Comparitive study between Intravenous Dexmedetomidine and Esmolol For Hypotensive Anaesthesia in Middle Ear Surgeries

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Abstract
Background and Aim: This study was done to compare the efficiency of Dexmedetomidine and Esmolol in inducing deliberate hypotension and providing a better surgical field exposure during middle ear surgery. Parameters like MAP, HR and blood loss are compared between both the drugs.

Materials and Methods: This present study included patients aged between 18 to 60 years of ASA physical status I or II, who are planned to undergo a microscopic operation in the middle ear with informed consent. These were divided into Dexmedetomidine(D) group of 30 patients and Esmolol (E) group of 30 patients. Patients in the dexmedetomidine group (D) received a loading dose of 1 μg/kg of dexmedetomidine in 200 ml of 0.9% normal saline, before induction over 10 mins and subsequent maintenance doses of 0.5 μg/kg/h after intubation throughout the surgery. Whereas, patients in esmolol group(E) received a loading dose of 1 mg/kg of esmolol, before induction over 1 min and subsequent maintenance doses at 0.5 mg/kg/h after intubation throughout the surgery. Then, patients are evaluated for hemodynamics like MAP, HR at regular intervals and blood loss noted for both drugs.

Results: Mean arterial pressure values were significantly decreased in Group D compared to that in Group E, except for the baseline value (p < 0.05). Blood loss is 104.15 ml in Dexmedetomidine group and 113.24 ml in Magnesium sulfate group, that is significantly low in Dexmedetomidine, hence quality of the surgical field and surgeon satisfaction score was better with D group at all intervals. Heart rate is significantly low in the Dexmedetomidine group at all intervals. Bradycardia is more prominent with Dexmedetomidine, with no major differences between other side effects.

Conclusion: Dexmedetomidine can provide more effective controlled hypotension and thus contribute to improved visibility of the surgical site.

Introduction
Intraoperative bleeding may be reduced most effectively by hypotensive anesthetic technique. Advantages of using the hypotensive anesthetic technique during the middle ear surgeries are reduction in blood loss leading to reduction in blood transfusion rate, improvement in the surgical field, and reduction of the duration of surgery. In this technique, there should bereduction of the systolic blood pressure to 80-90 mm Hg, or baseline mean arterial pressure (MAP) is reduced by 30% or MAP was kept at 50-65 mm Hg(1).

Several pharmacologic agents have been used to produce deliberate hypotension. Direct vasodilators such as nitroprusside(2) and nitroglycerine, alpha-2 adrenergic agonists such as clonidine and dexmedetomidine, beta adrenergic antagonists such as propranolol and esmolol, alpha and beta adrenergic antagonists such as labetalol, inhalational anaesthetics such as isoflurane(3) and sevoflurane,µ-receptors agonist

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such as remifentanil\(^4\), and N-methyl D aspartate antagonist such as magnesium sulfate\(^5\) were all used to induce hypotension during middle ear surgery.

Disadvantages with these drugs are tachyphylaxis with nitroglycerine, cyanide toxicity with sodium nitroprusside, delayed recovery from anesthesia with high doses of inhaled anesthetics, and resistance to vasodilators. So, an ideal agent is required for inducing hypotension, having properties like short onset time, rapid elimination without toxic metabolites, and dose-dependent effects. Postural variation, like reverse Trendelenburg position for decreasing bleeding, has increased the incidence of air embolism.

This study is designed to compare the efficiency of both the drugs in causing hypotensive anesthesia, with least side effects. Blood loss is also compared between both drugs.

**Aims and Objectives**

1) To evaluate the efficiency of the drugs in producing hypotensive anesthesia in middle ear surgeries.

2) To compare variables like hear rate and blood loss between both the drugs.

**Materials and Methods**

- **Design**: Cross sectional randomised study
- **Study Period**: 23 months (September 2017 to August 2019)
- **Setting**: Operation theater (OT) in a tertiary care hospital.
- **Study Population and Size**: All patients admitted in Government E.N.T. Hospital, Visakhapatnam

**Inclusion Criteria**

This present study included patients aged between 18 to 60 years of ASA physical status I or II, who are planned to undergo a microscopic operation in the middle ear with informed consent.

