Evaluation of the efficacy of desflurane with or without labetalol for hypotensive anesthesia in middle ear microsurgery

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Abstract

Background and Aims: Hypotensive anesthesia technique is used to reduce intraoperative bleeding and to improve the visibility of the operative field. The aim was to evaluate the efficacy of desflurane with and without labetalol for producing hypotensive anesthesia.

Material and Methods: Sixty adult patients undergoing elective middle ear surgery were administered general anesthesia and randomly divided into two groups – Group D and Group L. The target mean arterial pressure (MAP) was 55–65 mmHg during hypotensive period. Group D patients received an increasing concentration of desflurane alone. Group L patients received 3% desflurane plus labetalol (loading dose 0.3 mg/kg intravenously, followed by 10 mg increments every 10 min). Student's t-test and paired t-test were used to compare the hemodynamic parameters. Visibility of the operative field, anesthetic and rescue drug requirement, partial pressure of oxygen in arterial blood, time taken for induction and reversal of hypotension and recovery characteristics were noted.

Results: Target MAP was achieved in both the groups. Group D was associated with a higher mean heart rate compared with Group L (77.3 ± 11.0/min vs. 70.5 ± 2.5/min, respectively; P < 0.001) during the hypotensive period, along with a higher requirement for desflurane (P = 0.000) and metoprolol (P = 0.01). Time taken to achieve target MAP was lesser in Group L compared with Group D (33.7 ± 7.1 vs. 39.8 ± 6.2 min, respectively; P = 0.000). Time taken to return to baseline MAP was faster in Group D (P = 0.03). Emergence time was longer with desflurane alone (P = 0.000) resulting in greater sedation (P = 0.000) in the immediate postoperative period.

Conclusion: Although desflurane is effective for inducing deliberate hypotension in middle ear microsurgery, the combination of desflurane with labetalol is associated with decreased requirement of desflurane, absence of reflex tachycardia, faster induction of hypotension, faster recovery from anesthesia, and less postoperative sedation.

Keywords: Desflurane, hypotensive anesthesia, labetalol, middle ear microsurgery

Introduction

Deliberate or induced hypotension is an anesthetic technique which is used in various types of surgeries to reduce intraoperative bleeding and to provide a clear operative field. It has been found to be beneficial in neurosurgery, plastic surgery, major orthopedic procedures, head and neck surgery, radical cancer operations, and procedures on the middle ear.[1-4] For successful microsurgery of the middle ear a bloodless operative field is essential to improve the surgical outcome of patients.

Inhalational anesthetics, vasodilators, autonomic ganglion blockers, and adrenergic receptor antagonists have been...
successfully used for producing deliberate hypotension in middle ear surgery. Desflurane induces hypotension by producing peripheral vasodilation and a subsequent decrease in systemic vascular resistance. In healthy individuals, the cardiac output remains unchanged, although in older or chronically hypertensive patients there may be a decrease in cardiac output.

Labetalol is a competitive antagonist at both alpha-1 and beta adrenergic receptors. Deliberate hypotension with labetalol is associated with either no change in heart rate (HR) or bradycardia. Therefore, combining labetalol with inhalational agents may offer the advantage of producing hypotension while maintaining the cardiac output.

We hypothesized that a combination of desflurane and labetalol would not only produce deliberate hypotension while maintaining the cardiac output but would also help to decrease the dose of desflurane, which could be beneficial in high-risk patients. The purpose of this study was to evaluate the efficacy of desflurane with or without labetalol, for providing hypotensive anesthesia in middle ear microsurgery.

Material and Methods

The study was conducted after written informed consent from the patients and after being approved by the Institute Ethics Committee.

Sixty adult patients (18–60 years) of either sex, American Society of Anesthesiologists physical status Grade 1, undergoing elective middle ear surgery were included in the study. Patients with major hepatic, renal, cerebral or cardio-respiratory dysfunction, anemia or other hematological disorders, diabetes mellitus, pregnancy, neuromuscular disease, malignant hyperthermia, intracranial hypertension or known allergy to any of the drugs used were excluded from the study.

