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RESEARCH ARTICLE

RANDOMIZED DOUBLE BLIND STUDY COMPARING DEXMEDETOMIDINE WITH FORTWIN & PHENERGAN COMBINATION FOR TYMPANOPLASTY UNDER MONITORED ANESTHESIA CARE (MAC)

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A B S T R A C T

In middle ear surgery under Local anesthesia with monitored Anesthesia Care, Dexmedetomidine, a newer drug seems to be a better choice than the age old traditional regime. Local anaesthesia with sedation is a well established approach used for Tympanoplasty1. The comfort of patient as well as surgeon play important role throughout the surgery which aids to Anaesthesiologists' satisfaction 2. In this study, satisfaction score and effectiveness of sedation with Dexmedetomidine were compared with a combination of Intra venous (IV) Fortwin- Phenargan.

INTRODUCTION

Tympanoplasty is the procedure of reconstructing the perforated tympanic membrane with or without Ossiculoplasty.[1] It is usually done under local Anesthesia with sedation under monitored anaesthesia care (MAC). The comforts of patient as well as surgeon are two important factors throughout the surgery which aids to Anaesthesiologists' "Sedation score" and "Satisfaction score" [2]. Commonly used medications for MAC are Benzodiazepines, Pentazocine, Promethazine etc. Midazolam which is a very commonly used Benzodiazepine has quick onset, but its relatively long half‑life can cause prolonged sedation after repeated administration. Combining Midazolam with Pentazocine (Fortwin) increases the risk for drowsiness and respiratory depression. The addition of Promethazine (Phenargan) has been reported to cause oversedation with respiratory depression[3].

Dexmedetomidine, a comparatively newer drug which centrally acts as α2 receptor agonist with analgesic and conscious sedative effect without major respiratory depression, has been reported significantly effective both during and after Surgery [4]. In addition, it has a sympatholytic effect that can attenuate the stress response to surgery (tachycardia and hypertension) and maintains desired controlled hypotension[5].

In our study, satisfaction score and sedation scores are used to compare the effectiveness of Dexmedetomidine (D) and a combination of Intra venous (IV) Fortwin- Phenargan (FP). We considered primary end point as patient satisfaction score and intra operative need of rescue analgesia to maintain a calm and quiet state of the patient was the secondary end point. We have used these two drugs for the comparison because this traditional combination is widely used for MAC.

MATERIALS AND METHODS

After obtaining approval from Institutional Ethical Committee and valid, written informed patients' consent, 80 American Society of Anesthesiologists (ASA) I & II patients, aged 18-60 years, of both sex, who were planned for Tympanoplasty under local Anesthesia, were enrolled in this randomised double‑blind study. Those having any cardiac disease, 2nd or 3rd degree heart block, chronic obstructive lung disease, renal and hepatic insufficiency, endocrine, metabolic or central nervous system disorders, pregnant and lactating female, sensitivity to local Anesthetic drug (Lignocaine), allergy to study drugs, α2 agonist or antagonist therapy taken earlier , and active upper respiratory tract infection, were excluded from the study. The patients were counselled about sedation, comfort, local Anaesthesia as well as the operative procedure. All the patients were examined a day before surgery and were thoroughly investigated according to the institutional protocol.

The patients were randomly divided into two equal groups, Group D (Dexmedetomidine) and Group FP (Fortwin-Phenergan) on basis of a computer‑generated randomization scheme. The Anesthesiologist who had administered Anesthesia to the patient attended the the case till shifting to the ward from post Anesthesia care unit (PACU) and the patients were blinded to group assignment."Data was recorded by a blinded observer in the peri operative period and the drugs were prepared by an Assistant who was neither

involved in patient management nor in data collection. After confirming adequate period of starvation and checking the consent patient was shifted to OT.

Routine monitoring which includes ECG, SpO_2 and noninvasive blood pressure was done by a multimodal device. Intra operatively, all the patients received Oxygen via Hudson's mask/nasal catheters @ 3 L/minutes. Group D: Dexmedetomidine group: received a loading dose of 1 µg/kg (infused over 10 min).Dexmedetomidine infusion was continued throughout the operation @ 0.3- 0.5 µg/kg/hour. Group FP: Received a standard dose of Pentazocine @0.5mg/Kg (maximum dose not exceeding 360mg) and Inj.Promethazine 25 mg IV or IM once at the onset of surgery followed by close observation for response. An additional dose, maximum up to 50 mg, was administered during the surgery to achieve the desired satisfaction point.

