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Original Research Article

Comparison of Propofol with Dexmedetomidine and Propofol with Fentanyl Combination for Middle Ear Surgery under Monitored Anesthesia Care (MAC): A Prospective and Randomized Study

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Conflict of interest: Nil

Abstract:

Introduction: Middle ear surgery, a delicate and intricate procedure, demands meticulous anesthesia management to ensure optimal patient outcomes. This study aims to compare the efficacy and safety of two anesthesia regimens: Propofol with Dexmedetomidine and Propofol with Fentanyl for middle ear surgery performed under monitored anesthesia care (MAC).

Aim: The primary objective is to assess the sedation and analgesia in patients undergoing middle ear surgery with two different combinations. Secondarily, we aim to compare the efficacy of these combinations of drugs to provide a near bloodless microscopic surgical field, hemodynamic and respiratory effects, surgeon and patient satisfaction, and adverse effects

Materials and Methods: This prospective, randomized controlled trial includes 100 patients scheduled for middle ear surgery under MAC. Participants will be randomly assigned to the (Propofol-Dexmedetomidine) **Group DP** or the (Propofol- Fentanyl) **Group FP**. Sedation, Analgesia Intraoperative and postoperative parameters like hemodynamic and respiratory stability, postsurgical recovery time, surgeons' and patients' satisfaction about quality of anaesthesia, will be closely monitored and evaluated.

Results: Group DP had lower intra-operative hemodynamic changes when compared to Group FP, which was statistically significant. Group DP had better quality of the surgical field; surgeons' and patients' satisfaction when compared with Group FP. Group DP had reduced need for rescue analgesia. Group DP had significantly and consistently quicker post-operative recovery time. Group DP had lower post-operative pain when compared to Group FP.

Conclusion: Propofol-Dexmedetomidine combination is good alternative to Propofol-Fentanyl combination for MAC in middle ear surgery since it produces quicker post-operative recovery time and reducing post-operative pain with better quality of the surgical field and reduced need for rescue analgesia. Propofol-Dexmedetomidine was well tolerated with no clinically significant effects on blood pressure or heart rate.

Keywords: Dexmedetomidine, Propofol, Fentanyl, Sedation, Middle ear surgery, monitored anesthesia care.

Introduction

Monitored anesthesia care (MAC) has been described as a specific anesthesia service for diagnostic or therapeutic procedures performed under local anesthesia along with sedation and analgesia, titrated to a level that preserves spontaneous breathing and airway reflexes, according to American Society of Anesthesiologists (ASA). Analgesia, anxiety management for the patient, and safe sedation are among the key components and goals of MAC. [1,2] Both local and general anaesthesia can be used during middle ear surgery (MESs). [9] Local anesthesia offers several advantages, including reduced bleeding, faster recovery, postoperative pain relief, cost-effectiveness, and most importantly, the ability to assess the patient's hearing during the operation.

Middle ear surgeries commonly performed under monitored anesthesia care (MAC) include tympanoplasty, myringoplasty, stapedectomy, and ossiculoplasty. [3]

During surgery under local anaesthesia with MAC, opioids, benzodiazepines, propofol, nalbuphine, and α2 agonists are often used drugs for sedation. [4,9] Combining two medicines can improve patient control and prevent side effects by allowing fewer dosages of each individual medication to be used.

Fentanyl is a potent lipophilic synthetic opioid. Fentanyl is a μ receptor agonist with a short onset time and moderate duration of action. Side effects from fentanyl include respiratory depression and pruritus. [2,8]

An α2 agonist that acts centrally, dexmedetomidine has a conscious sedative and analgesic action without causing respiratory depression. In addition to its sympatholytic properties, dexmedetomidine helps reduce the stress response that follows surgery, preserving hemodynamic stability. [6,7,9]

The medication most frequently used for sedation during MAC is propofol. Because of its antiemetic and euphoric qualities, propofol is an ultra-short acting sedative hypnotic drug with a fast start of action, significant potency, very short recovery time, and great patient satisfaction. [8,9]

Under this study, we examine the effects of propofol-fentanyl and propofol-dexmedetomidine combination on sedation and analgesia under monitored anesthesia treatment.

