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COMPARISON OF EFFECTS OF DEXMEDETOMIDINE AND MIDAZOLAM FOR SEDATION AND HAEMODYNAMIC CHANGES IN PATIENTS UNDERGOING TYMPANOPLASTY AND MODIFIED RADICAL MASTOIDECTOMY UNDER MONITORED ANAESTHESIA CARE: A PROSPECTIVE RANDOMIZED DOUBLE BLIND STUDY

Anaesthesiology

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ABSTRACT

Background: Monitored anaesthesia care (MAC) has become increasingly used for middle ear surgeries which usually combines a local anaesthetic agent with intravenous sedation. Dexmedetomidine has gained popularity for intravenous sedation for the procedures to be done under MAC. So this study was aimed at to compare the efficacy of dexmedetomidine with midazolam for sedation, analgesia, patient and surgeon satisfaction along with various haemodynamic changes and side effects.

Methods: Eighty adult patients of either sex aged 18-60 years with ASA grade I and II undergoing tympanoplasty and modified radical mastoidectomy under MAC were randomly allocated into two groups. Group D (n = 40) received intravenous dexmedetomidine 1 µg/kg diluted up to 30 ml by normal saline given over 15 min followed by a continuous infusion of 0.5 µg/kg/h and Group M (n = 40) received intravenous midazolam 0.05 mg/kg diluted up to 30 ml normal saline given over 15 min followed by continuous infusion of 0.01 mg/kg/h. Ramsay sedation score (RSS), Visual analogue score (VAS), rescue sedative and analgesic requirement, patient and surgeon satisfaction scores ,haemodynamic parameters and side effects were recorded and compared in both groups. The data were analysed using different statistical tests.

Results: The mean RSS was significantly more in Group D (3.0±0.0) as compared to Group M (2.85±0362),(P<0.05).The mean VAS was significantly lesser in Group D in comparison to Group M,(P<0.05).The total number of patients and number of doses of rescue sedative required were significantly lesser in Group D [12(30%),0.3±0.464)] as compared to Group M [36(90%),1.3±0.648],(P<0.05).Similarly, the total number of patients and number of doses of rescue analgesic were significantly lesser in Group D [4(10%),0.10±0.308] as compared to Group M [14(35%),0.38±0.540],(P<0.05). The patient and surgeon satisfaction scores were significantly better in Group D,(P<0.05).The HR was reduced significantly in Group D,P<0.05, while SBP and DBP remained comparable to their respective baseline values in both groups,(P<0.05). In Group D, four patients had experienced bradycardia.

Conclusion: Dexmedetomidine could be a safer and effective alternative to midazolam for tympanoplasty and modified radical mastoidectomy done under monitored anaesthesia care.

KEYWORDS:

Dexmedetomidine, Midazolam, Monitored Anaesthesia Care, Fentanyl, Tympanoplasty, Sedation Score

INTRODUCTION

Middle ear surgeries like tympanoplasty and modified radical mastoidectomy are usually done under local anaesthesia or local anaesthesia with sedation under monitored anaesthesia care (MAC) in adult patients.[1,2] This technique of local anaesthesia with sedation have various advantages including less bleeding, better postoperative analgesia, rapid recovery, increased cost effectiveness with the ability to test hearing during the procedure or surgery.[3-5]

Various drugs have been used for sedation along with local anaesthesia for MAC including benzodiazepines, propofol, opioids and α2 agonists either alone or in combination.[6,7] Midazolam, a short acting benzodiazepine, has become the most frequently used drug for procedural sedation, as it has hypnotic, amnesic and anxiolytic properties which are desirable for procedures under MAC. However, it can cause prolonged sedation and respiratory depression after repeated administration of bolus doses.[8] The newer drugs, like dexmedetomidine, a highly selective α2 adrenoceptor agonist, has emerged as an alternative drug for intravenous sedation and gained popularity nowadays, as it has both sedative and analgesic properties. It provides conscious sedation without significant respiratory depression along with shorter half life and wider margin of safety which makes it a suitable agent to be used for procedures under MAC.[9-11] Dexmedetomidine also attenuates the stress response to surgery due to its sympatholytic effect and has opioid sparing effect which provides stable haemodynamics both during and after surgery.[11]

So based on above hypothesis , this prospective, randomized, clinical study was undertaken to compare efficacy of dexmedetomidine and midazolam for sedation and analgesia along with various haemo dynamic changes during tympanoplasty and modified radical mastoidectomy under monitored anaesthesia care.

