

Effect of Dexmedetomidine on Isoflurane Consumption in Middle Ear Surgery

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Abstract

Background: With the introduction of intentional hypotensive anesthesia in the surgical field to achieve a relatively bloodless surgical field along with the use of the operative microscope, it has revolutionized the middle ear surgery practice. Dexmedetomidine is a relatively new and potent α_2 agonist prototype found efficient in rendering bloodless intra-surgical field and inducing controlled hypotension during the surgeries of the middle ear. The objective is to present prospective study was aimed at evaluating with and without dexmedetomidine infusion effect on end-tidal isoflurane concentration for lowering blood pressure by 30%, awakening time and quality of bloodless surgical field during middle ear surgical procedure. **Subjects and Methods:** 54 patients who were to undergo middle ear surgery and had ASA I and II were randomly divided into the two groups. In Group I Dexmedetomidine was used and in Group II Normal saline. Effect of Dexmedetomidine infusion on end-tidal isoflurane concentration for lowering blood pressure by 30%, awakening time, quality of bloodless surgical field during middle ear surgical procedure, heart rate was evaluated. The data collected were statistically analyzed. **Results:** The mean values of the heart rate were statistically non-significant between the groups when recorded at the baseline, whereas, a statistically significant difference was seen in the values for heart rate intra-operatively. The mean values for heart rates were significantly higher for the placebo group. A significant difference in Isoflurane concentration was found with dexmedetomidine requiring a percentage of 0.6 ± 0.4 and normal saline 1.8 ± 0.5 . Less bleeding was seen with dexmedetomidine. **Conclusion:** Dexmedetomidine is a potent hypotensive agent which also reduces the requirement of Isoflurane compared to the normal saline placebo. The use of dexmedetomidine is relatively safe and provide a relatively bloodless surgical field, hence, increasing efficacy, and improving visibility at the surgical site.

Keywords: Dexmedetomidine, Middle Ear Surgery, Bloodless Surgical Field. Hypotensive Anaesthesia, A2 -Adrenoceptor, Heart Rate.

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Introduction

In the last decade, low-flow anesthesia has gained wide popularity in adult surgical procedures. This can be attributed to the less atmospheric pollution and also reduce the wastage associated with the anesthetic agents who are volatile as well as expensive. [1] Isoflurane is a low-flow anesthetic agent used widely in present days for surgical procedures requiring general anesthesia. Besides, Isoflurane does not affect the cardiac output by a concentration up to 2 MAC (Minimum Alveolar Concentration), and also lead to a dose-dependent decrease of MAP (Mean Arterial Pressure). [2] Although Isoflurane can cause reflex tachycardia and the phenomenon of rebound hypertension. This associated rebound hypertension associated with the isoflurane can lead to difficulty during the surgi-

cal procedures by imposing the difficulties to attain hypotension desired by surgeons. The hypotension/ intentional reduction of blood pressure is desirable during various surgical procedures. This controlled hypotension is achieved to attain a bloodless field during various operative procedures including the microsurgeries of the middle ear. [3,4] The primary objective of attaining the controlled hypotension is to achieve a relatively bloodless surgical field, besides, this also improves visualization in the surgical field. [4]

With the introduction of intentional hypotensive anesthesia in the surgical field to achieve a relatively bloodless surgical field along with the use of an operative microscope, it has revolutionized the middle ear surgery practice. [5] Traditionally, practiced approaches to minimize the blood loss during middle ear surgeries included topical application/infiltration

of epinephrine (1:2,00,000 or 1:50,000) and 15° head elevation. In recent studies, the advantages and disadvantages of various intravenous and inhalational anesthetic agents and techniques intra-operatively have been assessed. [6-9] Various pharmacological agents/ techniques have proved to effectively lower the blood pressure and achieve hypotension during surgeries. These agents range from drugs like sodium nitroprusside and nitroglycerine to inhalation agents including isoflurane, halothane. [10]

Nitroglycerine and sodium nitroprusside control the blood pressure accurately. This can be attributed to their short duration of action and rapid onset, but they require continuous monitoring of the intra-arterial blood pressure and electrocardiogram (ECG) record with the analysis of the S-T segment. Remifentanyl at an infusion of 10 - 20 µg/kg/h is also effective but is associated hyperalgesia as a side effect. Recently, clonidine addition, which is an α₂ agonist has shown to promote hypotensive anesthesia in surgeries of the middle ear. [7,11,12] Another new prototype of α₂ agonists, Dexmedetomidine, have shown effects similar to the clonidine. Also, it has shown to reduce the reflex tachycardia and sympathetic outflow and also diminishes the phenomenon of rebound hypertension. Dexmedetomidine has promising effect in reducing the heart rate and mean arterial pressure and hence can be used as a budding agent for inducing controlled hypotension. [13]