**Exclusion Criteria**

Patients who refused for the study, patients of ASA grade III and IV, patients with renal, hepatic impairment or cardiac disease, who are hypertensive or on antihypertensive drugs and those with known allergy to the study drugs are excluded from the study.

**Methodology**

The surgeon and the nursing staff who follow-up the patients in the post-anesthesia care unit (PACU) were blinded with the type of drug used. Preoxygenation with a face mask for 3 min done, premedicated with Inj. Glycopyrrolate 5μ/kg, Inj. Midazolam 0.05mg/kg, Inj. Fentanyl 2μ/kg, followed by induction of anesthesia with Inj. Thiopentone 5mg/kg body wt. Thereafter, Inj. Vecuronium at a dose of 0.01mg/kg body wt is given intravenously, followed by positive pressure ventilation with the face mask until adequate relaxation obtained. Intubation was performed with a suitably sized endotracheal tube.

Patients in the dexmedetomidine group (D) (n = 30) received a loading dose of 1 μg/kg of dexmedetomidine in 200 ml of normal saline 0.9% before induction, and subsequent doses of 0.5 μg/kg/h after intubation. Whereas, patients in the esmolol group (E) (n = 30) received 1 mg/kg of esmolol before induction as loading dose, and subsequent maintenance doses at 0.5 mg/kg/h after intubation, throughout the procedure.

General anesthesia was maintained with O2 and N2O (33% and 67% respectively), fentanyl, vecuronium, and sevoflurane. Patients were kept under controlled ventilation at a respiratory rate of 14 cycles/min and a tidal volume (VT) of 8 ml per kg. Sevoflurane percentage was titrated to maintain mean blood pressure around 30% descents in the blood pressure (Target MAP 60-70mm of Hg). Blood pressure, oxygen saturation, and HR were recorded. Intraoperatively fluid volume of 5 ml/kg/h of 0.9% saline was given. The total amount of blood loss during surgery was calculated (by Gravimetric method) as follows: (Volume of bloody fluid in the suction container– Volume of the irrigating fluid) + (and amount of wet gauze pieces and mops dry weight). After the correct and secured placement of the tympanic membrane graft, the test drugs were discontinued.
and the blood pressure allowed to return to its baseline value. At the end of the surgery, anesthetic drugs were discontinued, and reversal of muscle relaxation was done with intravenous 0.005 mg/kg glycopyrrolate followed by 0.05 mg/kg neostigmine. After the return of reflexes, extubation was performed. They were followed up for blood pressure, HR, oxygen saturation, and pain through a visual analogue scale.

The duration of the surgery (skin incision to the end of the surgery) and awakening time (last dose of muscle relaxant to sustained eye-opening on command after reversal) were recorded. Patients were monitored for SpO2, HR, and BP at intervals 15 min, 30 min, 45min, 60min, 90min, and 120min.

Side effects of the drugs, such as nausea, vomiting, bradycardia, hypotension, dry mouth were recorded. Bradycardia was managed with a small dose of atropine 0.02 mg/kg IV. Hypotension was managed with fluids and a small dose of Mephenteramine (6–12 mg) if needed.

**Statistical Analysis:** Data was entered in Microsoft MS Excel and analysis was done in MS Excel and MEDCALC software on a personal computer. Categorical data will be expressed in proportions and quantitative data by means and standard deviation. A p-value of 0.05 was taken as the level of significance.

