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Comparison of Dexmedetomidine vs. Pentazocine – Promethazine for Tympanoplasty under MAC: A Randomized Double Blind Study

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Abstract

Aim: To compare effectiveness of Dexmedetomidine with Pentazocine - Promethazine combination for intraoperative sedation under MAC for tympanoplasty under local anesthesia (LA). *Methodology*: Total 120 patients undergoing tympanoplasty under LA divided in to two groups randomly to receive either IV dexmedetomidine 1 µg/kg over 10mins followed by 0.2 µg/kg/h infusion (Group D) or Pentazocine 0.6mg/Kg and Inj. Promethazine 0.5 mg/kg IV diluted in 10ml normal saline over 10mins followed by 0.2 µg/kg/h infusion of normal saline (Group P). Sedation was titrated to RSS of 3. Vital parameters like HR, BP, SpO_2, requirement of rescue analgesics, intraoperative bleeding scale, surgeon satisfaction score (Likert Scale) and Post Anesthesia Recovery Score (Modified Aldrete Score) were recorded and analyzed. *Results*: Intraoperative HR and MAP in Group D were lower than the baseline values and corresponding values in Group P ($p<0.05$). Intraoperative sedation in Group D was more than Group P (4 vs. 2 in a scale of 6). Intraoperative bleeding scale and surgeon satisfaction score was better in Group D than Group P (median interquartile range (IQR) 9 (8-10) vs. 8 (6.5-9.5) and 9 (8.5-9.5) vs. 8 (6.75-9.25), $p = 0.0001$ for both). Mean VAS for pain was more in group D than group P. Time for rescue analgesic was high with Group P while modified Aldrete score was high in Group D. Rate of occurrence of adverse drug reaction (ADR) was not statistically significant among two groups ($p > 0.05$). *Conclusion*: Dexmedetomidine is comparable to pentazocine - promethazine combination for sedation and analgesia in tympanoplasty with better surgical field and surgeon satisfaction, with better hemodynamic stability.

Keywords: Dexmedetomidine; Pentazocine - Promethazine; Sedation; Tympanoplasty; Monitored Anesthesia Care.

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Introduction

One of the commonest conditions encountered in ENT outpatient department are Perforation of the tympanic membrane and middle ear pathologies. Middle ear surgeries can be carried out under general or local anesthesia [1-3]. Tympanoplasty, most commonly performed ear surgery, involves reconstruction of perforated tympanic membrane with or without reconstruction of ossicles [1]. It is usually done with under local anesthesia (LA) with Monitored anesthesia care (MAC). Less bleeding, cost effectiveness, early recovery and assessment of ontable hearing during tympanoplasty are advantages of using local anesthesia. Patient's anxiety caused by noise during surgery, dizziness and discomfort due to positioning of head and neck etc are most common disadvantages of local anesthesia during tympanoplasty [2-5]. These problems can easily be overcome by administering appropriate sedatives as monitored anesthesia care. Most

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important elements of MAC are sedation, analgesia and control of anxiety [6]. During surgical procedure inhibition of movement by patient can be bring by Judicious use of MAC and patient still can respond to verbal commands as required for the surgical stage of operation.

During MAC, wide variety of centrally active IV and inhaled drugs have been used including barbiturates, benzodiazepines, ketamine, propofol, opioid and nonopioid analgesics, α-agonists, and nitrous oxide [7,8]. Usually two or more drug groups are combined and these drugs are administered pre-operatively in doses which can achieve desired clinical response with minimal respiratory depression and hemodynamic fluctuations [9-12]. Benzodiazepines and opioids combination increases risk of hypoxia and apnoea [9,10]. Opioids can be used as the sole supplement to local anesthetics but they fail to produce reliable sedation in absence of respiratory depression. α_2-agonists usually reduce central sympathetic outflow and have shown to produce anxiolysis and sedation at doses which produces relatively very less adverse effects [11]. These drugs also help in attenuating the hemodynamic responses associated with anaesthesia by reducing sympathetic outflow. Nausea-vomiting caused by Pentazocine can becounteracting by a sedative drug Promethazine. So, combination of pentazocine - promethazine is preferred for MAC [13].