Dexmedetomidine is a relatively new and potent α₂ agonist prototype. It is used as a subservient with general anesthesia during surgical procedures. Its effects are similar to the clonidine. There is scarce research in the literature regarding the efficacy of dexmedetomidine and its peri-anesthetic infusion for rendering bloodless intra-surgical field and inducing controlled hypotension during the surgeries of the middle ear. [13] It is used as sedative agent pre-operatively, as an analgesic and hemodynamic agent during the surgery, and to avoid respiratory depression postoperatively. Dexmedetomidine is beneficial as it is a dose-dependent and predictable hemodynamic agent, along with its analgesic and anesthetic effect. [14,15]

The present prospective study was aimed at evaluating the with and without dexmedetomidine infusion effect on end-tidal isoflurane concentration for lowering blood pressure by 30%, awakening time, and quality of bloodless surgical field during middle ear surgical procedure.

Subjects and Methods

The present prospective study was carried out at the Department Of Anaesthesia, Late Shree ABVM Medical College, Rajnandgaon, Chhattisgarh, India.

54 patients who were to undergo middle ear surgery in the period of August 2019 to March 2020, and had ASA I and II were randomly divided into the two groups. In Group

I Dexmedetomidine was used and Group II Normal saline was used as a control at the place of dexmedetomidine. The inclusion criteria for the present trial were males and females within the age group of 18 years to 56 years having ASA I and II admitted to the institution for middle ear surgical procedures. Informed consent was obtained from all the study subjects. Patients who did not give consent were excluded from the study along with ASA III and ASA IV patients. Also, patients who were less than 18 years and more than 56 years of age were excluded from the trial. The exclusion criteria also had patients having anesthetic medication allergy, cardiac, renal, respiratory diseases, obese patients, patients taking sedatives or hypnotics, and patients having coagulation or bleeding disorders. Study subjects underwent a thorough pre-anesthetic evaluation before enrolment in the study. Pre-operative blood pressure, ECG, heart rate, and oxygen saturation were recorded for all the patients just before infusion with dexmedetomidine.

All the patients were premedicated with inj. Glycopylorate, ondansetron and fentanyl. all patients were induced with inj. Propofol and vecuronium and maintenance of anaesthesia was done on oxygen and isoflurane. After recording the baseline parameters, an intravenous line was established and Group I patients were infused with dexmedetomidine using the pump for infusion, and Group II patients were infused with normal saline as a placebo at the same infusion rate as dexmedetomidine. The infusion for both dexmedetomidine and normal saline was stopped 15 minutes before the surgery. Intra-surgical anesthesia was kept with 1.5 volume percent isoflurane and 60% nitrous oxygen for the initial 10 minutes. This was then titrated to achieve mean arterial blood pressure lower than 30% of the values recorded at the baseline. The values for all the recorded parameters at baseline were repeated every 5 minutes during the surgery included blood pressure, heart rate, oxygen saturation, and ECG record.

Intra surgical blood at the site of surgery was evaluated using the following criteria and scoring

Grade 0 – no bleeding excellent surgical fields;

Grade 1- minimal bleeding; sporadic suction needed;

Grade2 - diffuse bleeding repeated suction needed; and

Grade 3 –considerable troublesome bleeding and continuous suction needed

Post-surgical assessment of awakening time was also done using the following criteria

Awakening Time 1: last dose of muscle relaxant to the appearance of spontaneous breathing

Awakening Time 2: administration of reversal of neuromuscular blockade to sustained eye-opening (for > 5 seconds) on command. Post-operative assessment of nausea, vomiting, or any other significant findings was recorded for 30 minutes.

The data were collected and recorded for all the variables assessed and the collected data were statistically analyzed.

Results

The present study was aimed at evaluating the dexmedetomidine infusion effect on end-tidal isoflurane concentration for lowering blood pressure by 30%, in middle ear surgical procedures under the general anesthesia microsurgically. The present study included 56 study subjects and all of them completed the trial with no subjects backed out or excluded due to any reason. The data for the various parameters mentioned were recorded and were statistically evaluated.

The patients included in the study were in the age range of 18 to 56 years and other demographic details included age, weight, ASA status, gender, and the time taken for surgery in the two groups were recorded, and are being summarized in [Table 1]. The data were statistically evaluated using one-way ANOVA.