Patients were premedicated with oral diazepam 5 mg the night before and 2 h before surgery. In the operating room, standard monitoring was established and preoperative vital parameters were recorded: HR; systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP); oxygen saturation (SpO₂) and electrocardiogram (ECG). Anesthesia was induced with fentanyl (2 µg/kg) and propofol (till loss of verbal response). Orotracheal intubation was facilitated with vecuronium (0.1 mg/kg). The left radial artery was cannulated for the purpose of invasive blood pressure monitoring. Anesthesia was maintained with oxygen (O₂) in nitrous oxide (fraction of inspired O₂ concentration, FiO₂ 0.33), desflurane, fentanyl (intermittent boluses of 0.5 µg/kg every hour) and vecuronium using circle system.

Head end of the operating table was elevated by 15°. The skin behind the ear was infiltrated with 5 ml of normal saline containing 1:200,000 adrenaline.

Deliberate hypotension was maintained during the reconstruction of the tympanic space (period of microsurgery/hypotensive period), target MAP being 55–65 mmHg. For the period of hypotension, patients were randomized (computer generated random number table) into two groups - Group D: Hypotension was induced with desflurane alone, and Group L: Hypotension was induced with a combination of desflurane and labetalol. In Group D, vaporizer concentration of desflurane was gradually increased till target MAP was reached (till a maximum of 9%). In Group L, vaporizer concentration of desflurane was kept constant at 3%. In addition, labetalol was administered intravenously in a loading dose of 0.3 mg/kg slowly over 2 min, followed by 10 mg increments every 10 min till the target MAP was achieved. Thereafter, 5–10 mg increments of labetalol were given every 30 min or when MAP increased to >65 mmHg. Fresh gas flow (FGF) was kept at 4–6 L/min initially in both groups. It was reduced to 1 L/min after MAP was achieved in Group D and 10 min after induction in Group L.

In case target, MAP was not achieved in any of the groups and remained >65 mmHg; nitroglycerine infusion was started. If MAP was <55 mmHg, desflurane was decreased or stopped. In addition, intravenous fluids and ephedrine were given, if required. If HR was >80/min and MAP was in the desired range, metoprolol was given in increments of 1 mg. If HR was <60/min and MAP was <55 mmHg, atropine 0.6 mg was administered.

Fluids were replaced as per period of fasting and calculated losses in the intraoperative period. At the end of the period of induced hypotension, desflurane was decreased to 3% in Group D and was stopped approximately 15 min before the end of surgery in both groups. Ondansetron 4 mg IV was administered 30 min before the end of surgery in both groups. Residual neuromuscular block was antagonized with neostigmine (0.05 mg/kg) and glycopyrrolate (0.01 mg/kg).

Intraoperatively, ECG, HR, blood pressure (SBP, DBP, and MAP), SpO₂ and end-tidal carbon dioxide concentration were monitored continuously and recorded at 5 min intervals. Visibility of the operative field at exposure, during the procedure and at closure was assessed by the surgeon (blinded to group allocation) using a quality scale proposed by Fromm and Boezart (0: No bleeding; 1: Slight bleeding-blood evacuation not necessary; 2: Slight bleeding-sometimes blood has to be evacuated; 3: Low bleeding-blood has to be often evacuated, operative field is visible for some
seconds after evacuation; 4: Average bleeding—blood has to be often evacuated, operative field is visible only right after evacuation; 5: High bleeding-constant blood evacuation is needed, sometimes bleeding exceeds evacuation, surgery is hardly possible.\[8\] Anesthetic dose requirements of desflurane (total volume consumed as indicated on the vaporizer), fentanyl and vecuronium were recorded in both the groups. The requirement of labetalol in Group L and that of rescue drugs such as nitroglycerine, metoprolol, ephedrine, and atropine was also noted. Arterial blood gas analysis was performed before, during and after the hypotensive period. Time taken to achieve target MAP after induction of hypotension with desflurane/labetalol, time taken to achieve baseline MAP at the end of microsurgery and time taken after administration of reversal till eye opening and following of commands (emergence time) was noted.