Material and Methods

This prospective, double-blind, randomized, comparative study was carried out after obtaining institutional ethical approval. (Approval number: PUIECHR/PIMSR/00 /081734/3102. We included 100 patients of either sex, ASA Grades I and II, between the ages of 20 and 60, undergoing supervised anesthesia treatment for MESs (tympanoplasty, myringoplasty, and stapedectomies). All enrolled patients provided written informed consent.

In this study, we evaluated the sedative and analgesic effects of a propofol-dexmedetomidine combination compared to a propofol-fentanyl combination in monitored anesthesia care.

The degree of sedation and analgesia attained was the primary conclusion. Secondary conclusions included the ability of these drug combinations to create a nearly bloodless microscopic surgical area. Effects of drugs on respiration, hemodynamics, patients' and surgeons' contentment, side effects (any) were also studied and analysed.

Following patients were excluded from the study: (a) patients with known sensitivity to local anaesthetics, allergies to the study drugs, (b) patients with second or third-degree heart block, renal or hepatic insufficiency, uncontrolled diabetes or hypertension, obesity (BMI >30 kg/m²), (c) pregnant or lactating female.(d) patients not giving consent. Preoperative examinations (PAC) and routine investigations were performed on all patients.

Patients were detailed about the methodology and instructed to keep NPO status for 6 hours prior to surgery.

A Computer and website (www.calculator.net) were used to generate a random number table for all patients, who were then divided into two equal groups of 50 subjects each. Sealed paper covers were prepared for the allotment of patients (Fig-1).

Just prior to premedication, an anesthesiologist who was not involved in the study opened the envelope and prepared the necessary medication, all the while maintaining blinding by not participating in management or observations. The anesthesiologist who recorded the data and administered the study medicines was also blind to the groups to which they were assigned. On the operating table, patients were positioned supine with their heads turned away from the ear that needed surgery. Monitors were attached to all patients with Peripheral oxygen saturation (Spo2), Electrocardiogram (ECG), heart rate (HR) and non-invasive blood pressure (NIBP) attachments. Intravenous (IV) access 22-gauge was taken and injection glycopyrrolate was given as premedication. All patients received 2 l/min O2 oxygen through nasal prongs. [9] Following are the 2 study groups: (a) **Group DP** – received intravenous bolus injection Propofol 0.75mg/kg IV, injection Dexmedetomidine 1 μg/kg IV (over 8-10 min) followed by an infusion started at 0.4 μg/kg/h IV. (b) **Group FP-** received intravenous bolus injection Propofol 0.75mg/kg IV, injection Fentanyl 1 mcg/kg followed by an infusion started at 1 mcg/kg/hr IV.

The Ramsay Sedation Score (RSS) was used to gauge the degree of sedation. [9,10] Adequate level of sedation was defined as RSS ≥3. (1 = anxious, restless; 2 = cooperative, oriented; 3 = responds to commands; 4 = brisk response to light glabellar tap or noise; 5 = sluggish response to light glabellar tap or loud noise; 6 = no response). If we found RSS was <3, we supplemented rescue sedation with a bolus dose of midazolam 0.01 mg/kg. Using all antiseptic precautions, the surgical area was painted draped at the same time. The operating surgeon (who was not aware of the group randomization) used lidocaine (2%) with adrenaline for local anesthetic infiltration (1:200,000) for giving great auricular nerve field block and auriculotemporal nerve (tympanic branch) block. Pain during surgery was assessed using visual analogue scale (VAS) [8,9]. If the patient complained of pain (VAS ≥3) during the surgery, IV

paracetamol infusion (15mg/kg) was given as intraoperative rescue analgesic and the surgeon supplemented a dose of local anaesthetic agent. [9]