**Observations and Results**

**Demographic Data**

Sixty patients were taken into the study aged between 18 to 60 years of ASA physical status I or II, who are planned to undergo a microscopic operation in the middle ear with informed consent. These were divided into Dexmedetomidine(D) group of 30 patients and Esmolol(E) group of 30 patients. Patients in the dexametomidine group (D) received a loading dose of 1 μg/kg of dexametomidine in 200 ml of 0.9% normal saline, before induction over 10 mins and subsequent maintenance doses of 0.5 μg/kg/h after intubation throughout the surgery. Whereas, patients in esmolol group(E) received a loading dose of 1 mg/kg of esmolol, before induction over 1min and subsequent maintenance doses at 0.5 mg/kg/h after intubation throughout the surgery. Then, patients are evaluated for hemodynamics like MAP, HR at regular intervals and blood loss noted for both drugs. The mean age in Dexmedetomidine group was 23.43±4.03 years, and in Esmolol group was 24.04±5.03 years and is comparable (p-value >0.05 ). In dexametomidine group, 13 of the patients were males, and 17 of the patients were females. In esmolol group, 16 of the patients were males, and 14 of the patients were females with a p-value >0.05, showing no significant difference between the groups.

Hemodynamic variables like heart rate and Mean arterial pressure was measured at baseline, after loading dose of the study drug, after induction, After intubation, 5 min after intubation, at an interval of 5 min intra operatively, after reversal, after extubation. Blood loss was recorded. The postoperative side effects such as nausea and vomiting, shivering and dry mouth were observed.

### Demographic Variables

| Demographic Variables | Dexmedetomidine group (D) | Esmolol group(E) | P-value |
|-----------------------|---------------------------|-----------------|---------|
| Age                   | 23.43±4.03                | 24.04±5.03      | 0.5     |
| sex                   | 13/17                     | 16/14           |         |
| weight                | 56.9 ± 5.36               | 57.1 ± 4.21     | 0.87    |
| ASA status (i/ii)     | 25/5                      | 28/2            | --      |
| Type of surgery (tympanoplasty / mastoidectomy) | 19/11 | 14/16 | -- |
| Amount of Blood loss  | 104.15 ml                 | 113.24 ml       | 0.04*   |

*P value <0.05 considered significant, p value > 0.05 considered as non significant.

Datasuggest that there is no statistical significance in age, gender, weight, ASA status of patients and type of surgery in between both groups. Amount of blood loss is less with Dexmedetomidine group compared to Esmolol group.
Comparison of MAP in Group D and Group E

| Time of measurement | Group D       | Group E       | P value |
|---------------------|---------------|---------------|---------|
| Baseline            | 86.3±5.9      | 93.1±4.6      | 0.19*   |
| After loading dose  | 76.2±5.6      | 86.3±4.5      | 0.00*   |
| After induction     | 72.1±6.9      | 80.8±3.1      | 0.00*   |
| After intubation    | 69.3±3.9      | 80.3±5.2      | 0.00*   |
| 5 mins after intubation | 68.6±2.7  | 76.8±5.4      | 0.00*   |
| Average intraoperatively | 80.4±0.9 | 88.3±1.2      | 0.00*   |
| After reversal      | 72.8±3.8      | 82.5±3.9      | 0.00*   |
| After extubation    | 89.5±4.5      | 91.3±1.8      | 0.00*   |
| 5 mins after extubation | 82.1±3.9  | 89.3±2.0      | 0.00*   |

*P value <0.05 considered significant , p value > 0.05 considered as non significant

The MAP was significantly lower in group D compared to group E after infusion of study drugs, after induction of anesthesia, after intubation and 5 min after intubation, average intra operatively, after reversal, after extubation, 5 mins after extubation (P < 0.05) [Table 2]. However, the desired MAP for intra operative induced hypotension could be achieved in both groups. None of the patients experienced bradycardia, resistant hypotension or hypertension during the study period. None of them required additional atropine or mephentermine.

Comparison of mean HR in both groups
| Time of measurement          | Group D         | Group E         | P value |
|-----------------------------|----------------|----------------|---------|
| Baseline                    | 80.93 ± 8.82   | 87.97 ± 10.75  | 0.01*   |
| After induction             | 78.20 ± 7.95   | 87.67 ± 10.53  | 0.00*   |
| After intubation            | 75.87 ± 7.18   | 86.87 ± 12.40  | 0.00*   |
| Average intraoperatively    | 75.17 ± 10.73  | 89.2± ±11.35   | 0.00*   |
| After reversal              | 77.40 ± 8.70   | 87.13± ±8.85   | 0.00*   |
| After extubation            | 74.87 ± 7.66   | 86.7± ±7.87    | 0.00*   |

*P value < 0.05 considered significant, p value > 0.05 considered as non significant.