METHODS

This prospective randomized comparative study was conducted after obtaining approval from local ethical committee including eighty adult patients of either sex, aged [18-60] years with American Society of Anaesthesiologists grade I and II, undergoing tympanoplasty and modified radical mastoidectomy under monitored anaesthesia care. The patients with known sensitivity to local anaesthetic drug lidocaine, allergy to any of the study drugs, pregnant and lactating females, history of use of any opioid or sedative medications in the week prior to surgery, patients with any cardiac disease, patients on psychotropic drugs, patients with significant systemic disorders and obese patients with body mass index more than 28 were excluded from the study.

The patients were randomly allocated into two groups with 40 patients in each group; Group D (Dexmedetomidine) and Group M (Mida zolam) using computer generated tables of random numbers and sequentially numbered opaque sealed envelopes were prepared. For the purpose of double blinding, the anaesthesiologist not involved in the study had prepared the study drugs after opening the sealed envelope while the other anaesthesiologist who administered the study drugs and observed the parameters, was also blinded to the study groups.(Figure 1)

All patients have undergone routine pre-anaesthetic evaluation the day before surgery, written informed consent was taken and were kept nil per oral for a minimum duration of eight hours before surgery. On arrival of the patient in the operating room, an 18-gauge intravenous cannula was inserted and an infusion of DNS (dextrose normal saline) was started @ 2 ml/kg. The baseline haemodynamic and vital parameters were recorded including heart rate (HR), non-invasive blood pressure (NIBP), capnography (EtCO2), electrocardiogram (ECG) and arterial oxygen saturation (SpO2).

After that, the patients were premedicated with glycopyrrolate 4µg/kg given intravenously. Oxygen was supplemented via oxygen mask @ 4 litres/min. Group D (n = 40) received intravenous dexmedetomidine 1 µg/kg diluted up to 30 ml by normal saline given over 15 min followed by a continuous infusion of 0.5 µg/kg/h and Group M (n = 40) received intravenous midazolam 0.05 mg/kg diluted up to 30 ml normal saline given over 15 min followed by continuous infusion of 0.01 mg/kg/h. The maintenance infusions in both the groups were initiated immediately, once the loading infusion was stopped. During this period the patients were assessed every five minutes using Ramsay

sedation score12 (RSS); (1 = agitated, restless; 2 = cooperative, tranquil; 3 = responds to verbal command while sleeping; 4 = brisk response to glabellar tap or loud voice while sleeping; 5 = sluggish response to glabellar tap or loud voice; 6 = no response to glabellar tap or loud voice). The target end point for RSS was to achieve a score equal to [3]. After completing the loading infusion of the drugs and when RSS of 3 was achieved, the surgeon was allowed to administer the local anaesthetic agent (lidocaine 2% with 1:200000 adrenaline) thereafter sedation level (RSS) was assessed every 10 min till 65 min and if RSS < 3 midazolam 0.01 mg/kg was administered intavenously as a common rescue sedative in both the groups.

The visual analogue scale (VAS) was used to evaluate pain both during intraoperative and postoperative period. VAS (0-10, where 0 indicated no pain while 10 corresponded to maximum pain), was explained to the patient during the preoperative period and the target was to achieve a score of 3 or less. If VAS >3, then fentanyl 1 µg/kg was given intravenously as rescue analgesic in both the groups. The number of rescue doses along with total number of patients who required rescue midazolam and fentanyl were recorded. The standard protocol was followed for rescue sedation and analgesic which included to give maximum three rescue doses each of midazolam and fentanyl in both groups. At any time during the study if the amount of rescue drugs had reached their specified limits, this sedation technique was abolished along with discontinuation of the study drug. RSS and VAS were assessed every 5 min during loading infusion of the study drugs and thereafter at 10-min intervals till 65 min, the maintenance infusions were discontinued towards the completion of surgery. Intraoperative haemodynamic parameters i.e. HR, SBP,DBP and SpO2 were recorded every 5 min during loading infusion of the study drugs and thereafter at 10-min intervals till 65 min.