By considering benefits of dexmedetomidine and pentazocine - promethazine, safety of use and desired therapeutic response achievement lead to increase in their use for the day care surgeries now a day. It is a common practice to use combinations of drugs for sedation and analgesia and focus is also shifting from the physician controlled techniques to patient controlled techniques due to level of stimulation and discomfort produced during ambulatory surgical procedures varies widely among different patients. There is no standard dosage regimen or dosage formulation that can be applied to all patients undergoing MAC. The need of the current anesthetic practice is tailor made approach for each patient. Proper knowledge and skills are required for designing such regimens and to use all the drugs effectively.

Therefore, this study was planned to compare effectiveness of intraoperative sedation as MAC between Dexmedetomidine and Pentazocine - Promethazine for tympanoplasty surgery under local anesthesia.

Methodology

This randomized, prospective, controlled, double blind study was carried out in patients undergoing tympanoplasty surgery in otorhinolaryngology department of a tertiary care, teaching, rural hospital in western India.

Ethical Consideration

The study protocol was approved by ethics the institutional committee of the institute. Written informed consent was obtained from all the participants before enrolling them for the study.

Participant Selection

Total 120 patients meeting inclusion-exclusion criteria could be enrolled for the study after screening all the patients undergoing tympanoplasty. Inclusion criteria for the study were age of 18-50 years and of either gender, patients having grade ASA I & II, having Mallampati grading of airway I & II and planned for tympanoplasty under LA. Exclusion criteria were patients with any cardiac disease, chronic obstructive lung disease, renal and hepatic insufficiency, CNS disorders, pregnant and lactating female, and sensitivity to LA drug and allergy to drugs.

Study Procedure

The patients were counseled in detail about sedation, LA and operative procedure.All the patients were underwent Pre-anaesthetic checkup including detailed history, general and systemic examination and investigations. The visual analogue scale (VAS) (0-10, where 0 indicated no pain while 10 indicated maximum pain) was explained to the patients. Preoperatively patients were advised to remain nil by mouth for atleast 8 hours. Patient was shifted to operation theatre after confirming starvation and consent. All baseline vital parameters; HR, SBP, DBP, MAP and SpO_2 were recorded by multi-para monitor. Ringer lactate solution was started after Intravenous (IV) access was secured. All the patients were given oxygenat 2 L/min via nasal cannula. As pre-medications, Inj. Ranitidine 1mg/kg, inj. Ondansetron 0.08mg/kg and inj. Glycopyrolate 0.004mg/kg IV were given to all patients

All eligible patients were allocated in two groups randomly by chit method. The anesthesiologist conducting the case, patients and anesthesiologist in the post anesthesia care unit (PACU) were all blinded to group assignment.Blinded observer

recorded the data and the anesthesiologist who did not participate in patient management or data collection had prepared the drugs

Group D: This group received Dexmedetomidine 1 μg/kg in 10ml normal saline (NS) over 10 minutes followed by it's infusion at a rate of 0.2 μg/kg /hr through infusion pump.

Group P: This group received a standard dose of Pentazocine 0.6mg/kg and Inj.Promethazine 0.5 mg/kg IV in 10ml NS over 10 minutes followed by infusion of 0.2 μg/kg/hr of NS through infusion pump.

LA was administered by surgeon using 2% Lignocaine with Adrenaline (1:2,00,000) to block greater auricular, lesser occipital, auriculotemporal nerves and four quadrants of the external auditory canal, After RSS of 3 was achieved. 2% Lignocaine and Adrenaline (1:1,00,000) were used for the Infiltration of operative field. Surgery was commenced after confirmation of adequate analgesia. Patient's response to LA infiltration was evaluated for pain and body movement. Pain was recorded on 10 point VAS.