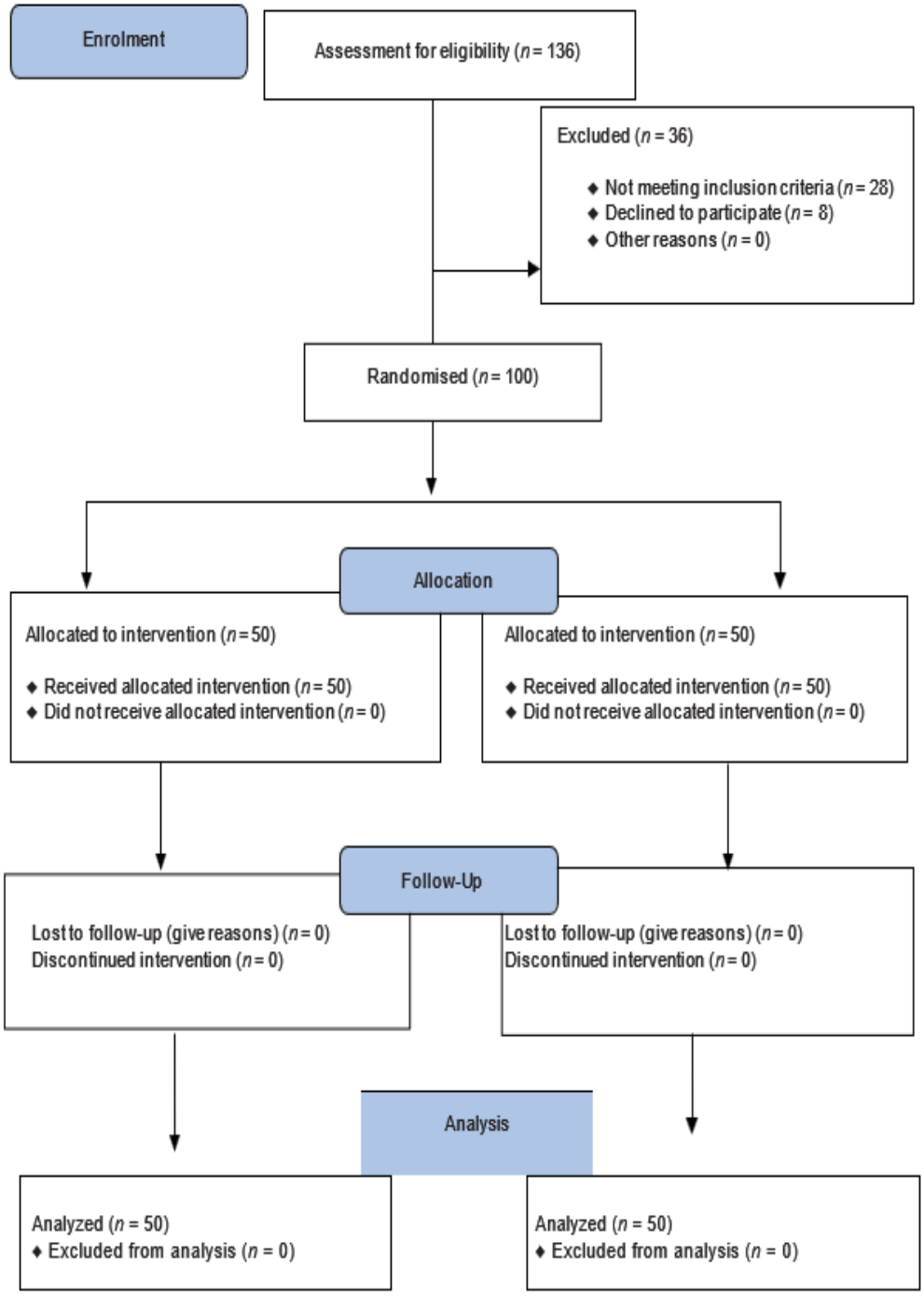

Figure 1: Consort diagram showing the number of patients included excluded and analysed