Postoperatively, HR and BP were recorded and sedation was assessed on a 4-point scale (A - awake and alert, D - drowsy but cooperative, P - responds to pain, U - unconscious) every 15 min in the 1st h and hourly thereafter for the next 4 h.\[9\] The presence of pain and other adverse effects such as nausea and vomiting were also noted.

**Statistical analysis**

The primary objective of this study was to assess visibility of the operative field using Fromm and Boezart scale.\[8\] For sample size calculation, a difference of 25% in the acceptable visibility of the operative field (Grade 0 or 1) between the two groups was defined as clinically relevant. Using a two-tailed alpha value (0.05) and a beta value (0.2), thirty patients per group were considered sufficient to detect a significant difference.

Data were collected on a standard proforma and tabulated on Microsoft Excel sheet. Statistical Package for the Social Sciences statistical software version 21.0 (2012, IBM, Armonk, NY, United States of America) was used for statistical analysis. Student’s t-test and paired t-test were used to compare the hemodynamic parameters between the groups and within each group, respectively. Nonparametric Wilcoxon Mann–Whitney U-test was used to compare visibility of the operative field, anesthetic and rescue drug requirement, partial pressure of oxygen in arterial blood (PaO\(_2\)) values, time taken to achieve target and baseline MAP and emergence time between the groups. Chi-square test was used to compare postoperative sedation score and side effects. \(P < 0.05\) was considered to be statistically significant.

**Results**

Both groups were comparable with respect to age, sex, and weight of the patients. Mean duration of surgery, duration of anesthesia, and period of hypotensive anesthesia were also similar between the groups.

Mean HR was comparable between the groups at baseline and immediately after induction. The overall mean HR (beats/min) was higher in Group D (77.3 ± 11.0) as compared to Group L (70.5 ± 2.5) during microsurgery (hypotensive period); \(P < 0.001\). Mean HR was comparable between the groups at 25 min after the end of microsurgery [Figure 1].

Mean SBP was comparable between the groups at baseline, after induction and during and after microsurgery [Figure 2]. Mean DBP was comparable between the groups at baseline, and before and during microsurgery. Mean DBP was significantly lower in Group D at 25 min after the end of microsurgery; \(P = 0.000\) [Figure 2].

Mean visibility of the operative field was comparable between the groups at exposure, during microsurgery, and at closure. The mean \(\text{PaO}_2\) before, during, and after reversal of hypotension, was also comparable between the groups [Table 1].

Mean requirement of desflurane was higher in Group D than in Group L; \(P = 0.000\). No significant difference was found in the mean requirement of fentanyl and vecuronium between the groups. The mean requirement of metoprolol was found to be significantly higher in Group D than Group L; \(P = 0.01\). There was no difference in the mean requirement of nitroglycerine, atropine, and ephedrine between the groups [Table 2].

![Figure 1: Heart rate before, during and after microsurgery. B = Baseline, AI0 = Immediately after induction, AI30 = 30 min after induction (\(P = 0.000\)), M = At beginning of microsurgery (\(P = 0.000\)), M30 = 30 min after start of microsurgery (\(P = 0.004\)), M60 = 60 min after start of microsurgery (\(P = 0.000\)), AM0 = At end of microsurgery (\(P = 0.002\)), AM25 = 25 min after end of microsurgery](image)
Time taken to achieve target MAP was significantly shorter when labetalol was used along with desflurane to induce hypotension; \( P = 0.000 \). Time taken to return to baseline MAP was shorter (\( P = 0.03 \)) and emergence time was longer in the desflurane group (3.3 ± 0.8 min) as compared to the labetalol group (1.3 ± 0.5 min); \( P = 0.000 \) [Table 3].

