patient complained of pain during surgery, Inj. Fentanyl 1 mcg/kg was given as rescue analgesic and additional dose of local anaesthetic 2-3 ml (not exceeding the maximum dose) was repeated by surgeon, if required. Heart rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean arterial pressure (MAP), Respiratory Rate (RR), Oxygen Saturation (SpO_2) were recorded at the start of loading infusion, 5 minutes after, at the end of loading infusion and thereafter at 15 minutes interval till the end of surgery and every 15 minutes in the post operative period up to 2 hours. The maintenance infusions were discontinued approximately

15 minutes before the end of surgery. Adverse events like Bradycardia (PR<60 bpm), Hypotension (MAP< 65 mm Hg), Desaturation (SpO_2), nausea, vomiting, dry mouth or any other events were noted. Bradycardia was treated with Inj. Atropine 0.01 mg/kg. and Hypotension was treated with Inj. Ephedrine 5 mg bolus and IV fluids. Any time during the procedure if dosage of rescue drugs crossed the acceptable dosage, the technique was discontinued and converted to any alternative sedative or anesthetic technique. Such incidents were noted and the subjects were withdrawn from further analysis. Patients were shifted to Post Anaesthesia Care Unit (PACU) after completion of surgery and were monitored for hemodynamic parameters. Pain was assessed postoperatively using Visual analog scale and if VAS >3, then Inj. Diclofenac 1.5mg/kg I.V was given. At the end of surgery, surgeons were asked to grade their satisfaction using Likert scale; score of 4 and 5 were taken as acceptable.

Various scores used in the study are as follows:

Ramsay Sedation Scale

[1 - Anxious, agitated or restless, 2 - Cooperative, oriented and tranquil, 3 - Responds to command, 4 - Asleep but has a brisk response to light glabellar tap or loud auditory stimulus, 5 - Asleep has a sluggish response to a light glabellar tap or loud auditory stimulus, 6 - Asleep no response]

Surgeon Satisfaction score

[1- Very dissatisfied, 2- Dissatisfied, 3- Neither satisfied nor dissatisfied, 4- Satisfied, 5- Very satisfied]

Statistical analysis

All characteristics were summarized descriptively. For continuous variables, the summary statistics of N, mean, standard deviation (SD) were used. For categorical data, the number and percentage were used in the data summaries. Chi-square ($\chi 2$)/Fisher exact test was employed to determine the significance of differences between groups for categorical data. The difference of the means of analysis variables was tested with the unpaired t-test. If the p-value was < 0.05, the results were considered to be significant. Data was analyzed using SPSS software v.23.0.

RESULTS

This comparative clinical study was conducted on 96 patients of ASA Grade I & II, aged between 18 - 60 yrs, undergoing middle ear surgeries to evaluate and compare the effects of intravenous infusion of Inj. Dexmedetomidine and Inj. Midazolam in terms of sedation, analgesia and hemodynamic stability intraoperatively and postoperatively. All these patients were operated under Monitored Anaesthesia Care using local infiltration with 2% Lignocaine with Adrenaline 1:200000 and sedation using either Dexmedetomidine or Midazolam infusion.

The patient characteristics and demographic data are shown in Table 1.

The mean sedation score in Group D was 3.77±0.18 and in Group M was 3.69±0.64. p value was >0.05 and was not statistically significant.

Table 1. Demographic Parameters

Parameter	Group D	Group M
Age (years) (mean± sd)	37.8±12.1	35.2±12.3
Sex : males	29	29
Females	19	19
Weight (kg)	61.5±8.0	59.5±8.0
Asa grade i	39	38
Ii	9	10
Duration of surgery (minutes)	85.6±11.6	88.1±15.4

Surgeon satisfaction score was high in Group D compared to Group M (p<0.001) (Figure 1). 31 out of 48 surgeries (64.6 %) in Group D were rated 5 on Surgeon satisfaction score compared to 14 out of 48 (29.2 %) surgeries in Group M. (Figure 2)