The results regarding the demographic characteristics depict that all the parameters including age, gender, and weight values were statistically non-significant between Group I and Group II with the values of $p < 0.5$. The value of time spent during the surgery was significantly higher statistically for Group II compared with the dexmedetomidine group (Group I) with the p-value of 0.00001.

The mean heart rate values were monitored at baseline to a period after extubation and data were recorded as summarized in [Table 2]. The mean values of the heart rate were statistically non-significant between the groups when recorded at the baseline, whereas, a statistically significant difference was seen in the values for heart rate intra-operatively. The mean values for heart rates were significantly higher for group II (the group treated with saline placebo).

The study also evaluated the required percentage of isoflurane required to reach and maintain the systemic blood pressure 30% below the baseline value. On intergroup comparison, it was found that the percentage of isoflurane required was lower, i.e., 0.6 with a standard deviation of 0.4 for the dexmedetomidine infusion group (Group I) as compared to Group II (placebo using normal saline), which had a value of 1.8 with a standard deviation of 0.5 and this value difference was statistically significant with a p-value of < 0.05 .

The present study also evaluated the surgeon's perspective of bleeding in the surgical field microscopically which was assessed on the following grades and assessment is described in [Table 3]. None of the patients showed Grade 0 as some bleeding is well expected during any surgical procedure. In Group I most of the patients depicted Grade 1 bleeding, Grade 2 bleeding was seen in few patients and none of the patients showed the troublesome bleeding. For Group II, the majority of the patients showed bleeding of Grade 3, and few depicted

troublesome bleeding of Grade 3.

Post-operative instructions given to patients were followed well by all the patients. Three patients from Group II showed bradycardia. This bradycardia was well managed. Awakening time, respiratory rates, recovery rate, and levels of peripheral oxygen did not show any statistically significant differences between the two study groups. No intra-operative or post-operative side effect was related to dexmedetomidine or anesthetic agent was reported by any study subject.

Discussion

With the advancements in medical field, microscope use was introduced in various surgical procedures including middle ear surgical procedures. The bloodless surgical field has become an important parameter to improve the surgeon's work and visibility under the microscope. Various techniques have been introduced in the literature to achieve this goal including controlled hypotension.^[16,17] Along with this, various vasodilating agents (nitroglycerine and nitroprusside),^[18] β adrenergic antagonists (propranolol and esmolol), α -2 adrenergic agonists, inhalation agents, μ receptor agonists (remifentanyl), and alpha and beta-adrenergic receptor antagonists (labetalol) have also been tried.^[19,20]

Middle ear surgeries should not induce nausea and vomiting in the postoperative period. Dexmedetomidine is a potent selective α_2 receptor agonist. It has currently gained popularity owing to its potential role in various surgeries and sedative procedures as an analgesic, sedative, sympatholytic, anxiolytic, opioid, and antinociceptive with no respiratory depression. Among various suggested techniques and agents, dexmedetomidine is the most recently introduced drug to provide hypotensive anesthesia during middle ear surgery.^[21,22]

In the present study, dexmedetomidine was tested against normal saline as a placebo for its efficacy in providing a bloodless surgical field in ASA I and II patients undergoing middle ear surgery. The results showed that the patient group receiving dexmedetomidine infusion had an oligoemic surgical field with better visibility when compared to Group II subjects receiving normal saline as a placebo. A total of 56 patients were divided into two groups with 28 patients in each group where either dexmedetomidine or normal saline was used along with the isoflurane. One such similar study was conducted by Nasreen F et al,^[14] in 2009 where authors also compared dexmedetomidine with the saline and concluded that dexmedetomidine reduces the requirement of the halothane and provide the relatively bloodless surgical field with hypotension. Concerning the isoflurane, Gupta et al,^[23] in their study of 2015 concluded that oligoemic surgical fields, as well as the reduction in requirement of isoflurane, were found with the dexmedetomidine for middle ear surgical procedures. The findings proving dexmedetomidine as a better

Table 1: Demographic Characteristics of study subjects

Characteristic	Group I	Group II	p-value
Number (n)	28	28	-
Age (in years)	36.75±11.81	36.21±11.41	0.8636
Gender (Female/Male)	12/16	13/15	-
Weight (in kgs)	53.78±3.38	54.25±3.70	0.6264
ASA Status (I/II)	23/5	26/2	-
Time spent in surgery (in mins)	97.07± 3.43	101.75±4.83	0.00001