Any of the adverse haemodynamic variations including bradycardia (HR < 60 beats per minute), hypotension (fall in SBP or DBP >20% of baseline value or MAP < 60 mmHg), hypertension (an increase in SBP or MAP > 20% of baseline value), respiratory depression (respiratory rate < 10 breaths/min), desaturation (SpO2 < 90%) and other side effects like nausea, vomiting and dry mouth during or within immediate postoperative period of the procedure were observed. Bradycardia was treated with atropine (0.01mg/kg) given intravenously, hypotension was managed either by fluid replacement or if required mephentermine 6 mg given intravenously in incremental doses. Desaturation was treated either by increasing the oxygen flow or if required, using 100% O2 with bag mask (bain's circuit) ventilation. Both, the surgeons and patients were asked to rate their satisfaction using seven point scale, the Likert scale13 [1- Extremely dissatisfied; 2- Dissatisfied; 3- Dissatisfied somewhat; 4- Undecided; 5- Somewhat satisfied; 6- Satisfied; 7- Extremely satisfied].

All the patients remained in the Post Anaesthesia Care Unit (PACU) for a minimum of 1 hour after discontinuation of the study drug. In PACU the RSS, VAS and haemodynamic parameters (HR,SBP,DBP,SpO2) were recorded at arrival, 30 min and 60 min.

Statistical analysis: The sample size was calculated to be 40 patients in each group based on the results of a previous study and to demonstrate a power of 0.8 and type 1 error of 0.05.The above sample size was required to demonstrate a significant difference in sedation scores between the two groups. Categorical data i.e. demographic data and side effects were analyzed using chi square test and were expressed as number or percentage. Haemodynamic variables were analyzed using paired t-test and unpaired t-test for intragroup and intergroup comparisons respectively. Quantitative data were expressed as Mean± Standard Deviation. P<0.05 was considered as significant.

RESULTS

The two groups were comparable with respect to demographic profile of the patients including mean age, mean weight, gender, ASA grade and mean duration of surgery, (P>0.05).(Table 1)

The mean RSS was found to be higher in Group D than Group M i.e. the mean RSS was 3.0±0.0 and 2.85±0.362 in Group D and Group M respectively at the end of 15 min of loading infusion which was statistically significant, (P = 0.0255). Similarly the mean RSS was found to be statistically significant at all time intervals except at 25 min and 65 min, (P= 0.0355). In PACU, it was also significantly higher in Group D at 30 min and 60 min, (P< 0.05).(Table 2) The number of patients required rescue dose of midazolam in Group M were more (36, 90%) as compared to Group D (12, 30%). Similarly the total number of rescue doses of midazolam needed were higher in Group M (1.3±0.648) compared to Group D (0.3±0.464) and was found to be statically significant, (P < 0.001).(Table 3)

The mean VAS was found to be significantly lower in group D than Group M compared at various time intervals. Similarly, at arrival in the recovery room the VAS was significantly lower in Group D as compared to Group M; (P < 0.05),however it remained comparable thereafter in both groups till 60 min.(Table 2) The number of patients required rescue dose of fentanyl in Group M were more (14, 35%) as compared to Group D (4, 10%), also the total number of rescue doses of fentanyl needed were higher in Group M (0.38±0.540) compared to Group D (0.10±0.308); (P<0.05).(Table 3)

Surgeon satisfaction scores were 6.55±0.7494 and 4.75±0.5430 in Group D and Group M respectively, while patient satisfaction scores were 6.5±0.679 and 4.8±0.686 in Group D and Group M respectively and both were significantly higher in Group D, (P= 0.001).(Table 4)