Once patient achieves Ramsay sedation score (RSS)of 3, the blinded ENT surgeon administered LA using 2% Lignocaine with Adrenaline(1:2,00,000), (6-7 ml/Kg) in the postauricular area to block greater auricular and lesser occipital nerves, in the incisura terminalis to block auriculotemporal nerve and the four quadrants of the external auditory canal. Surgery was commenced after confirmation of adequate analgesia. Operative field was infiltrated with 2% Lignocaine and 1/100,000 epinephrine and surgery was started. Patient's response to Local Anesthetic infiltration was evaluated for pain and body movement. Pain was recorded on 10 point visual analogue (VAS) scale where, 0 indicated no discomfort and 10 indicated maximum discomfort.

A rescue bolus @1 µg/kg was given to all those patients responding with the pain score >4 or showing movement during infiltration. Heart rate (HR), mean arterial pressure (MAP), respiratory rate (RR), and peripheral oxygen saturation (SpO2) were recorded every 10 min till the end of surgery. Intraoperative bleeding was assessed by bleeding scale (0–4), acceptable bleeding score being 0–2, if bleeding score >2 bolus Dexmedetomidine @ 1 µg/kg was given in D group. All adverse events like bradycardia (HR < 55 beats/min), hypotension (MAP < 50 mmHg sustained for >10 min), respiratory depression (respiratory rate< 10 bpm), oxygen desaturation, (SpO2 < 90%), nausea or vomiting were recorded.

After the completion of surgery patients were shifted to the PACU and were monitored for hemodynamic parameters, degree of analgesia and adverse events, if any for 2 hours. RSS was assessed immediately on arrival in the PACU and every 30 min thereafter till transfer to surgical ward. Requirement of postoperative analgesia was noted. The first rescue dose of analgesic was given at VAS >4 and was documented.

Various Scores Used in the Study

Ramsay sedation scale Score Response

1	Anxious, agitated or restless
2	Cooperative, oriented and tranquil.
3	Asleep, 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 without response

Intraoperative bleeding scale

0	No bleeding
1	Slight bleeding; no suctioning of blood required
2	Slight bleeding; occasional suctioning required. Surgical field not threatened
3	Slight bleeding; frequent suctioning required. Bleeding threatened surgical field a few seconds after suction was Removed.
4	4-Moderate bleeding; frequent suctioning required. Bleeding threatened surgical field directly after suction Was removed.

Likert scale

1	Extremely dissatisfied
2	Dissatisfied
3	Somewhat dissatisfied
4	Undecided
5	Somewhat satisfied
6	Satisfied
7	Extremely satisfied

Visual Analogue Scale VAS (0–10cm)

0	No pain
2	
4	
6	
8	
10	Worst pain

Postanesthesia recovery score (Modified Aldrete Score)

Parameters	2	1	0
Activity	moves all activities on command	Moves two activities on command	Unable to move extremities
Respiration	Breaths deeply and coughs spontaneously	Dyspnoea or shallow breathing	Apnoeic
Circulation	BP within 20 mm of Pre operative value	BP ≥20 – 50 mm of pre operative value	BP ≥50 mm of pre operative value
Level of consciousness	Fully awake	Arousable on calling	Not arousable
Oxygen saturation SpO_2	≥94% on room air	Supplemental O_2 needed to maintain ≥90%	≤90% with supplemental O_2

RESULTS

All data were analysed using Statistical Package of Social sciences version 15.0.The demographic data of the two study groups are summarized in Table 1. Statistical analysis revealed non-significant differences between the two study groups as regards age, gender distribution, body weight and duration of surgery.

Table 1 Patients' demographic profile and operative data, expressed as Mean (SD) or number (proportion)

Study variables	Dexmedetomidine n=40	Fortwin-Phenargan n=40
Age (years)	45 ±7.5	44.9 ± 8.1
Sex M:F	45:55	47:53
Weight (Kg)	59.9 ± 10.8	58.4 ± 7.2
ASA I/II	38/12	36/14
Duration of surgery	90 ± 12	55 ± 14

* Values are expressed as means +- s.d
ASA= American Society of Anesthesiologists

Intraoperative sedation was measured by using Ramsay sedation score. It revealed that there was statistically significant difference between the two studied groups, where the D group (4 in a scale of 6) showed more sedation than the FP group (2 in a scale of 6) Table 2.