Following vitals were taken every 10 minutely: (a) Heart rate (HR), (b) Spo2, (c) mean arterial pressure (MAP) (d) respiratory rate (RR) ,till the end of surgery. Patient was then shifted to recovery room where vitals were monitored for next 2 hours. Boezaart grading scale was utilised to grade intraoperative (surgical site) bleeding. 9 Acceptable

bleeding score was: 0,1,2. (0 = no bleeding; 1 = slight bleeding, no suctioning required; 2 = slight bleeding, occasional suctioning required, surgical field not threatened; 3 = slight bleeding, frequent suctioning required, 4 = moderate bleeding, frequent suctioning required, bleeding threatened surgical field directly after suction was removed). [9,11,22]

Following complications were recorded: (a) hypotension (fall in blood pressure by 20% from the baseline or an absolute MAP <60 mmHg), (b) bradycardia (HR <50 bpm or 20% decrease from the baseline value), (c) desaturation (SpO2 <94%), (d) bradypnea (RR <8 breaths/min), (e)nausea and vomiting, (f) dryness of mouth or (g)any other events during or within 2 hours after the procedure. [9,13] Hypotension was managed with a bolus of IV crystalloids or with increments of injection mephentermine 3 mg Bradycardia was treated with IV injection atropine 0.6 mg,. Desaturation was treated with supplemental oxygen administration using face mask up to 5-6 L/min. Antiemetics (Inj Ondansetron 4mg IV) were given to treat vomiting if needed. Patient with RSS >5 was graded as 'over sedated' and administered standard general anaesthesia with appropriate sized endotracheal tube intubation. [9,11] Following surgery, patients were moved to the recovery room, where the following procedures were carried out: (a) Post-operative pain was assessed using VAS (0–10); if VAS was >3, post-operative rescue analgesia was provided with IV Paracetamol 15mg/kg IV.(b) Post-operative recovery was assessed using Aldrete score in the recovery room every 5 min, till score of 10 was achieved. We recorded the time to achieve Aldrete score of 10. 9,11

The satisfaction score of surgeons and patients were evaluated. After surgery, operating surgeon was asked to mark their experience using the seven point Likert verbal rating scale at the end of surgery. Patient's experience was marked by asking them to answer the question: 'How would you rate your experience during surgery?' using a 7-point Likert verbal rating scale. This question was asked in patients' native language. To minimize the effects of sedation on the patient's judgment, this evaluation was completed right before the patient was sent to the ward. Rating Scale: (1 = extremely dissatisfied; 2 = dissatisfied; 3 = somewhat dissatisfied; 4 = undecided; 5 = somewhat satisfied; 6 = satisfied;7 = extremely satisfied). Acceptable satisfaction score of both the patient and surgeon was 5–7. [9,11]

Sample size calculation: Data analysis was based on the results of a previous study. [9] Sample size calculation was based on a Population Standard Deviation (σ) of 1.1 with 0.8 (80%) power and 5% Alpha error (probability of rejecting the null hypothesis when it is true.). The formula to calculate the sample size for a two-group parallel study

$$n = \left(\frac{Z_{\alpha/2}+Z_{\beta}}{\delta}\right)^2 \times 2$$

Where:

- $Z_{\alpha/2}$ is the critical value for a two-tailed test at the desired significance level.
- Z_{β} is the critical value for the desired power.
- δ is the minimum clinically significant difference.

A sample size of 48 patients each group was calculated using this formula. 50 patients were included in each group to improve the validity of the findings. With the use of Google Sheets, Microsoft Excel, and SPSS Statistics, Ver. 22.0, data was entered, reviewed, and analysed. For quantitative variables, data are expressed as mean ± standard deviation; for categorical variables, they are expressed as numbers and percentages. Chi square tests and the Student t test were employed to compare groups. It was deemed statistically significant when $P < 0.05$. [6,9]

Results:

Age, gender, body mass index, and ASA grade were equivalent between the two groups in terms of demographic features ($P > 0.05$, Table 1). Baseline vital signs (MAP, SpO2, and HR) were comparable between the two groups ($P > 0.05$, Table 1). Patients underwent stapedectomy, tympanoplasty, or myringoplasty as the surgical procedures.