The baseline mean HR,SBP,DBP and SpO2 were comparable in both groups,(P>0.05). In Group D, the mean HR was found to be significantly lower at 5,55 and 65 min compared to baseline values, (P < 0.05) and rest of the time HR was comparable to baseline values. At arrival in PACU , mean HR was significantly lower from baseline value, (P = 0.001) after that HR was comparable to baseline values till 60 min. However, in Group M, the HR did not show any statistical difference from their baseline values at any time interval, (P>0.05).(Figure 2) However, the intra group comparison of SBP and DBP at different time intervals from their respective baseline values was found to be statistically not significant till 65 min,(P>0.05) in both groups. Similarly, no statistically significant difference was observed till 60 min in the recovery room,(P>0.05) in both groups.(Figure 3 and 4) The mean SpO2 observed in Group D was significantly higher as compared to Group M, (P<0.05).(Figure 5)

The bradycardia was observed in 4 (10 %) patients in Group D while none of the patients had any episode of bradycardia in Group M and this was statistically significant, (P = 0.0402). The bradycardia was reversed easily with atropine in titrated doses. However no other side effects (hypotension,hypertension,dryness of mouth and PONV) were observed in both groups.(Figure 6)

DISCUSSION

MAC is one of the methods of outpatient anaesthesia which usually combines a local anaesthetic agent with parenteral drugs for sedation, anxiolysis and analgesia. It requires proper selection of drugs with adequate titration of doses so that there would be minimal physiol ogical alterations and adverse effects associated with rapid recovery. It has become increasingly used for middle ear surgeries like tympanoplasty and modified radical mastoidectomy.[11] Dexmedet omidine, a highly selective α2 adrenoceptor agonist, can be used effectively for the procedures or surgeries to be done under conscious sedation and monitored anaesthesia care.[14]

The primary objective of our study was to compare the level of sedation using RSS between the two groups. In our study all the patients in Group D achieved RSS=3 at the end of loading drug infusion whereas only 34 patients achieved RSS=3 in Group M, as the target end point of RSS was 3 at the end of 15 min. We observed that mean RSS was significantly higher at almost all time intervals in Group D. This implies that the level of sedation was found to be significantly better with dexmedetomidine and the patients remained calmer and co-operative during surgery, which is desirable for the surgeries to be done under sedation and MAC. In recovery room, the mean RSS was also found to be significantly higher in Group D which showed that the recovery of patients in dexmedetomidine group was somewhat delayed but clinically patients remained calm and arousable as sedation scores were in acceptable range.This may be attributed to sustained therapeutic plasma concentration of dexmedetomidine as it has elimination half life of 2 hours. Our results concurs with the study done by Parikh DA et al[7] who found better sedation with dexmedetomidine when compared to midazolam fentanyl combination in patients for tympanoplasty under MAC. Similarly Mohamed MH et al11 also showed higher sedation scores in dexmedetomidine group than midazolam group in ear surgeries under

monitored anaesthesia care.Nallam SR et al[1] also found significantly higher sedation scores in dexmedetomidine group as compared to propofol group, P< 0.01 in middle ear surgeries under MAC ,however they have used nalbuphine as a common drug in both groups.

The total number of rescue doses and number of patients required rescue doses of midazolam to achieve RSS 3 was significantly lesser in dexmedetomidine group which was consistent with the findings of Parikh DA et al7 and Gupta P et al10, and also with some other studies too.1,6,11 This could be explained by the fact that dexmedetomidine has both sedative and analgesic properties by acting on spinal cord and locus ceruleus and thereby reduced the requirement of rescue midazolam and the target level of sedation had achieved with dexmedetomidine alone.[14-17]

The mean VAS values were found to be lower in dexmedetomidine group when compared to midazolam group as the target VAS was less than [3]. Mohamed MH et al[11] and Nallam SR et al1 were found significantly higher VAS in midazolam group and propofol group respectively while comparing it with dexmedetomidine and these results were in concordance with our study too.