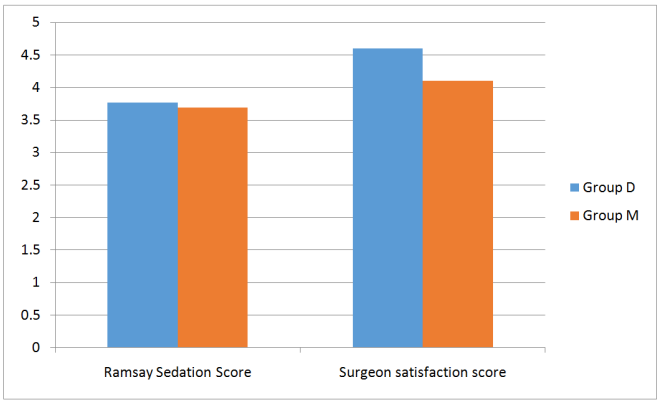

Figure 1. Comparison of RSS and Surgeon Satisfaction score

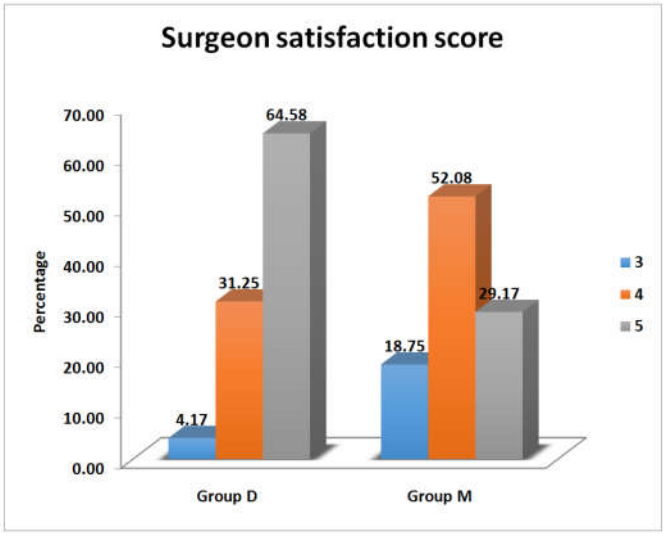

Figure 2. Surgeon satisfaction score

Pain scores calculated using Visual analog scale were significantly lower in Group D (0.76±0.71) compared to Group M (2.22±0.50) in the intraoperative period (p <0.001) (Figure 3). Pain scores in the postoperative period were lower in Group D (0.62±0.77) compared to Group M (2.47±0.8) (p<0.001). (Figure 4). Table 3 and Figure 5 show requirement of rescue sedation (RSS< 3) and rescue analgesic (VAS> 3) among both groups. 5 out of 48 patients required rescue analgesic in Group D in comparison to 15 out of 48 patients in Group M. The difference was statistically significant with p<0.05. 2 out of 48 patients in Group D required rescue sedation compared to 5 out of 48 patients in Group M. The difference was not statistically significant.

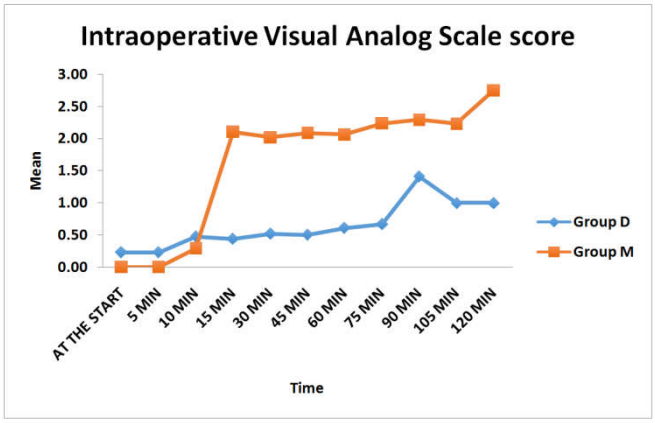

Figure 3. Intraoperative VAS

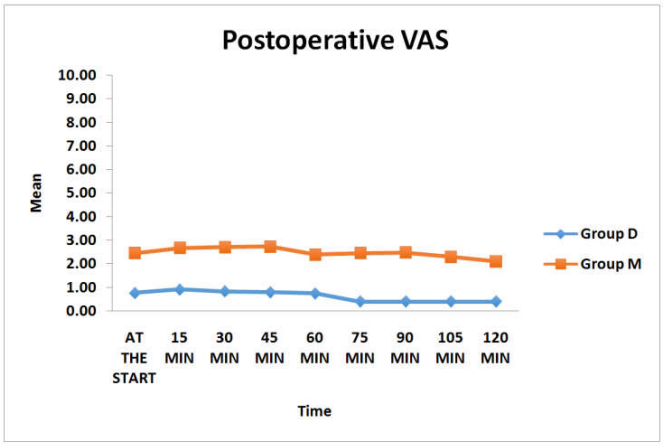

Figure 4. Postoperative VAS

Table 2. Requirement of Additional drugs

Additional requirement	Group D		Group M		Total		p value
	N	%	N	%	N	%	
Additional analgesic	5	10.4	15	31.3	20	20.8	0.012*
Additional sedation	2	4.2	5	10.4	7	7.3	0.128
Total	48	100.0	48	100.0	96	100.0	