Vital parameters were recorded intraoperatively every 2 minutes during loading dose of study drugs and at 10 minutes intervals till the end of surgery. At, every 10 minutes sedation level was assessed by RSS, if RSS <3 IV midazolam 0.01mg/kg was administered in either group. VAS was used for Intraoperative pain evaluation. LA infiltration at surgical site (2-3 ml) and rescue IV fentanyl 1μg/kg was used for inadequate analgesia.Approximately 15 min before end of surgery, maintenance infusion was discontinued at the time of closure. All adverse events like bradycardia (HR<45 beats/min), hypotension (MAP<50 mmHg sustained for >10 min), respiratory depression (respiratory rate <10bpm), oxygen desaturation, (SpO_2< 90%), nausea or vomiting were recorded. Bradycardia was managed with IV Atropine and IV fluids or IV Mephenteramine used for management of Hypotension.Surgical field was graded in terms of bleeding by the blinded surgeon using the scale developed by Boezaart at the end of surgery [11,12]. Likert scale was used for assessment of surgeon's satisfaction.

Patients were shifted to post anesthesia care unit and monitored for hemodynamic parameters, analgesia and adverse events if any within 2 hours after completion of surgery. Every 30 min RSS was assessed and first rescue analgesic was given at VAS >4 and was documented. patients were observed for 24 hours post operatively. All data were recorded in a structured case record form.

Statistical Analysis

All the data were recorded as appropriate as actual frequency, percentage, mean, standard deviation. Data entry was done in Microsoft excel andepi info software was used for analyzing data. The Chi Square Test was used for analyzing all the qualitative data and students' paired and unpaired t test as appropriatefor quantitative data. p value<0.05 was considered statistically significant.

Results

There were total 60 patients in each group.In group D, all 60 patients had received Dexmedetomidine and all 60 patients in group P had received a standard dose of Pentazocine in combination with Promethazine. Basic profile of study participants was shown in Table 1. Both the groups had no statistically significant difference in respect to mean age and mean weight. There were total 22 participants of ASA I and 38 participants of ASA II in group D where as in group P, there were total 40 participants of ASA I and 20 participants of ASA II.

Figure 1 shows comparison of trend of mean heart rate of both the groups at different time starting from a baseline to at the end of procedure and till post operative phase.In Group P, a steady decline of heart rate was observed.

Figure 2 shows comparison of mean of systolic and diastolic blood pressure in both groups at different time. sy Blood pressure was well maintained in both the groups. It was observed that, In Group D both stolic and diastolic blood pressure was maintained at lower side in in comparison with Group P. It was seen from the figure 3 that Mean Arterial Pressure (MAP) was slightly lower in Group D than Group P.

Table 2 shows comparison of means of difference of heart rate at different time. The mean and standard deviation of Difference between heart rate at baseline and at 30 mins for all participants was taken and was noted in both groups. It was shown that difference heart rate between observations at baseline and at 30 mins was statistically significant (p-Value < 0.05). Similarly, there is also statistically significant mean of difference between heart rate at Baseline and at the end of surgery was noted in both groups.

Ramsay sedation score was used to measure Intraoperative sedation. There was statistically significant difference between the two studied groups revealed, where the P group (2 in a scale of 6) showed less sedation than the D group (4 in a scale