The lesser number of rescue doses of fentanyl were required in dexmedetomidine group. Similarly the number of patients who required rescue doses of analgesic were significantly lesser in Group D as compared to Group M, P <0.05.Turan et al[18] found that total diclofenac consumption as rescue alalgesic was significantly higher in propofol group in comparison to dexmedetomidine group in septoplasty and endoscopic sinus surgeries, which was similar to results of our study. Similarly, Karaaslan K et al[19] also found that rescue tramadol required was significantly higher with midazolam as compared to dexmedetomidine in endoscopic nasal surgeries. Mohamed et al[11] also showed in their study that use of rescue analgesic was significantly more in midazolam group in comparison to dexmedetomidine group. Similar results were also found in other studies.[5,7,20] The reduced requirement of rescue analgesic with dexmedetomidine may be attributed to its additional analgesic property which provides better control of pain along with reduced level of anxiety. Similarly the mean VAS values were lesser with dexmedetomidine because of this property of dexmedetomidine only.[10,21,22]

In our study, both patient and surgeon satisfaction scores were found to be better with dexmedetomidine. Delmade MA et al8 demonstrated significantly better patient and surgeon satisfaction scores in dexmedetomidine group while comparing with midazolam group in ENT surgeries under MAC. Our results are also consistent with the finding of Nallam SR et al[1], Vyas DA et al[3], Alhashemi JA et al[9], and Gupta P et al10 who found better patient and surgeon satisfaction scores in their studies too.The patient's satisfaction score was better with dexmedetomidine as it provides better sedation which allays anxiety along with adequate analgesia which makes the patient more comfortable and pain free during the surgery. Similarly surgeon's satisfaction score was found to be higher with dexmedetomidine as it provides bloodless field along with calm and co-operative patient which is desirable for the surgeries to be done under sedation with MAC.[6,9,23-26]

Our study demonstrated a significantly lower mean HR in Group D when compared to their baseline values both during intraoperative and postoperative period. However, both SBP and DBP were found to be comparable to their baseline values in individual groups respectively. Although dexmedetomidine affected both HR and MAP in various studies by significantly decreasing both parameters but in our study the SBP and DBP remained stable throughout both intraoperative and postoperative period, which is somewhat contrary to these studies.[5,7,10,25]

The decreased sympathetic activity might be responsible for lower mean HR in dexmedetomidine group.[7,21,25,26] Parikh DA et al7 found significantly lower mean HR in dexmedetomidine group from their baseline values and corresponding values in midazolam fentanyl group, P<0.05.MAP was also found to be significantly lower in their study but our results regarding SBP and DBP were found to be not in concordance to study done by Parikh DA et al. Similar results were found by Alhashemi et al[9]. Kazim Karaaslan et al[19] while comparing mean HR between dexmedetomidine and midazolam group. Delmade MA et al[8] also found similar decrease in mean HR from their baseline values in dexmedetomidine group when comparing midazolam in ENT surgeries under MAC.

The bradycardia was observed in four patients in dexmedetomidine group while no patient had any episode of bradycardia in midazolam group. However this was reversed with atropine in titrated doses. No other side effect like hypotension, hypertension, dryness of mouth and PONV were reported in any of the patients in both groups.

Conclusion: Dexmedetomidine could be a better alternative to midazolam for providing sedation in various middle ear surgeries done under monitored anaesthesia care as it provides better level of sedation with adequate intraoperative and postoperative analgesia along with reduced rescue sedative and analgesic requirements which makes the patient more calm and co-operative leading to better patient and surgeon satisfaction which is desirable for the surgeries to be done under MAC. Dexmedetomidine was also associated with no significant haemodynamic changes and any other adverse events except for bradycardia which could be managed effectively.

Table 1: Demographic data and duration of surgery

Variables	Group D (n=40)	Group M (n=40)	P value
Mean Age (years)	25.73±1.309	25.55±1.461	0.921
Gender (M/F)	22/18	21/19	0.8226
Mean Weight (kg)	55.05±0.879	53.38±1.129	0.245
ASA (I/II)	30/10	28/12	0.616
Mean Duration of surgery(min)	91.43±15.07	95.29±15.29	0.236
*P value > 0.05, not significant. * Data expressed as Mean ± SD or number.			