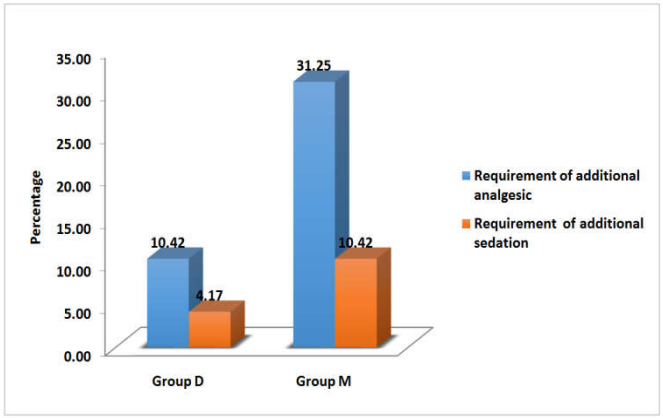

Figure 5. Requirement of Additional drugs

Systolic and Diastolic blood pressure decreased significantly in Group D than in Group M after the start of infusion ($p<0.05$) as shown in Figure 6 & 7. There was significant reduction in Heart rate in Group D compared to group M ($p<0.05$) (Figure 8).

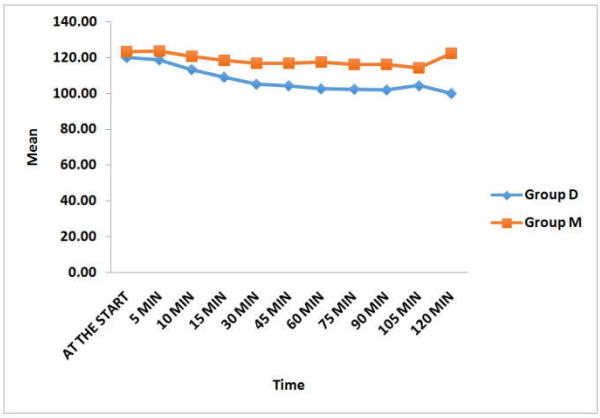

Figure 6. Changes in Systolic blood pressure

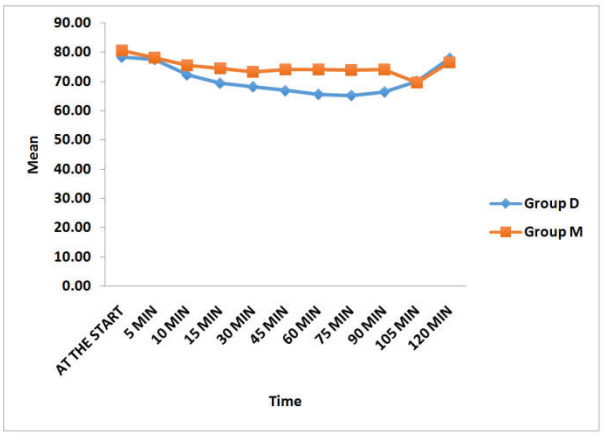

Figure 7. Changes in Diastolic blood pressure

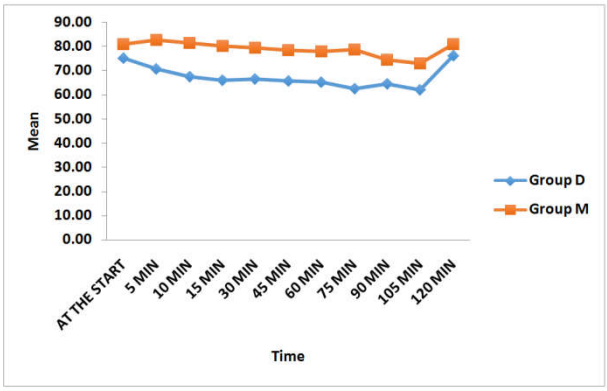

Figure 8. Changes in Heart rate

DISCUSSION

Monitored anaesthesia care (MAC) may be used in various ENT surgeries which require adequate sedation and analgesia for comfort of both the patient and surgeon. MAC involves administration of local anaesthesia with intravenous sedatives, anxiolytic and analgesic drugs with detailed monitoring of vital parameters. It has many advantages such as less bleeding, cost-effectiveness, postoperative analgesia, faster recovery and ability to test hearing intra operatively. Thus the primary objective in providing MAC is to ensure patient comfort, safety, and satisfaction during surgery (Ronald D. Miller, 2009). Verbal communication between the anaesthesiologist and patient is important in order to facililtate patient cooperation, reassure the patient and evaluate the level of sedation. A level of sedation that allows verbal communication

should be optimal for the patient's comfort and safety. If the level of sedation is deepened to the extent that verbal communication is lost, most of the advantages of monitored anesthesia care are also lost, and the risk of this technique almost approaches to general anesthesia with an unprotected and uncontrolled airway. American Society of Anaesthesiologists (ASA) Standards for Basic Anaesthetic Monitoring that is applicable to all levels of anesthesia care includes monitored anesthesia care too. It includes Pulse Oximetry (SpO_2), Electrocardiography (ECG), NIBP Monitor. It is important to continually evaluate patient's response to verbal commands in order to titrate the level of sedation and to allow early detection of neurologic or cardiopulmonary dysfunction. It is equally important to have a bloodless surgical field as far as possible for better visibility. Bleeding control is usually achieved with the use of epinephrine. Pain during surgery may lead to sympathetic stimulation and a restless patient may have tachycardia and hypertension, leading to increased bleeding in the surgical field, therefore adequate analgesia is needed.Several drugs have been used for sedation during surgery under local anesthesia with monitored anesthesia care including Propofol, benzodiazepines and opioids. However, Propofol may cause over sedation and disorientation (Maze and Tranquilli, 1991), Benzodiazepines may result in confusion, particularly in elderly and opioids are associated with increased risk of respiratory depression (Avramov *et al*., 1996). All of these untoward effects hamper patient's cooperation during surgery and make these agents less ideal for sedation in MAC.