Table 2: Inter-Group Comparison of Heart Rate

Heart Rate (in beats/min)	Group I	Group II	p-value
At Baseline	88±4.48	89.82±5.54	0.1775
Before Induction	76.57±4.57	76.96±5.10	0.7629
After Induction	73.34±6.78	72.22±6.11	0.7345
10 mins	71.57±4.39	71.60±5.34	0.9783
60 mins	64.07±2.32	84.89±2.85	< 0.00001
120 mins	62.17±2.12	82.35±2.24	< 0.00001
After extubation	82.21±2.20	92.35±2.24	< 0.00001

Table 3: Surgeon’s perspective of intra-surgical bleeding

Grade	Bleeding Assessment	Group I (n)	Group II
0	No bleeding excellent surgical fields	0	0
1	Minimal bleeding; sporadic suction needed	22	1
2	Diffuse bleeding repeated suction needed	6	21
3	Considerable troublesome bleeding and continuous suction needed	0	6

agent in providing an oligoemic surgical field can be attributed to the reduction in the sympathetic activity leading to a decrease in heart rate and blood pressure and hence blood loss.

In recent literature, various intravenous or inhalational anesthesia techniques are studied to assess the ideal intra-operative conditions required for the middle ear surgical procedures. One in such a series study was carried out by Jellish et al. in 2005, and the authors concluded that the intravenous anesthesia techniques are better comparatively in terms of less movement, faster emergence, and hemodynamic control during middle ear surgical procedures.^[6] Also, other studies by Lee YY et al,^[24] in 2007 and Tanskanen PE et al,^[25] in 2006 showed that short-acting inhalational anesthetics agents like isoflurane and desflurane provide favorable conditions for middle ear surgery. These studies are in agreement with the present prospective study.

The result of the present trial showed that the use of dexmedetomidine infusion reduced the percentage of isoflurane concentration to maintain a systolic blood pressure 30% below baseline values. These findings were in agreement with the previous study by Khan et al. in 1999 which also showed that dexmedetomidine use reduces the inhalational anesthetic agent requirement.^[26] The present study was also consistent with the studies by Aho et al,^[27] in 1991 and Aantaa et al.^[28] in 1997, which also reported a decrease in the isoflurane requirement and also established the symbiosis between isoflurane and dexmedetomidine. Regarding the bradycardia, a study by Bekker et al. in 2008 suggested that intraoperative infusion of dexmedetomidine was effective for reducing the hemodynamic responses peri-operatively with no subject reported hypotension or bradycardia.^[29] The present clinical study was consistent with the study by Bekker et al as all the study sub-

jects were stable concerning the hemodynamic parameters.

One study similar to the present trial was conducted by Tobias et al where they evaluated dexmedetomidine for controlled hypotension in spinal surgery and authors concluded that dexmedetomidine could be used to maintain desired mean arterial pressure without causing tachycardia.^[30] The present trial used dexmedetomidine as an alliance with isoflurane for controlled hypotension in the middle ear surgery and showed that dexmedetomidine was effective in doing so.

The present study also considered the awakening time where no statistically significant difference was found between the two groups. This finding was in contrast with the studies by Raul A et al,^[31] in 2005 and Curtis FG et al,^[32] in 2002 where the authors found less awakening time in the dexmedetomidine group. This can be attributed to the use of halothane in these studies compared to isoflurane in the present study.

For the present study, no study subject presented any minor or major complications in the postoperative period. Both Isoflurane and dexmedetomidine were tolerated by the entire subjects well. Recovery was not delayed in any of the patients. No respiratory depression in the post-operative period was presented by any patient. This was consistent with the study by Ebert et al,^[33] in 2009 where the use of dexmedetomidine was not related to any hypoxemia or airway obstruction in the post-operative period with the usage of sedation. This can be attributed to the usage of appropriate dexmedetomidine use.

Conclusions

Dexmedetomidine reduces the requirement of Isoflurane compared to the normal saline placebo. The use of dexmedetomidine is relatively safe and provide a relatively bloodless surgical field, hence, increasing efficacy, and improving visibility at the surgical site. Also, the decrease in sympathetic response and blood pressure is seen with its use. All the hemodynamic parameters remained stable with dexmedetomidine use. No major or minor complication in the peri-operative period was presented with the dexmedetomidine use. The recovery and awakening time was also prudent with dexmedetomidine use. There were few limitations in the study including the non-consideration of measuring middle ear blood flow and depth of anesthesia.

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