Table 2 Patient satisfaction and Surgeon satisfaction (Intra operative bleeding) score and Sedation score. Expressed as Median (IQR) and P value

Study variables	Dexmedetomidine n=40 (Median)	Fortwin-Phenargan n=40(Median)	P value
Patients' satisfaction score	6 – 7(5.5)	3 -4(3.6)	0.0173
Intra operative bleeding	1-2(1)	2-3(2.4)	0.0162
Sedation score	3-4(4)	1-2(2)	0.024

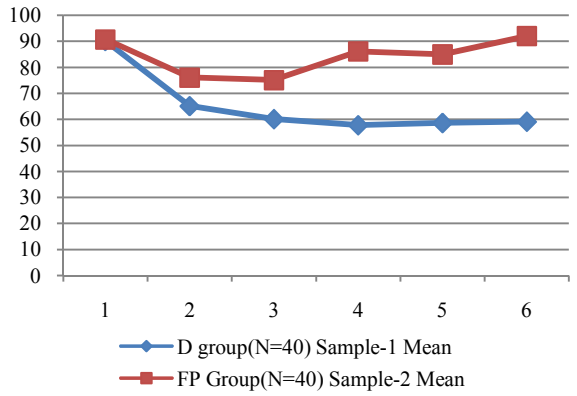

Figure 1 Chart comparing Heart rate (hourly) in D and FP groups

Mean arterial pressure and HR and Respiratory rate values during sedation and recovery were significantly lower than those at baseline in both groups [Figures 2 and 3], but intra operative MAP ($P < 0.001$) and Heart rate was significantly lower in *D* group as compared to FP group Table 3.

Table 3 Pain score and measured particular time until need for post operative analgesics

Study variables	Dexmedetomidine n=40(Median)	Fortwin-Phenargan n=40(Median)
VAS pain score	3-5(3.5)	6-7(6.8)
Time to first rescue analgesic (min)	75-90(82)	90-120(100)
Time to achieve Aldrete score of 10 (min)	30-45(32)	60-90(88)

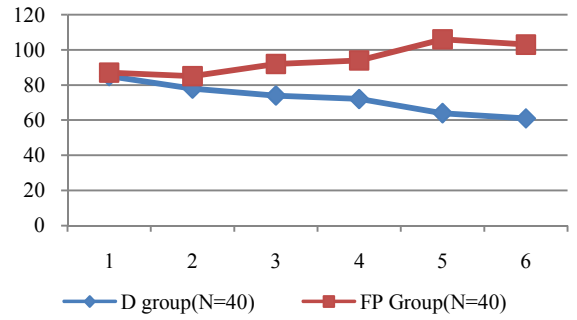

Figure 2 Chart comparing Mean Arterial pressure(MAP) in D and FP groups

A total of 6 (15%) patient in FP group showed tachycardia (HR>100) and 2 (5%) in D group developed hypotension (MAP < 60 mm Hg), which was managed by either giving fluid or injection Phenylephrine. Four patients (10%) in D group had bradycardia and these patients were successfully treated with 0.6 mg IVAtropine. Respiratory rate (>14/min) and SPO2 (>96%) were maintained in both the groups with no incidence of respiratory depression in either of the two groups.

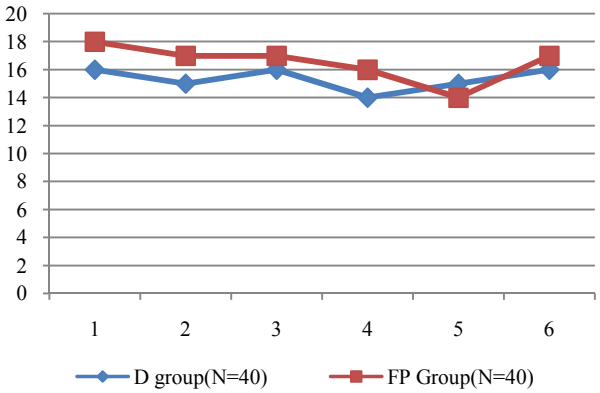

Figure 3 Chart comparing rate of respiration (hourly) in D and FP groups

A total of 4(10%) patients in D group and 8 (20%) patients in group FP complained of dry mouth in the postoperative period, but 12 (30%) patients had nausea and vomiting too. Statistically, a significant difference between two groups was observed in maintaining hypotension and leading to less bleeding in D group, better patient satisfaction in group D better sedation and less pain in group D (Table 3). Requirement for rescue analgesia was also less in group D than group FP (Table 4).

Table 4 Adverse reactions

Study variables	Dexmedetomidine n=40	Fortwin-Phenargan n=40
Nausea & Vomiting	0	12
Dry mouth	4	8
Tachycardia	0	6
Bradycardia	4	0
Hypotension	2	0

However, no major adverse events were observed in this study and no patients had to be converted to an alternative sedative or anesthetic therapy in either of the groups.