Midazolam is a potent imidazobenzodiazepine which has hypnotic, amnestic, anticonvulsant and anxiolytic activity. Midazolam is most commonly used for sedation in MAC and reported to be well tolerated by patients. Midazolam causes sedation by GABA receptor activation. α_2 receptors are found densely in the locus ceruleus, which is an important source of sympathetic nervous system innervations of the forebrain and a vital modulator of vigilance. The sedation effects evoked by α_2 agonists most likely reflects inhibition of this nucleus. Midazolam has a number of beneficial effects when used for sedation like fast onset and limited duration of action. Despite having a number of beneficial effects, it is far from an ideal agent having untoward side effects such as restlessness, paradoxical reaction, cognitive impairment, amnesia, and respiratory depression. (Bergendahl *et al*., 2005; Bergendahl *et al*., 2006) Dexmedetomidine is a highly selective α_2-adrenoceptor agonist with eight times higher specificity for the receptor compared to clonidine. Dexmedetomidine provides dose-dependent sedation, analgesia, sympatholysis and anxiolysis without causing respiratory depression. Hypotension and bradycardia are frequently observed with Dexmedetomidine. These effects are known to be related to the dose, route of administration and infusion rate (in intravenous administrations) (McCutcheon *et al*., 2006). Reports of its use state that, alpha-2 agonist effect is observed on administration of low and moderate doses and at slow rates of infusion and alpha 1 agonism is seen at high dose and faster rate of infusion. (Venn *et al*., 1999) Use of continuous intravenous infusion of short acting sedative - hypnotic drugs has been found to be associated with fewer side effects and shorter recovery times than the traditional intermittent bolus techniques. It also provides stable level of sedation. Taking this into account, we decided to use a loading dose of 1 µg/kg Dexmedetomidine, in order to avoid side effects associated with high infusion rates. A short distribution half life of 5 minutes necessitates that it be given as a maintenance infusion. Recent multicenter trial indicated that it was an effective baseline sedative for patients undergoing a broad range of surgical procedures under MAC, providing greater patient satisfaction, less opioid requirements, and less respiratory depression compared with the placebo. (Candiotti *et al*., 2010)