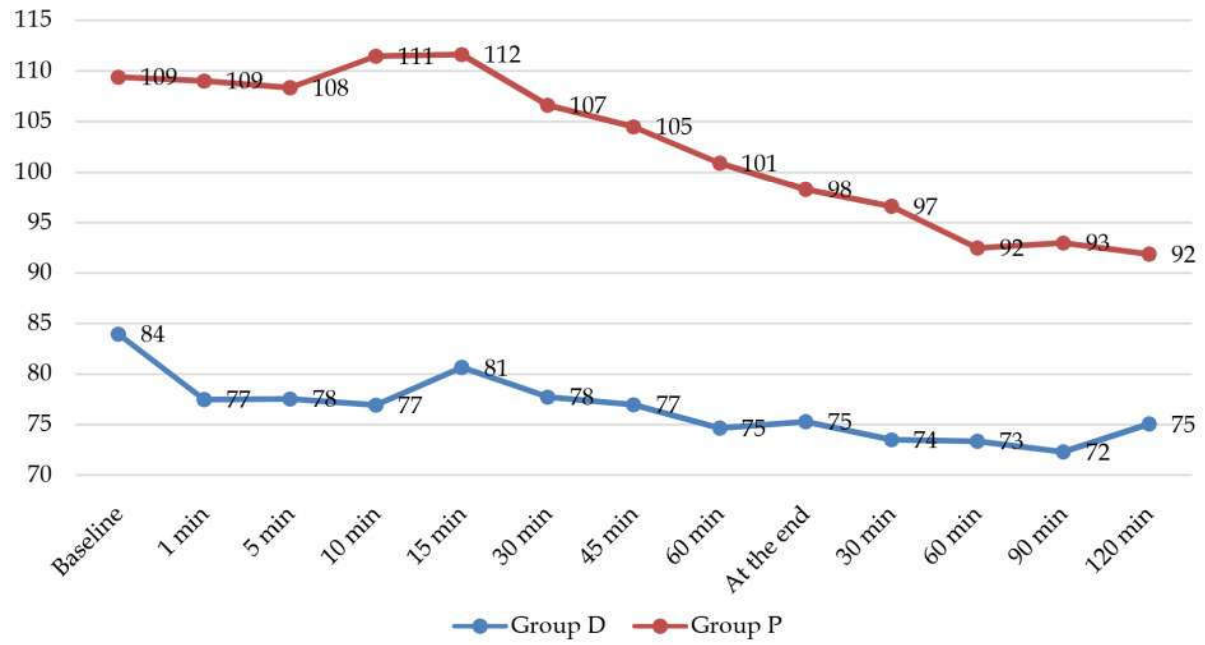

Fig. 1: Trend of Mean HR in both group

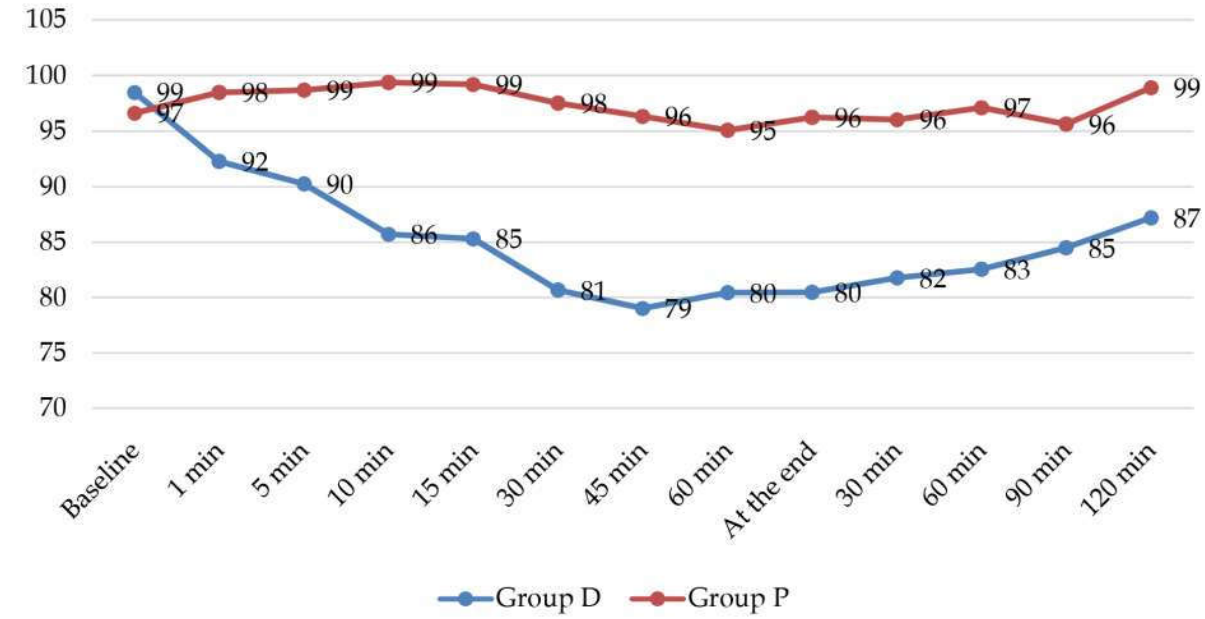

Fig. 2: Trend of SBP and DBP in both group

Table 1: Demographic profile of patients

Parameter	Group D (n=60)	Group P (n=60)	p-Value*
Age (Years)	33.3± 11.8	33.03± 13.52	0.93
Weight (kg)	52± 12.93	49.74± 11.20	0.47
Sex (M:F)	13:17	16:14	-
ASA(I/II)	38:22	40:20	-

Expressed as mean and SD and proportion; Chi square test- p value <0.05 was considered significant
Group D: dexmedetomidine group
Group P: pentazocine – promethazine group

of 6) as shown in Table 3. As shown in Table 4, Mean VAS for pain, time to rescue analgesic was high with P group as compared to D group while time to achieve Aldrete score of 10 was high in D group.

Different adverse events encountered in the study participants were shown in Table 5 . In group P, 5 patients reported nausea and vomiting while 8 patients developed tachycardia and 3 patients developed respiratory depression. In group D, 8 and 4 patients respectively reported bradycardia and hypotension. There is not any statistically significant difference in rate of occurrence of ADR among the two groups (p>0.05).