Between the two study groups, the distribution of these procedures and the average duration of operation were similar and comparable ($P > 0.05$, Table 1).

Table1: Pre-operative variables

Variables	Group DP	Group FP	p
Demographic data			
Age(years)	40.24±12.29	38.74±12.07	0.27
Gender(male: female)	33:17	30:20	0.36
BMI(kg/m^2)	21.92±1.42	21.89±1.08	0.9
ASA(I:II)	45:05	43:07	0.37
Baseline vital signs			
HR(bpm)	83.46±5.08	84.38±6018	0.41
MAP(mmHg)	84.07±6.87	84.96±8.02	0.55

SpO2(%)	98.86±0.73	98.72±0.78	0.35
Type of surgeries (%)			
Tympanoplasty	25 (50%)	27 (54%)	0.78
Myringoplasty	14 (28%)	11 (22%)	
Stapedectomy	11 (22%)	12 (24%)	
Duration of surgery(min)	61.28±8.88	58.86±2.07	0.063

Data are represented as mean±SD or percentage. SD – Standard deviation; BMI – Body mass index; ASA – American Society of Anaesthesiologists; SpO2 – Peripheral oxygen saturation; HR – Heart rate; MAP – Mean arterial pressure

The mean RSS (Ramsay sedation score) was significantly higher in Group DP (4.02 ± 0.8) than in Group FP (3.06 ± 0.74) (P < 0.0001). The target sedation level (Ramsay sedation score RSS ≥3) was attained by a significantly higher proportion of patients in Group DP (92%, n = 46) compared to Group FP (58%, n = 29). Additionally, significantly fewer patients in Group DP (8%, n = 4) required rescue sedation with midazolam to achieve the target sedation score compared to Group FP (42%, n = 21) (P < 0.0001, Table 2).

In our study, there were no instances of patients experiencing over sedation.

Table2: Requirement of rescue sedatives and analgesics

Variables	Group DP	Group FP	p
Sedation score	3.06±0.74	4.02±0.80	<0.0001
Rescue midazolam (%) Yes:no	07:43	23:27	0.00048
Rescue LA infiltration (%) Yes:no	10:40	22:28	0.01
Rescue paracetamol (%) Yes:no	06:44	16:34	0.015
Intraoperative bleeding score (0-2)	39/50	25/50	0.0035

Values are expressed as number (percentage Yes). LA – Local anaesthetic. A significantly higher number of patients in Group FP (n = 16, 32%) required intraoperative rescue analgesia (paracetamol infusion) compared to Group DP (n = 6, 12%) (P = 0.015). Furthermore, the postoperative visual analog scale (VAS) score was significantly lower in Group DP (3.48 ± 0.86) than in Group FP (5.1 ± 0.9) (P < 0.0001). Postoperatively, 22 patients (44%) in Group DP and 42 patients (84%) in Group FP required rescue analgesia with injection paracetamol (P = 0.0022, Table 3).

Table 3: Post-operative variables

Variables	Group DP	Group FP	p
VAS	3.48±0.86	5.1±0.97	<0.0001
Post-operative rescue analgesic (if VAS >4)	22/50	42/50	0.00225
Time to achieve to 10 in Aldrete score	14.84±2.96	14.34±2.47	0.3614
Patient satisfaction score (5-7)	42/50	27/50	0.0011
Surgeon satisfaction score (5-7)	41/50	29/50	0.0088

Values are expressed as mean±SD, number (percentage). SD – Standard deviation; VAS – Visual analogue scale

A greater proportion of patients in Group DP (n = 39, 78%) achieved an acceptable bleeding score (0-2) compared to Group FP (n = 25, 50%) (P = 0.0035). The time taken to achieve a score of 10 in the Aldrete score was 14.84 ± 2.96 (min) in Group DP, slightly longer than the 14.34 ± 2.47 (min) in Group FP (P > 0.05, Table 3).

