



Efficacy of dexmedetomidine infusion as an anesthetic adjuvant to provide oligemic surgical field in middle ear surgeries

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Abstract

Background and Aims: *Controlled hypotension is required for middle ear surgery to achieve a bloodless operative field. A highly selective alpha2 adrenergic agonist like dexmedetomidine, by virtue of its central sympatholytic, sedative and analgesic-sparing effect may provide such desired operating conditions. The present study was designed to evaluate the clinical effects of dexmedetomidine infusion as an anesthetic adjuvant to provide oligemic surgical field in middle ear surgeries.*

Methods: *Forty patients of American Society of Anesthesiologists (ASA) physical status I and II, aged 18-58 years, weighing 45-80 kg, scheduled for elective middle ear surgery, were enrolled for this prospective placebo controlled observational study. After induction of general anaesthesia, Patients of Group A received infusion of dexmedetomidine 0.5 µg/kg/h and patients of Group B received placebo infusion of normal saline during middle ear surgery till 20 min before completion of surgery. All patients were assessed intraoperatively for bleeding at surgical field, haemodynamic changes, awakening time and postoperative recovery.*

Results: *The mean heart rate was found to be higher in patients of Group B after the extubation while patients of Group A did not show much variation in their mean heart rate values. In Group A, the Bleeding Scores and the Final Opinion on Bleeding Score were significantly lower when compared with Group B. None of the patients of Group B had significant reduction in bleeding at surgical site, thus it is evident that patients receiving dexmedetomidine infusion had a better surgical field as compared to patient of Group B.*

Conclusions: *Dexmedetomidine was found to significantly reduce intra operative bleeding. This, in turn, improves operative field visibility and increases surgeon's satisfaction during middle-ear surgery under general anesthesia.*

Keywords: *Dexmedetomidine, anesthesia oligemic surgical field, Middle ear.*

Introduction

Maintenance of relatively dry bloodless field is favored by surgeons during middle ear surgery

under operating microscope as it produces better visibility, ease of operation and reduces operating time.¹

The primary methods to minimize blood loss during middle ear surgery included mild head elevation of 15°, and infiltration or topical application of epinephrine (1: 50,000 or 1: 200,000). Currently, many inhalational or intravenous anesthesia techniques were evaluated to offer ideal intra operative conditions for middle ear surgery with their advantages and disadvantages.^{2,3}

Numerous pharmacological agents lower the systemic blood pressure for hypotensive anesthesia.⁴ Controlled hypotension is defined as a reduction of systolic blood pressure 80 mm Hg to 90 mmHg, a reduction of mean arterial pressure to 50 mm Hg to 65 mm Hg in patients without hypertension, or a reduction of 30% of baseline mean arterial pressure in patients with hypertension. A slightly elevated position of the head reduces arterial and venous pressures in areas above the heart; however, it increases the risk of air embolism. In the presence of hypotension, elevating the head will further compromise perfusion of the head and neck region.⁵

Pharmacologic agents used for controlled hypotension in ear, nose, and throat surgery include: inhalation anesthetics (e.g. isoflurane and sevoflurane), vasodilators (e.g. sodium nitropruside and nitroglycerin), beta adrenoceptor antagonists (Labetalol and Esmolol), alpha-2 adrenergic agonists (clonidine and dexmedetomidine), opioids (remifentanyl), and more recently magnesium sulfate.⁶

The alpha-2 adrenoceptor agonists, clonidine and dexmedetomidine, have sedative and analgesic properties. They also markedly reduce catecholamine secretion, are anesthetic sparing, and produce moderate bradycardia and hypotension.⁷ Remifentanyl is an ultra-short acting receptor agonist. It is able to decrease systemic blood pressure, reduce blood flow to the middle ear, and produce better visibility in the operative field without impairing autoregulation of the middle ear microcirculation. The proposed mechanism of action is via central sympathetic blockade.⁸

Dexmedetomidine has become of the frequently used drugs in anesthetic armamentarium, along with routine anesthetic drugs, due to its haemodynamic, sedative, anxiolytic, analgesic, neuroprotective and anesthetic sparing effects. Other claimed advantages include minimal respiratory depression with cardio protection, neuroprotection and renoprotection, thus making it useful at various situations including offsite procedures. α -1 to α -2 ratio of 1:1600 makes it a highly selective α -2 agonist compared to clonidine, thus reducing the unwanted side effects involving α -1 receptors. High selectivity of dexmedetomidine to α -2A receptors (which mediate analgesia and sedation) has been exploited by various authors in regional anesthesia practice. Due to its central sympatholytic effect, dexmedetomidine is useful in blunting haemodynamic responses in perioperative period. It is successfully used in intravenous doses varying from 0.25 to 1 mcg/kg for attenuating intubation response.⁹