Parikh *et al*. (2013) compared Dexmedetomidine verus Midazolam-Fentanyl in 90 patients undergoing tympanoplasty surgeries and concluded that both drugs were comparable in terms of sedation. In their study, rescue sedation with Propofol was required in 1 patient in Group D and 4 patients in Group M. In our study, sedation score was slightly higher in Group D compared to Group M, but p value was > 0.05 indicating no statistical difference between both groups. In our study 2 out of 48 patients in Group D required additional sedation in comparison to 5 out of 48 patients in Group M. Similar findings were also noted in study conducted by Vyas *et al*. (2013) where difference in sedation score among both groups was found to be statistically insignificant. In our study, we found that perioperative VAS scores were significantly lower in Group D compared to Group M. ($p<0.001$), suggesting that analgesia is better with Dexmedetomidine than Midazolam. Similar findings were reported by Karaaslan *et al*. (2007), who compared Dexmedetomidine and Midazolam with Tramadol PCA as rescue analgesic in 70 patients undergoing Septoplasty or Endoscopic sinus surgery under MAC. They found that the amount of rescue analgesia needed in Dexmedetomidine group was significanty lower compared to Midazolam group ($p<0.001$), suggesting that better analgesic effect was achieved with Dexmedetomidine. Padmaja and Varma (2015) compared efficacy of Midazolam versus Dexmedetomidine in minor ENT procedures and concluded that Dexmedetomidine reduces the doses of rescue analgesics making it a more favourable choice for ENT surgeries. In our study only 5 out of 48 patients in Group D required rescue analgesia with Fentanyl in comparison to 15 out of 48 patients in Group M.($p<0.001$).

Karaaslan *et al*. (2007) found that Hemodynamic parameters like Systolic blood pressure, Diastolic blood pressure, mean arterial pressure and heart rate were higher in Midazolam group compared to Dexmedetomidine group. Dexmedetomidine leads to depressive effects on hemodynamic parameters at the loading dose of 1 µg/kg over 10 min, but this effect does not reach the level of severe impairment as shown by Eren *et al*. (2011). Parikh *et al*. (2013) found that intraoperative mean heart rate and mean arterial pressure was lower in Dexmedetomidine group than the baseline values and the corresponding values in Midazolam-Fentanyl group. In our study also, we found significant reduction in heart rate, Systolic blood pressure, Diastolic blood pressure and Mean arterial pressure in Group D compared to baseline values and corresponding values in Group M, suggesting that both drugs produce stable haemodynamics but Dexmedetomidine has a clinical advantage over Midazolam in providing better operative field for microscopic surgery. Durmus *et al*. (2007) evaluated this property of Dexmedetomidine for providing controlled hypotension in general anaesthesia for tympanoplasty cases and concluded that it is a useful adjuvant to decrease bleeding in cases where bloodless surgical field is required.

Vyas *et al*. (2013) compared Dexmedetomidine versus Midazolam for sedation during Tympanoplasty and Modified radical mastoidectomy under local anaesthesia in 50 patients

and found out that Surgeon's satisfaction score and patient's satisfaction score were higher in Group D. Parikh *et al*. (2013) compared Dexmedetomidine with Midazolam-Fentanyl for Tympanoplasty under local anesthesia and concluded that Dexmedetomidine is better than Midazolam-Fentanyl for sedation during Tympanoplasty with better surgeon and patient satisfaction scores. In our study, 31 out of 48 surgeries (64.6 %) in Group D were rated 5 on surgeon satisfaction score compared to 14 out of 48 (29.2 %) surgeries in Group M. The lower MAP and HR in Group D patients could have resulted in better surgical field thereby causing greater surgeon satisfaction compared to Group M. (p value <0.001). To summarize, Dexmedetomidine causes better sedation, without causing any ventilatory depression and better perioperative analgesia with reduced requirement of rescue analgesics. It also normalises the increases in blood pressure and heart rate caused by perioperative anxiety by virtue of its anxiolytic property. It also causes better surgeon satisfaction by creating an oligemic surgical field. It is cost effective and has no significant side effects.

Conclusion

Dexmedetomidine is a safe and attractive agent compared to conventional sedation with Midazolam in patients undergoing Middle ear surgeries under local anaesthesia with monitored anaesthesia care as it provides a calm patient, better perioperative analgesia, increased surgeon satisfaction and rapid recovery.

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