Table 2: Comparison of Ramsay sedation score (RSS), visual analogue score (VAS) at various time intervals

Time	RSS			VAS		
	Group D (n=40)	Group M (n=40)	P value	Group D (n=40)	Group M (n=40)	P value
Preop	1±0.0	1±0.0	0.9999	0.0±0.0	0.0±0.0	0.9999
5 min	2.70±0.304	1.85±0.361	0.002*	0.0±0.0	0.0±0.0	0.9999
10 min	2.60±0.496	2.40±0.504	0.2629	0.0±0.0	0.0±0.0	0.9999
15 min	3.0±0.0	2.85±0.362	0.0255*	0.30±0.52	1.2±1.34	0.0013*
25 min	2.80±0.405	2.80±0.405	0.9999	1.10±1.13	1.58±1.24	0.0611
35 min	3.0±0.0	2.70±0.438	0.0010*	1.08±0.94	1.47±1.11	0.1101
45 min	2.90±0.304	2.70±0.073	0.0482*	1.13±0.18	1.19±0.19	0.2749
55 min	3.0±0.0	2.70±0.464	0.0002*	0.70±0.72	1.98±1.09	0.001*
65 min	3.0±0.0	3.0±0.0	0.9999	0.20±0.46	2.10±1.43	0.001*
At postop arrival	3.0±0.0	2.80±0.362	0.0255*	0.50±0.82	1.20±1.11	0.0027*
30 min	2.41±0.495	2.02±0.719	0.0025*	0.28±0.55	0.48±0.64	0.1254
60 min	2.29±0.462	1.91±0.786	0.0018*	0.13±0.33	0.43±0.84	0.0686
*P value <0.05, significant. * Data are represented as Mean ± SD						

Table 3: Requirement of rescue Midazolam and Fentanyl in both groups

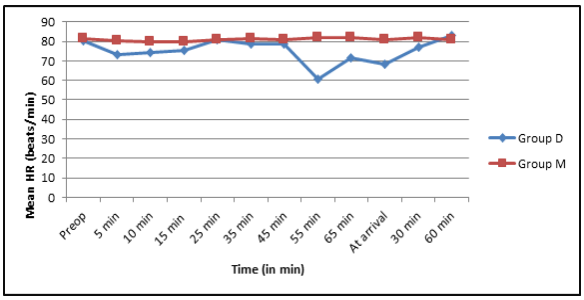
Variables	Group D (n=40)	Group M (n=40)	P value
Number of patients required rescue dose of midazolam	12 (30%)	36 (90%)	0.001

Total number of rescue doses of midazolam required	0.3±0.464	1.3±0.648	0.001
Number of patients required rescue dose of fentanyl	4 (10%)	14 (35%)	0.0074
Total number of rescue doses of fentanyl required	0.10±0.308	0.38±0.540	0.0118
*P value <0.05, significant. *Data are represented as Mean ± SD or number (%)			

Table 4: Patient and surgeon satisfaction scores in both groups

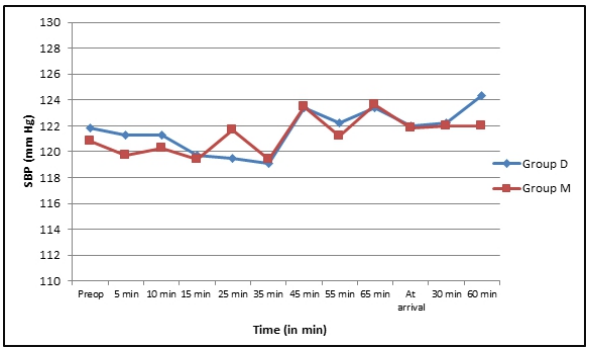
Variables	Group D (n=40)	Group M (n=40)	P value
Surgeon satisfaction score	6.655±0.749	4.75±0.543	0.001
Patient satisfaction score	6.5±0.679	4.8±0.687	0.001
*P value <0.05, significant. *Data are represented as Mean ± SD			

Figure 1: Comparison of mean heart rate (HR) at various time intervals in both groups'