The mean HR was significantly lower in group D compared to group E at all the times of measurements (P < 0.05) [Table 3].

### Comparison of Side Effects in both groups

| Side Effects           | Group D | Group E |
|------------------------|---------|---------|
| Nausea/Vomiting        | 1       | 3       |
| Hypotension            | 1       | -       |
| Bradycardia            | -       | -       |
| Respiratory depression | -       | -       |
| Excessive sedation     | -       | -       |
| Dryness of mouth       | 3       | -       |

Nausea and vomiting is more with Esmolol group compared to Dexmedetomidine group. Dryness of mouth is more with Dexmedetomidine group.

### Discussion

Middle ear surgeries like Tympanoplasty and Mastoidectomy are usually done under a microscopic view, so the bleeding has to be minimized during surgery, as even a minimal amount of blood may completely obstruct the vision through the operating microscope. Several approaches have been used to produce an oligemic field during surgery like reverse Trendelenburg position, use of vasoconstrictor drugs with a local anesthetic, and Pharmacological agents to reduce blood pressure.

Because of the potential advantages of the oligemic field during surgery like surgeon satisfaction, decreased blood loss, the present study was undertaken in sixty patients of age group between 18 to 60 yrs, for comparing the drugs dexmedetomidine and magnesium sulfate for producing an oligemic field.

The target M.A.P. between 60 and 70 mmHg was decided to achieve hypotensive anesthesia and good operating field without subjecting the patients to peripheral tissue ischemia. This target M.A.P. was determined after revising previous studies in which metabolic and hormonal responses were observed in patients subjected to induced hypotension.

Middle ear surgeries, either tympanoplasty or mastoidectomy admitted in Government E.N.T. hospital, Visakhapatnam was taken into this cross-sectional randomized controlled study belonging to A.S.A. grade I & II, of age group 18-60 yrs, scheduled for middle ear surgery after obtaining approval from the institutional ethics committee. Patients were randomly divided into two equal groups, 30 each (Randomisation done by computer-generated numbers). The sample size is comparable to other studies Table 10. To Dexmedetomidine group, inj. Dexmedetomidine i.v loading dose of 1 μg/kg in 200ml N.S. over 10min before induction of anesthesia was given and followed by maintenance infusion in the dose of 0.5 μg/kg/h after intubation via a syringe infusion pump. To Esmolol group, a loading dose of 1mg/kg Esmolol and subsequent maintenance of 0.5mg/kg/hr. Infusion is given during surgery. Hemodynamic variables like MAP, heart rate were measured at regular intervals. The postoperative side effects such as nausea and vomiting, hypotension, bradycardia, dry mouth were observed. Amount of blood loss was recorded for each case.
This study shows that both esmolol and dexmedetomidine are able to produce deliberate hypotension, where as the MAP was significantly lower in group D compared to group E after infusion in patients undergoing middle ear surgery. Heart rate is significantly lower in D group. Bleeding is less in Dexmedetomidine (D) group compared to Esmolol (E) group.

Yoshikawa and colleagues\(^6\) induced hypotensive anesthesia using a similar target M.A.P. of 60–70 mmHg in patients undergoing mandibular osteotomy. They measured blood pyruvate, lactate, and glucose and observed an insignificant increase in their levels. They concluded that induced hypotension with MAP between 60 and 70 mmHg could be safely administered.

Newton and colleagues\(^7\) targeted a M.A.P. of 55 mmHg in patients undergoing middle ear surgery. They also observed an insignificant increase in blood lactate and pyruvate levels.

Edram et al.\(^8\) assessed regional cerebral oxygen saturation using infrared spectroscopy during induced hypotension in patients who are undergoing rhinoplasty. They reported that when MAP was decreased to 50 - 60 mmHg, it resulted in cerebral desaturation in 10% of the patients. So, to prevent the occurrence of undistinguished cerebral hypoxia, it was decided to maintain the MAP above 60 - 70 mmHg in the present study.