Patient satisfaction was significantly higher in Group DP (84%) than in Group FP (54%) (P < 0.05). Similarly, surgeons' satisfaction was significantly higher in Group DP (82%) than in Group FP (58%) (P < 0.05, Table 3). In terms of intraoperative complications, 42% of patients in Group DP experienced bradycardia (HR < 50) compared to 14% in Group FP (P < 0.05) there was a statistically significant difference in mean arterial blood pressure between the two groups studied. Nineteen patients (38%) in Group DP experienced hypotension (MAP < 60 mmHg), while only 8 patients (16%) in Group FP experienced hypotension (P < 0.05). There was no significant difference between the two groups in terms of nausea and vomiting (P > 0.05). None of the cases had respiratory rate (RR) < 8/min or oxygen saturation (SpO2) < 94% (Table 4). Heart rate and mean blood pressure were significantly lower in Group DP than in Group FP from 10 minutes after the start of surgery to the end of the surgery (P < 0.05, Table 5).

Table 4: Intraoperative complications

Complication	Group DP	Group FP	*p*
Nausea and Vomiting	4	7	0.33
Dry mouth	7	9	0.58
Hypotension	19	8	0.013
Bradycardia	21	7	0.0018

Values are expressed as number (percentage)

Table 5: Intraoperative Vitals Monitoring

Variable	Time (min)	Group DP	Group FP	p
HR (bpm)	10	92.06±1.58	89.78±1	<0.0001
	20	64.24±1.22	75.06±1.42	<0.0001
	30	61.34±1.27	70.48±1.97	<0.0001
	40	60.14±0.86	69.98±1.20	<0.0001
	50	58.52±1.15	67.82±1.24	<0.0001
	60	61.04±1.05	68.74±2.57	<0.0001
	70	63.6±1.54	70.94±2.05	<0.0001
MAP (mmHg)	10	87.78±2.55	91.06±1.52	<0.0001
	20	74.22±4.25	90.26±1.05	<0.0001
	30	73.8±4.08	89.28±3.28	<0.0001
	40	72.68±3.44	87.84±4.85	<0.0001
	50	69.4±1.95	83.76±1.39	<0.0001
	60	66.06±0.84	79.56±2.04	<0.0001
	70	65.32±1.33	77.6±1.81	<0.0001

Values are expressed as mean±SD. SD – Standard deviation; HR – Heart rate; MAP – Mean arterial pressure

Discussion

Middle ear surgeries (MESs) are commonly performed under monitored anesthesia care (MAC) to achieve adequate sedation and analgesia without causing respiratory depression, ensuring comfort for both the patient and surgeon.

Using a single anesthetic agent for MAC may not provide sufficient control over the patient's condition, often requiring intraoperative rescue medications. Therefore, initiating the procedure with a combination of two anesthetic agents enables the use of lower doses of each agent. This strategy helps minimize the risk of adverse effects associated with individual agents while maximizing their therapeutic benefits.

In this prospective randomized study, we compared the safety and effectiveness of Propofol-Dexmedetomidine and Propofol-Fentanyl combinations as intravenously administered agents for monitored anesthesia care (MAC) during middle ear surgical procedures performed under local anesthesia. We observed that the mean Ramsay Sedation Score (RSS) was significantly higher in the Dexmedetomidine-Propofol group (Group DP) than in the Fentanyl-Propofol group. A significantly higher number of patients in Group FP (42%) required achieving the target sedation level (Ramsay score of 3) compared to Group DP (8%). Additionally, we found that a lower number of patients in Group DP (12%) required intraoperative rescue analgesia compared to Group FP (32%) ($P < 0.05$), which aligns with the findings of SR Arain. [13]