Bradycardia and hypotension are the major side effects observed following dexmedetomidine infusion. Bradycardia is attributed to reflex response for transient hypertension during initial part of infusion. Subsequent decrease in heart rate is due to decrease in central sympathetic outflow. Hypotension is attributed to decreased central sympathetic outflow. Transient hypertensive response has been observed with higher doses (1–4 mcg/kg). This is attributed to initial stimulation of α -2B receptors present in vascular smooth muscles. This hypertensive episode settles once there is decrease in central sympathetic outflow. The highly selective effect of dexmedetomidine promotes its use for intensive care unit (ICU) sedation. Reduced ICU stay, decreased duration of ventilation, haemodynamic stability and reduced agitation are claimed advantages.¹⁰ The present study was designed to evaluate the clinical effects of dexmedetomidine infusion as an anesthetic adjuvant to provide oligemic surgical field in middle ear surgeries.

Material and Methods

Study design and study population

This prospective placebo controlled observational study was conducted at the SMHS Hospital, Government Medical College Srinagar. A total of 40 patients of American Society of Anesthesiologists (ASA) physical status I and II of both genders, aged 18-58 years, weighing 45-80 kg, scheduled for elective middle ear surgery, were enrolled.

Patients were randomly divided into two groups of 20 patients each by computer generated random table number. Patients of Group A received infusion of dexmedetomidine 0.5 µg/kg/h and patients of Group B received placebo infusion of normal saline during middle ear surgery after induction of anesthesia till 20 min before completion of surgery. The study drug solution was prepared by an anesthesiologist who was blinded to study protocol and was not involved for intraoperative data collection. The surgeon and resident anesthetist were also blinded to the treatment regimen. All patients were admitted prior to the day of the surgery, and fasting of 6 hour was ensured. On arrival to the operation theatre, the baseline systemic blood pressure, heart rate, peripheral oxygen saturation (SpO₂) and ECG were recorded. After establishing the intravenous line, lactate Ringer solution was started and they were pre-medicated with ondansetron (0.1-0.3mg/kg), glycopyrrolate (10 µg/kg), midazolam (0.07-0.15 mg/kg) and fentanyl (2 µg/kg), 15 min before induction of anesthesia.

After pre-oxygenation for 3 min, anesthesia was induced with propofol (2 mg/kg) till loss of verbal command and tracheal intubation was facilitated with vecuronium 0.1 mg/kg. Anesthesia was maintained with 60% nitrous oxide in oxygen and isoflurane dial concentration was titrated to achieve a systolic blood pressure 30% below the baseline values. Patients were mechanically ventilated to maintain the endtidal concentration (EtCO₂) between 30 and 35 mm Hg. Intraoperatively, the heart rate, arterial blood

pressure, ECG, EtCO₂ and peripheral pulse oximetry (SpO₂) were monitored and recorded at 5 min intervals till end of surgery. Concentration of isoflurane was recorded in percentage every 15 min till conclusion of surgery. Hypotension was treated by decreasing the dial concentration of isoflurane.

During procedure, the bleeding at surgical site was assessed by the surgeon as G₀-no bleeding-excellent surgical conditions; G_I-minimum bleeding, sporadic suction needed; G_{II}-diffuse bleeding, repeated suction needed; and G_{III}-considerable, troublesome bleeding, and continuous suction needed as shown in table A.

Table: A: Assessment of bleeding

Grade	Suction requirement	Condition
G ₀ :	No suction	no bleeding
G ₁ :	Sporadic suction	minimum bleeding
G ₂ :	Repeated suction	diffuse bleeding
G ₃ :	Continuous suction	troublesome bleeding

After surgery, the residual neuromuscular blockade was antagonized with neostigmine (0.05 mg/kg) and glycopyrrolate (0.008 mg/kg). Patients were extubated after observing adequate motor recovery and spontaneous breathing efforts. Awakening time following reversal of neuromuscular blockade was recorded. This duration of awakening time comprised from administration of reversal of neuromuscular blockade till sustained eye opening on command. Patients were transferred to post anesthesia care unit for observation of any respiratory depression, haemodynamic changes, nausea/vomiting or any other drug induced side effects or complications. A total sample size of 40 patients ($n = 20$ each for two groups) was calculated using Power and Sample size calculator (PS version 3.0.0.34). To obtain a 40study sample size, a total of 55 patients were included; but 15 patients were excluded on the basis of exclusion criteria.