Effect of dexmedetomidine on the outcome of patients undergoing FESS surgery done by Guven et al.\(^9\) reported that dexmedetomidine group during surgery had less bleeding, postoperative pain, and nausea, as well as a better hemodynamic compared to normal saline group. Similarly, the result of the present study showed a significant reduction of bleeding with dexmedetomidine.

There are limited studies available that compare esmolol and dexmedetomidine. The results obtained in our study were similar to Yavascaoglu et al. 2008\(^10\) on whose study we based our dosage selection. They also concluded that, Dexmedetomidine is more efficient than Esmolol, in maintaining MAP. They found that fall in MAP and HR was more in Group D than in Group E, both the observations are in accordance with the present study.

Effect of nitroglycerine, esmolol, and dexmedetomidine for induced hypotension in Functional endoscopic sinus surgery was compared by Bajwa et al\(^{11}\) in 3 equal groups of 150 patients. The desired MAP was achieved in all the 3 study groups of 150 patients, but MAP and HR are significantly lower in dexmedetomidine group, compared to the esmolol group and Nitroglycerine group. Similarly, in the present study which was done in 60 patients of 2 equal groups, MAP, HR and bleeding is significantly lower in Dexmedetomidine group.

In another study Gogus et al., 2014\(^{12}\) results were comparable to our study as for heart rate, however, for blood pressure they showed a superior control of esmolol using a dosage of 2 mg/kg against 1mg/kg dexmedetomidine. This difference could be attributed to a proportionally double dosage of esmolol as compared to dexmedetomidine in their study.

In the present study, although esmolol produced a good attenuating response as far as blood pressure control is concerned; however it failed to provide a good control over heart rate. One of the explanations for this could be due to selection of a lower dose of esmolol in our study. Clinical studies like Cuneo et al.,1994\(^{13}\) have shown that esmolol has shown to have a delayed reduction in heart rate which is preceded by fall in blood pressure this could be the reason for selective action of esmolol on blood pressure and not on heart rate. As hemodynamic reflex is a transitory response, it is essential that the action of drug should be initiated within a short time. It also shows a dose dependent control on the heart rate and cardiac index.

In the present study dexmedetomidine group had significantly higher sedation Scores compared to group E similar to Shams et al\(^{14}\) who reported higher postoperative sedation scores with the intraoperative use of dexmedetomidine. Postoperative shivering was significantly lower in
the dexmedetomidine group. The most frequent side effect with dexmedetomidine is dry mouth.

**Summary**

Sixty patients of ASA 1 & 2, of age 18-60 yrs, of both sex, scheduled for middle ear surgery under general anesthesia, were included in the study. After approval of Ethics committee and written informed consent from all patients, patients were randomly divided into two equal groups of 30 each.

Group D (Dexmedetomidine) received Dexmedetomidine infusion of 1 μg/kg over 10 minutes before induction, followed by 0.5 μg/kg/hr after intubation. Group E (Esmolol) received Esmolol infusion of 1 mg/kg over 1 minute before induction, followed by a maintenance infusion of 0.5 mg/kg/hr after intubation. General anesthesia is maintained with O2 and N2O (33% and 67% respectively), sevoflurane, vecuronium, fentanyl.

Hemodynamic variables like MAP, Heart rate, Amount of blood loss, and postoperative side effects were recorded and statistically analyzed. Esmolol and dexmedetomidine are able to produce deliberate hypotension, where as the MAP was significantly lower in group D compared to group E after infusion in patients undergoing middle ear surgery.

Heart rate is significantly low in the Dexmedetomidine group at all intervals. Bradycardia is more prominent with Dexmedetomidine, with no major differences between other side effects.

Blood loss is 104.15 ml in Dexmedetomidine group and 113.24 ml in Esmolol group, which is significantly low in Dexmedetomidine, hence quality of the surgical field and surgeon satisfaction score was better with D group at all intervals.

**Conclusion**

Dexmedetomidine can provide more effective controlled hypotension and less bleeding compared to Esmolol, and thus contribute to improved visibility of the surgical site.

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