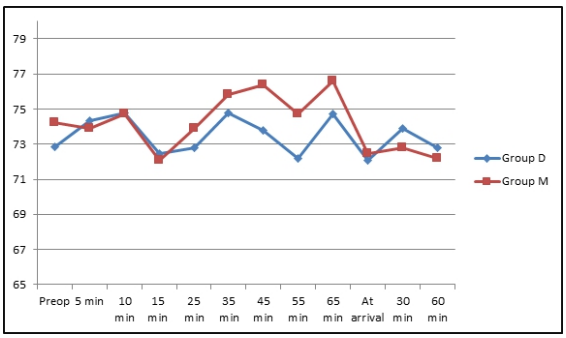
*Data expressed as Mean ± SD

Figure 2: Comparison of mean systolic blood pressure (SBP) at various time intervals in both Groups



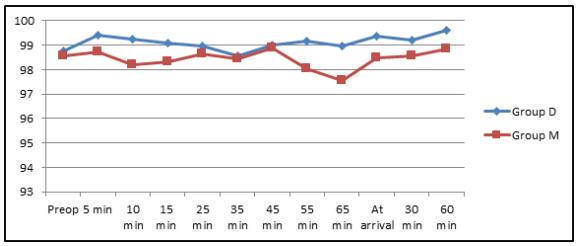
*Data expressed as Mean ± S

Figure 3: Comparison of mean diastolic blood pressure (DBP) at various time intervals in both groups