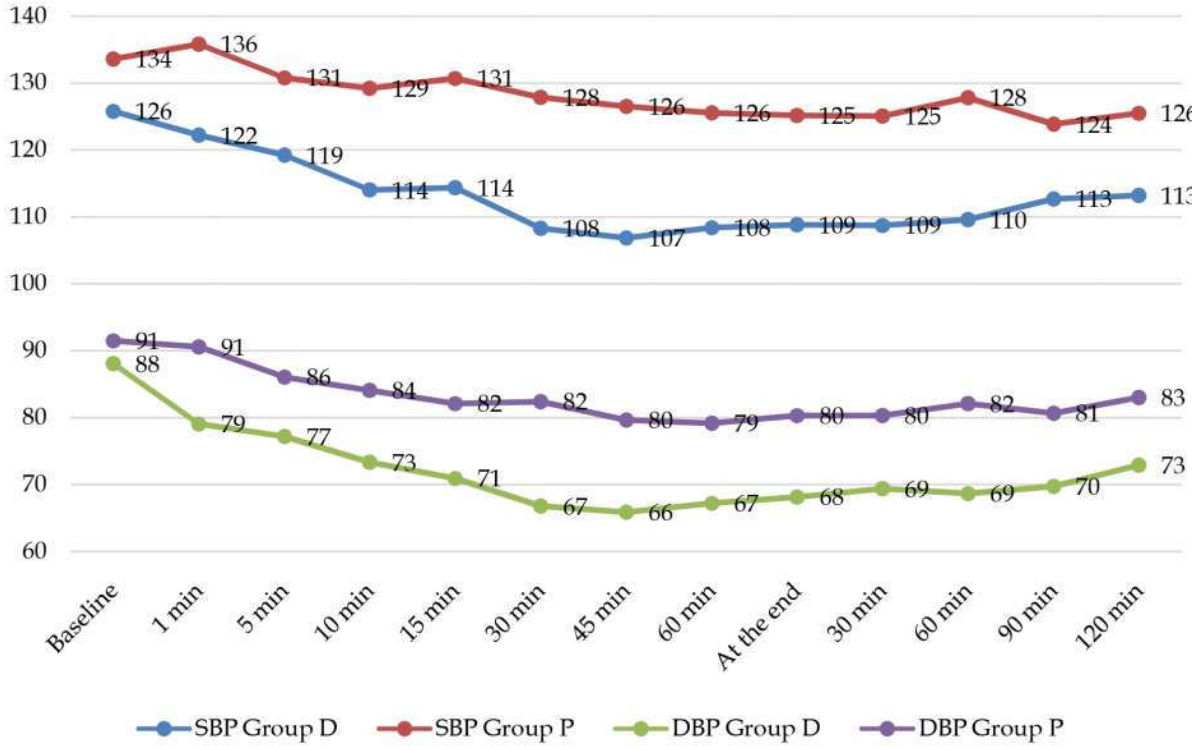

Fig. 3: Trend of MAP in both group

Table 2: Comparison of means of difference of heart rate at different time

Heart Rate	Group D	Group P	p-Value
Mean of difference between observations at Baseline and at 30 mins	11.0±9.6	20.0±19.0	0.02
Mean of difference between observations at Baseline and at the end of surgery	10.8±9.6	22.0±17.0	0.002

Expressed as mean and SD and proportion; Unpaired t test; p value <0.05 was considered significant
Group D: dexmedetomidine group
Group P: pentazocine – promethazine group

Table 3: Comparison of Surgeon satisfaction score, Intra operative bleeding score and Sedation score of patients in both groups

Study variables	Group D n=60 (Median)	Group P n=60(Median)	P value
Surgeon satisfaction score	6 – 7 (5.4)	3 - 4 (3.5)	0.01
Intra operative bleeding	1-2(1)	2-3 (2.5)	0.01
Sedation score	3-4(4)	1-2(2)	0.02

Expressed as Median (IQR) and P value
Group D: dexmedetomidine group
Group P: pentazocine – promethazine group

Table 4: Comparison of Pain score (VAS), F1irst rescue analgesic time and Modified Alderete score of patients in both groups

Study variables	Group D n=60 (Median)	Group P n=60(Median)
VAS pain score	3-5 (4.1)	6-7(6.3)
Time to first rescue analgesic (min)	70-92(81)	91-124 (100)
Time to achieve Aldrete score of 10 (min)	32-50(42)	62-98(78)

Group D: dexmedetomidine group
Group P: pentazocine – promethazine group

Table 5: Reported adverse events in study patients of both groups

Event	Group D	Group P
Nausea – vomiting	0	5
Tachycardia	0	8
Hypotension	4	0
Bradycardia	8	0
Respiratory depression	0	3
Dry mouth	2	0
Total	14	16

Group D: dexmedetomidine group
Group P: pentazocine – promethazine group

Discussion

Monitored anaesthesia careis being increasingly used for performing different ENT surgeries. Basic principle is to supplement sedation along with local anesthesia so that less bleeding during surgery occurs, hearing can be tested intra-operatively and any immediate complications can be detected early and managed accordingly [6-8]. If patient is screened and selected properly and counseled appropriately MAC can achieve good patient's as well as surgeon's satisfaction. Different drugs are used for MAC but no standard regimen can be designed which can be fitted to all patients. Primary aim of this study was to compare the effectiveness of dexmedetomidine with pentazocine-promethazine combination for MAC with local anesthesia.