Results

All the patients in treatment groups were compared with respect to age, weight, height, sex distribution, ASA class, and duration of surgery.

The demographic characteristics of the patients are given in the table 1.

Table 1: patient demographic characteristics:

Parameters	Group A	Group B
Number(N)	20	20
Age(years)	31.55±11.56	30.80±12.37
Weight(kg)	61.50±8.87	62.50±10.99
Height(cm)	166.3±4.610	168.4±5.547
Gender(M/F)	11/9	15/5
ASA status I/II	15/5	17/3
Duration of surgery	90.45±13.37	111.1±19.82

The baseline values of mean heart rate and systolic blood pressure were comparable between the groups with no statistical significance. Though mean heart rate values were comparable during intraoperative period between the groups but bradycardia (heart rate < 54 beats/min) was observed in two patients of Group A which promptly responded to intravenous atropine. The mean heart rate was found to be higher in patients of Group B after the extubation while patients of Group A did not show much variation in their mean heart rate values as shown in table 2.

Table 2: Changes in heart rate during anesthesia:

Heart rate(beats/minute)	Group A	Group B
Base line	76.10±10.66	71.10±13.16
After intubation	92.80±9.56	76.20±10.59
5 min	78.60±11.70	87.15±8.61
30 min	69.50±8.14	79.15±6.39
60 min	63.30±7.11	72.50±7.28
After extubation	90.55±9.34	99.40±7.70

The operating microscope was used throughout the middle ear surgery and surgeons observed Grade bleeding (minimum bleeding with sporadic suction) at surgical site in majority of patients of Group A and none of the patients had bleeding of Grade III. None of the patients of Group B had significant reduction in bleeding at surgical site, thus it is evident that patients receiving dexmedetomidine infusion had a better surgical field as compared to patient of Group B ($P < 0.05$). The difference in bleeding at surgical site was statistically significant between the groups as shown in table: 3.

Table 3: Assessment of intraoperative bleeding by surgeon

Grade	Suction requirement	Group A	Group B
G ₀ :No bleeding	No suction	0	0
G ₁ :Minimum bleeding	Sporadic suction	11	04
G ₂ :Diffuse bleeding	Repeated suction	09	10
G ₃ :Troublesome bleeding	Continuous suction	0	06

The awakening time from general anesthesia was calculated between the groups and was found insignificant with (P value of 0.365) as shown in table:4.

Table 4: Awakening time (in minutes)

Group	N	Mean	SD	Range	P-value	Remarks
Group A	20	5.00	1.5	4.0-6.0	0.365	NS
Group B	20	4.5	2.00	3.5-5.5		

All patients were able to obey the commands, and the duration of awakening time and recovery were comparable between the groups. Post-operative respiratory rate and peripheral SpO₂ were comparable with no episode of desaturation at any time. No side effect of dexmedetomidine infusion was observed during the study period.

Discussion

Middle ear micro surgery under general anesthesia is revolutionized with the introduction of hypotensive anesthesia that provides a relatively bloodless field. Currently, many inhalational or intravenous anesthesia techniques were used to offer ideal intra-operative conditions for middle ear surgery with their advantages and disadvantages. Even small amount of blood can obscure the microscopic operating field and decreasing the extravasation of blood may improve the results of surgical procedures. Different techniques, to minimize intra operative blood loss during middle ear surgery are used. The conventional techniques of electively lowering the blood pressure are positive pressure ventilation and administration of hypotensive drugs.^{11,12}

Dexmedetomidine has become of the frequently used drugs in anesthetic armamentarium, along with routine anesthetic drugs, due to its haemodynamic, sedative, anxiolytic, analgesic,

neuroprotective and anesthetic sparing effects. Other claimed advantages include minimal respiratory depression with cardio protection, neuroprotection and renoprotection, thus making it useful at various situations including offsite procedures.¹³

In our study, the dexmedetomidine infusion was used to produce oligoemic surgical field during middle ear surgery using operating microscope. It is evident from the study that the patient receiving dexmedetomidine infusion has oligoemic surgical field and better visibility when compared to patient receiving placebo. These findings can be attributed to the fact that dexmedetomidine reduces sympathetic activity, resulting in lower blood pressure and reduced heart rate thereby decreasing blood loss at the surgical site to improve the quality of the surgical field.