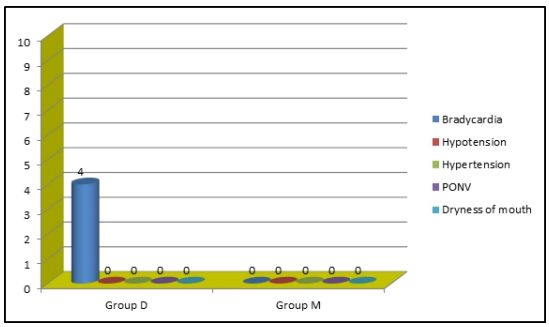
*Data expressed as Mean ±

Figure 4: Comparison of mean arterial oxygen saturation (SpO2) in both groups



*Data expressed as Mean ± SD

Figure 5: Comparison of side effects in both groups



Time (in min)*Data expressed as number

REFERENCES

1. Nallam SR, Chiruvella S, Reddy A. Monitored anaesthesia care – Comparison of nalbuphine/dexmedetomidine versus nalbuphine/propofol for middle ear surgeries: A double -blind randomised trial. Indian J Anaesth 2017;61:61-7
2. Liang S, Irwin MG. Review of anesthesia for middle ear surgery. Anesthesiol Clin 2010;28:519-28.
3. Vyas DA, Hihoriya NH, Gadhavi RA. A comparative study of dexmedetomidine vs midazolam for sedation and hemodynamic changes during tympanoplasty and modified radical mastoidectomy. Int J Basic Clin Pharmacol 2013;2:562-6.
4. Sarmento KM Jr, Tomita S. Retroauricular tympanoplasty and tympanomastoidectomy under local anesthesia and sedation. Acta Otolaryngol 2009 ;129(7):726-8.
5. A Padmaja, Varma T, Priya Darshini PP. Comparative Study of Dexmedetomidine Vs Midazolam for Monitored Anaesthesia Care during ENT Surgical Procedures, IOSR Journal of Dental and Medical Sciences (IOSR-JDMS) 2015;14(4):100-104.
6. Candiotti KA, Bergese SD, Bokesch PM, Feldman MA, Wisemandle W, Bekker AY. Monitored anesthesia care with dexmedetomidine: A prospective, randomized, double-blind, multicenter trial. Anesth Analg 2010;110:47-56.
7. Parikh DA, Kolli SN, Karnik HS, Lele SS, Tendolkar BA. A prospective randomized double-blind study comparing dexmedetomidine vs. combination of midazolam-fentanyl for tympanoplasty surgery under monitored anesthesia care. J Anaesthesiol Clin Pharmacol 2013;29:173-8.
8. Delmade MA, Parikh DA. A prospective randomized double blind study to compare dexmedetomidine and midazolam in ear nose and throat surgery for monitored anesthesia care. Int J Res Med Sci 2016;4:3159-63.
9. Alhashemi JA. Dexmedetomidine vs midazolam for monitored anaesthesia care during cataract surgery. Br J Anaesth 2006;96:722–6.
10. Gupta P, Joshi S, Jethava D, Kumar A. Dexmedetomidine ameliorates monitored anaesthesia care. Indian J Anaesth 2014;58:154-9.
11. Mohamed MH, Hakim KK. Comparative study between dexmedetomidine/nalbuphine and midazolam/nalbuphine in monitored anesthesia care during ear surgery. Egypt J Anaesth 2014;30:7-12.
12. Ramsay MA, Savege TM, Simpson BR, Goodwin R. Controlled sedation with alphaxone-alphadolone. Br Med J 1974;2:656-9.
13. Streiner DL, Norman GR. Scaling responses. In: Streiner DL, Norman GR, eds. Health Measurement Scales: A Practical Guide to Their Development and Use. Oxford: Oxford University Press,1995; 28–53.
14. Hall JE, Uhrich TD, Barney JA, Arain SR, Ebert TJ. Sedative, amnestic, and analgesic properties of small-dose dexmedetomidine infusions. Anesth Analg 2000;90:699-705.
15. Arain SR, Ebert TJ. The efficacy, side effects, and recovery characteristics of dexmedetomidine versus propofol when used for intraoperative sedation. Anesth Analg 2002;95:461-6.
16. Goksu S, Arik H, Demiryurek S, Mumbuc S, Oner U, Demiryurek AT. Effects of Dexmedetomidine infusion in patients undergoing functional endoscopic sinus surgery under local anaesthesia. Eur J Anaesthesiol 2008;25:22-8.
17. Dogan R, Erbek S, Gonencer HH, Erbek HS, Isbilen C, Arslan G. Comparison of local anaesthesia with Dexmedetomidine sedation and general anaesthesia during septoplasty. Eur J Anaesthesiol 2010;27:960-4.
18. Turan, A, Sapolyo O et al. Comparison of propofol and dexmedetomidine in monitored anaesthesia care of ear-nose-throat surgery: A-53.European Journal of Anaesthesiology. June 2004; 21, 14 Ambulatory Anaesthesia.
19. Karaaslan K, Yilmaz F, Gulcu N, Colak C, Sereflican M, Kocoglu H. Comparison of dexmedetomidine and midazolam for monitored anesthesia care combined with tramadol via patient-controlled analgesia in endoscopic nasal surgery: A prospective, randomized, double-blind, clinical study. Curr Ther Res Clin Exp 2007;68:69-81.
20. Ghali A, Mahfouz AK, Ihanamäki T, El Btarny AM. Dexmedetomidine versus propofol for sedation in patients undergoing vitreoretinal surgery under sub-Tenon's anesthesia. Saudi J Anaesth 2011;5:36-41.
21. Kamibayashi T, Maze M. Clinical uses of alpha-2 adrenergic agonists. Anesthesiology 2000;93:1345–9.
22. Guo TZ, Jiang JY, Buttermann AE, Maze M. Dexmedetomidine injection into the locus ceruleus produces antinociception. Anesthesiology 1996;84:873-81.
23. Demiraran Y, Korkut E, Tamer A, Yorulmaz I, Kocaman B, Sezen G, et al. The comparison of Dexmedetomidine and Midazolam used for sedation of patients during

upper endoscopy: A prospective, randomized study. Can J Gastroenterol 2007;21:25-9.
24. Na HS, Song IA, Park HS, Hwang JW, Do SH, Kim CS. Dexmedetomidine is effective for monitored anesthesia care in outpatients undergoing cataract surgery. Korean J Anesthesiol 2011;61:453-9.
25. Upendranath I, Amarnath RK, Bais DS, et al. Comparison of dexmedetomidine with fentanyl for sedation in tympanoplasty (ENT surgeries) done under monitored anaesthesia care. J. Evid. Based Med. Healthc. 2016; 3(16), 638-644.
26. Kewalramani A, Jaitawat SS, Gupta S, Gupta S. Comparative evaluation of iv dexmedetomidine versus dexmedetomidine with butorphanol as an adjuvant for monitored anaesthesia care in tympanoplasty and myringoplasty: A prospective controlled randomized double blind study. Indian Journal of Clinical Anaesthesia 2016; 3(1):96-101.