Dexmedetomidine is an imidazole compound and highly selective α2 adrenoreceptor agonist. Dexmedetomidine has been studied by many researchers and proven to have many advantages [14,15] Dexmedetomidine can reduce sympathetic over activity and related symptoms during anesthesia if administered in proper dosage. The drug is approved by United States Food and Drug Administartion (USFDA) and Drug Controller General of India (DCGI) for analgesia and sedation during different surgeries and in ICU [16-18]. Mechanism of action of dexmedetomidine is by activation of presynaptically located α2 receptor inhibits release of sympathetic neurotransmitter release leading to termination of pain signal propogation and Postsynaptic α2 receptor activation in CNS inhibits sympathetic activity in vasomotor centre leads to dose dependent decrease in BP and HR. [16-21]. Considering these advantages, dexmedetomidine is being used increasingly in anesthetic practice as MAC also. On other hand, pentazocine is synthetic, mixed agonist-antagonist type of opioid analgesic. Promethazine, a neuroleptic drug has strong sedative, antiemetic and anticholinergic property. Traditionally, this combination is used commonly for patients undergoing short surgeries under sedation or surgeries under MAC [13].

In this study, loading dose of Dexmedetomidine 1μg/kg was selected based on previous studies and because of its short distribution half-life of 5-6 minutes,it was given as infusion [22-24,30].On analyzing cardiovascular parameters in both study groups, there is statistically significant difference ($p<0.05$) between two group, HR and MAP maintained at lower side in group D than group P.Findings can be explained easily by property of dexmedetomidine to reduce sympathetic activity in body. The same findings have been reported in studies of Arain SR et al. [24] and Alhashemi JA [25]. This result also suggest dexmedetomidine helps in producing controlled hypotension which can be contributing factor for producing significantly more bloodless field at the operative site and less intraoperative bleeding in group D as compared to Group P ($p<0.05$). These findings are also conquering

with results of the similar study by Durums et al. [26]. Stable hemodynamics, controlled hypotension and decreased bleeding could be responsible for better surgeons' satisfaction score in group D in our study.

On analyzing safety of drugs used, predictable ADRs were reported in both groups,there was no statistically difference in rate of occurrence of ADR among the groups. In our study,promethazine was associated with some respiratory depression while dexmedetomidine caused no respiratory depression although both study drugs provide adequate levels of sedation. Dexmedetomidine does not cause respiratory depression as its effects are not mediated by GABA system. These findings are similar to other studies by Karaaslan K et al. [27], Parikh DA et al. [28], Cheung CW et al. [29] and Har A et al. [30].

Intra operative VAS pain score was lower in group D than group P. Due to very less half-life of dexmedetomidine; requirement of rescue analgesic was early after stoppage of infusion in group D. These findings are similar to studies of Hall JE, Arain SR, Ebert TJ et al. [24] and Karaaslan K et al. [27]. Due to involvement of natural sleep pathway of dexmedetomidine sedation and reduced sympathetic activity,the aldrete score was high in group D [28,29,30].

Although this study has compared the dexmedetomidine and pentazocine-promethazine in MAC, with local anesthesia, the study was single centered. Therefore, variations in genetic, racial and other factors could not be analyzed. Larger studies evaluating these aspects are required in future for enhancing quality of MAC for betterment of patients.

Conclusion

Our study demonstrates that dexmedetomidine has better sedation, analgesia, stable hemodynamics, lesser bleeding and better surgeon satisfaction for MAC compare to pentazocine-promethazine combination in tympanoplasty surgery under local anesthesia.

Ethical Considerations

The study protocol was approved by the Institutional Ethics Committee of the GMERS Medical College, Gandhinagar approval letter no: GMERSMCG/IEC/4/2017; dated 9th February 2017. All participants were explained clearly about nature and purpose of study and written informed consent was obtained.

Consent for Publication

All the participants were ensured about non-disclosure of their identity at any stage of study including publication of data and consent for publication was also obtained.

Availability of Data and Material

Details of all the data mentioned in the study can be obtained from corresponding author in case of any query of further clarification.

Competing interests / Conflict of interest: None

Funding source: None

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