Dexmedetomidine is a highly selective α_2 adrenergic agonist and used as adjuvant in anesthesia to reduce the intra operative anesthetic and analgesic requirement. It regulates the autonomic and cardiovascular systems by acting on blood vessels and neither inhibiting nor epinephrine release at sympathetic terminals, thereby attenuating the heart rate and blood pressure responses to intra operative stressful events of anesthesia. It effectively minimizes the surgical blood loss and improves the surgical field visibility. Its haemodynamic effects are predictable and dose dependent.^{14,15}

The result of our study indicates that the use of dexmedetomidine infusion reduced the percentage of isoflurane concentration to maintain a systolic blood pressure 30% below baseline values. These findings confirm with a previous study of Khan *et al.* which also showed that use of dexmedetomidine reduces the requirement of inhalational anesthetic.¹⁶ Aho *et al.*¹⁷ and Aantaa *et al.*¹⁸ also reported a reduction of isoflurane requirement in their study, thus confirm the synergism between isoflurane and dexmedetomidine.

In the study of Bekker *et al.*,¹⁹ patients received an initial loading dose of 1 $\mu\text{g}/\text{kg}$ of dexmedetomidine over 10 min, followed by a

continuous infusion of 0.5 $\mu\text{g}/\text{kg}/\text{h}$ and they determined that intra operative dexmedetomidine infusion was effective for blunting the perioperative haemodynamic responses with no incidence of hypotension or bradycardia. Our present study was in accordance with their study as all patients were hemodynamically stable, and none of them required vasopressor support or bolus administration of fluid to maintain haemodynamic status.

Ebert *et al.*,²⁰ did not observe any apnea, airway obstruction and hypoxemia with bolus doses of dexmedetomidine in their study, and they reported that the depression of respiration may be seen due to deep sedation. In our study, none of the patients suffered from respiratory depression as we did not use dexmedetomidine in high doses.

However, Hilal *et al.*,²¹ provided contrasting findings on effects of intraoperative surgical bleeding during tympanoplasty and septoplasty. They noted that dexmedetomidine played a significant role in reducing both intraoperative bleeding and fentanyl dosage requirement in septoplasty whereas in tympanoplasty, attenuation in intraoperative bleeding was not found to be significant. The authors attributed these findings to either inadequate sample size or the fact that blood loss is less in tympanoplasty than septoplasty operations generally.

In our study, it was observed that intraoperative dexmedetomidine infusion decreases bleeding and hemodynamic response to certain noxious stimuli like intubation, skin incision and attenuated the hemodynamic response during emergence from anesthesia. The main mechanism is attributed to the attenuation of the Sympathetic activity and stimulation of peripheral alpha 2 adrenoceptors of vascular smooth muscle. Reduction of the blood pressure and heart rate decreases bleeding within the surgical field thereby providing bloodless surgical site.²² Moreover, it has its advantages over other hypotensive anesthetics as it does not cause any respiratory depression. There are still inadequate studies stating the direct effect of

Dexmedetomidine on blood vessels and this needs further research.

A meta-analysis of previous studies showed that the incidence of bradycardia requiring intervention was increased when maintenance dosages of dexmedetomidine were used in excess of 0.7 µg/kg/h. In our study, no patients suffered from bradycardia as dexmedetomidine infusion was given in dose of 0.5 µg/kg/h and loading dose of dexmedetomidine was not given.

The loading and maintenance dose of dexmedetomidine in this study is comparable to doses used in similar previous studies.^{23,24} Aho et al.,²⁵ found that a dose of 0.3mcg/kg/hour as maintenance infusion on patients posted for gynecological surgery was ineffective in attenuating HR and SBP. On the other hand, in another study, they observed that a higher dose of dexmedetomidine infusion in the range of 0.6mcg/kg/hour resulted in hemodynamic instability.²⁶ so, a dose of 0.5mcg/kg/hour as continuous infusion of dexmedetomidine was selected for this study.

There are some limitations in our study, that we couldn't measure middle ear blood flow and depth of anesthesia. However, we assessed the quality of the surgical field in terms of blood loss, dryness and surgeon satisfaction by the same attending surgeon who was unaware of the pharmacological treatments. We found that infusion of dexmedetomidine achieved clear surgical field during middle ear surgery. In conclusion, present study showed that dexmedetomidine was effective in inducing consistent and sustained controlled hypotension, and achieved clear surgical field during middle ear surgery with no need for additional use of a potent hypotensive agent in low-flow anesthesia. Dexmedetomidine also reduced isoflurane and fentanyl requirements for deliberate hypotension and attenuated cardiovascular responses perioperatively.

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