We also noted that a greater number of patients in Group FP required injection paracetamol as postoperative rescue analgesia compared to Group DP, indicating the analgesic efficacy of dexmedetomidine. For dexmedetomidine, we chose a loading dose of 1 µg/kg based on previous literature, given its short half-life of only 5 minutes, necessitating a maintenance infusion. We selected a maintenance dose of 0.4 µg/kg/h because the surgery was primarily conducted under local anesthesia. [14,15] The bolus dose of injection fentanyl was 1 mcg/kg, followed by an infusion started at 1 mcg/kg/hr IV. The choice of a propofol dose of 0.75 mg/kg was based on a recent study by Gupta R et al., which found this dose to be comparable to dexmedetomidine 1 µg/kg in terms of sedation. We aimed to compare equivalent doses of the drugs to minimize bias in our results. Furthermore, both study groups were targeted to a predefined endpoint (Ramsay score of 3). [9,16]

The mean heart rate (HR) and mean arterial pressure (MAP) in Group DP were significantly lower compared to Group FP ($p < 0.05$, Table 5). This difference can be attributed to the decreased sympathetic activity induced by dexmedetomidine through its α2 agonist effect. [17] These findings suggest that dexmedetomidine offers a clinical advantage over fentanyl in creating a superior operative field for microscopic surgery. Our results align with previous studies where lower HR and

MAP were noted in the dexmedetomidine group. [18] AK But et al. investigated this characteristic of dexmedetomidine for achieving controlled hypotension in general anesthesia for tympanoplasty cases and concluded that it is a valuable adjunct for reducing bleeding when a bloodless surgical field is necessary [9,19].

Intraoperative bleeding was significantly reduced in Group DP compared to Group FP. Dexmedetomidine's ability to induce controlled intraoperative hypotension effectively reduces surgical blood loss, leading to improved exposure of the surgical field compared to propofol. This improvement in surgical field exposure is crucial for otology surgeries. [20,23]

In this randomized study, patient and surgeon satisfaction scores were notably higher in Group DP than in Group FP ($P < 0.05$), indicating a distinction in the sedation quality of both drugs. The lower heart rate (HR) and mean arterial pressure (MAP) in these patients likely contributed to a better surgical field, leading to increased surgeon satisfaction. Additionally, surgeons value the absence of patient movement during surgery for their satisfaction.

When comparing dexmedetomidine and fentanyl, no disparities were observed in the time from the end of surgery to discharge readiness and actual discharge. This finding is corroborated by our study, where all patients in both groups achieved a modified Aldrete score of 10 immediately after surgery. These findings were consistent with findings of Nallam SR et.al. [9]

Alhashemi JA reported a delayed readiness for discharge from the recovery room with dexmedetomidine compared to midazolam, which contrasts with our study findings. This delay may be due to the potential presence of a sustained therapeutic plasma concentration of dexmedetomidine upon arrival in the recovery room, attributable to its elimination half-life of approximately 2 hours and the maintenance of drug infusion until the conclusion of surgery in their study. [21]

Dry mouth is a recognized side effect of α2 agonists. Our observation revealed that a higher percentage of patients (18%) in Group DP experienced postoperative dry mouth compared to those in Group FP (14%), although this difference was not statistically significant. This lack of statistical significance may be attributed to the use of glycopyrrolate injection in premedication.

Conclusion

The combination of propofol and dexmedetomidine presents a feasible option compared to propofol-fentanyl for monitored anesthesia care (MAC) during middle ear surgery. It leads to quicker postoperative recovery and decreased postoperative pain, improving the quality of the surgical field and reducing the need for rescue analgesia, thereby enhancing both surgeons' and patients' satisfaction. Propofol-dexmedetomidine is well-tolerated, with no clinically significant impact on blood pressure, respiration or heart rate.

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