DISCUSSION

There are various advantages of doing operation under local anaesthesia with MAC[6-9], especially in day care surgeries. Middle ear surgeries pose a different set of challenges for the patient, surgeons and anaesthesiologists. Sympathetic stimulation and movements of an anxious patient cause increased bleeding and disturb the fine microscopic nature of the surgery which may even lead to graft failure. In other hand, a tranquil, peaceful patient with a bloodless field hastens the procedure with great surgeons' satisfaction. Dexmedetomidine, an imidazole compound, is the pharmacologically active dextroisomer of medetomidine that displays specific and selective ∞2-adrenoceptor agonism. Dexmedetomidine was approved by the Food and Drug Administration at the end of 1999 for use in humans as a short-term medication (<24 hours) for analgesia and sedation in the intensive care unit (ICU). The presynaptic activation of the ∞2 adrenoceptor inhibits the release of Norepinephrine, terminating the propagation of pain signals. Postsynaptic activation of ∞2 adrenoceptors in the central nervous system (CNS) inhibits sympathetic activity and thus can decrease blood pressure and heart rate. Combined, these effects can produce analgesia, sedation, and anxiolysis. Fortwin (Pentazocine) is a synthetically-prepared prototypical mixed agonist–antagonist narcotic (opioid) analgesic of two

enantiomers, named (+)-pentazocine and ( )-pentazocine. ( ). Levo Pentazocine is a κ-opioid receptor agonist, while (+) Pentazocine is not, instead displaying a ten-fold greater affinity for the σ receptor High dose may cause high blood pressure or high heart rate. Phenargan (Promethazine) is a neuroleptic medication and first generation antihistamine of the phenothiazine family. The drug has strong sedative and weak antipsychotic effects. It also has antiemetic and anticholinergic properties (via its action on the Dopamine receptor D2). We chose a loading dose of 1 mcg kg‑1 of Dexmedetomidine based on previous literature [8-11] and studies[12-15.] In view of its short distribution half-life of 5-6 minutes Dexmedetomidine necessitates that it be given as a maintenance infusion.

In our study, we have observed that both Dexmedetomidine and Promethazine provide adequate levels of sedation but clinically Dexmedetomidine caused no respiratory depression in the perioperative period, but use of Promethazine was associated with deeper level of sedation and some respiratory depression. Dexmedetomidine showed better hemodynamic effects in the form of controlled hypotension with excellent surgical field, no tachycardia even after local infiltration; where as Pentazocine administration was associated with exaggerated increase in Heart rate after administration of Local Anesthetics with Adrenaline. We compared Dexmedetomidine with Fortwin –Phenargan because this combination has been used commonly over years for Patients undergoing surgery under MAC.

Though requirement of rescue analgesics was early after stoppage of Dexmedetomidine infusion in Dexmedetomidine group but there was less requirement of rescue analgesic intra operatively as VAS pain score was lower than the other group, which is consistent with the findings of Arain and Ebert. This is because the half life of Dexmedetomidine is very less. In D group post operatively the Aldrete score was higher shortly after shifting to PACU and less time was taken to achieve 10 score in D group, in compared to FP groupfor the same reason may be.

As per as the adverse effects are concerned less significantly less number of patients developed nausea, dry mouth and tachycardia. Four patients in D group developed bradycardia, which were successfully managed with injection Atropine. An increase in vagal activity may be involved in the hemodynamic effects of Dexmedetomidine. But both surgeon comfort and patient satisfaction regarding sedation was more in D group which is due to sympathetic blockade and effects on locus coeruleus. Through presynaptic activation of the alpha 2 adrenoceptors, it inhibits the release of norepinephrine and subsequently decreases sympathetic tone. It also attenuates the neuroendocrine and hemodynamic responses to anesthesia and surgery, leading to good sedation and analgesia. These findings lead to the conclusion that the major sedative and antinociceptive effects of dexmedetomidine are attributable to its stimulation of the alpha 2 adrenoceptors in the locus coeruleus.

Limitations of our study were as follows: number of patients was not very large and few patients could not be convinced to give consent for the study, secondly, some surgeons refused to give patients local anesthesia , so they were excluded from the study,so collecting 80 patients for this study was difficult.

In this study we used two types of agents for performing MAC for Tympanoplasty and myringoplasty: Dexmedetomidine and classical cocktail of Pentazocine and Promethazine. We found that Dexmedetomidine alone is superior to Fortwin/Phenargan combination as regards level of sedation, satisfaction and operative conditions.

CONCLUSION

Dexmedetomidine is an excellent choice in Tympanoplasty under sedation with MAC in compared to Fortwin-Phenargan combination for better operative condition, patients' and surgeons' satisfaction.

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