In the immediate postoperative period, a significantly greater number of patients had sedation score “D” in Group D as compared to Group L; (27 vs. 0 patients respectively; \( P = 0.000 \)). Sedation scores at 1, 2, and 4 h were comparable between the groups. The incidence of postoperative nausea and vomiting immediately and at 1, 2, and 4 h postoperatively was comparable.

**Discussion**

Inhalational anesthetics offer the benefit of being hypnotic and hypotensive agents at clinical concentrations and are used alone or in combination with adjuvant agents for producing deliberate hypotension. Provision of surgical anesthesia, rapid onset and offset of hypotension and easy titrability make them popular as hypotensive agents. The efficacy of desflurane has been previously studied. To the best of our knowledge, this is the first study comparing desflurane and labetalol for hypotensive anesthesia. Though propofol is popular for providing hypotensive anesthesia, it does not significantly improve the surgical field, decrease total blood loss, or the operation time.\(^{[10,11]}\)

In our study, the desired degree of hypotension (target MAP 55–65 mmHg) was achieved using desflurane with or without labetalol, thus providing satisfactory operating conditions in both the groups. In the desflurane group, hypotension was achieved at the cost of an increase in HR, necessitating the use of metoprolol. Onset of hypotension was faster with labetalol, whereas return to baseline MAP occurred earlier with desflurane. Use of labetalol decreased the requirement of desflurane needed to achieve the target MAP, thereby facilitating a faster recovery from anesthesia.

The mean HR, before and after induced hypotension, was comparable between the groups. However, during the hypotensive period, HR was significantly higher in the desflurane group, and this was controlled by the administration of metoprolol. The hypotensive effect of desflurane is due to peripheral vasodilation which leads to a decrease in the systemic vascular resistance. This is accompanied by a moderate compensatory rise in HR.\(^{[5]}\) The lower HR in the labetalol group can be attributed to its beta-1 antagonist action, which prevents reflex tachycardia during induction of deliberate hypotension.\(^{[7]}\) Similar results have been reported by other investigators.\(^{[1,12-14]}\) Saarnivaara et al. used labetalol and

### Table 1: Visibility of operative field and arterial blood gas analysis

| Time                         | Mean±SD | \( P \) |
|------------------------------|---------|---------|
| **Group D**                  | **Group L** |
| Visibility at exposure       | 1.4±0.7 | 1.3±0.5 | 0.611 |
| Visibility during procedure  | 1.07±0.3 | 1.00±0.0 | 0.887 |
| Visibility at closure        | 1.00±0.0 | 1.00±0.0 | 0.891 |
| PaO₂ before start of hypotension (mmHg) | 173.3±9.8 | 171.1±9.2 | 0.766 |
| PaO₂ during hypotension (mmHg) | 166.1±10.9 | 170.9±9.8 | 0.891 |
| PaO₂ after reversal of hypotension (mmHg) | 172.35±7.7 | 175.11±7.8 | 0.787 |

\( \text{SD} = \text{Standard deviation} \)

### Table 2: Requirement of anesthetic and rescue drugs

| Drug                  | Mean±SD | \( P \) |
|-----------------------|---------|---------|
| **Group D**           | **Group L** |
| Desflurane (ml)       | 104.5±17.3 | 65.5±3.4 | 0.000 |
| Fentanyl (\( \mu g \)) | 201.0±29.5 | 206.7±25.6 | 0.891 |
| Metoprolol (%)        | 16.7 | 0 | 0.01 |
| Nitroglycerine (%)    | 6.7 | 0 | 0.733 |

\( \text{SD} = \text{Standard deviation} \)

### Table 3: Time taken to achieve target mean arterial pressure, baseline mean arterial pressure, and emergence time

| Time                              | Mean±SD | \( P \) |
|-----------------------------------|---------|---------|
| **Group D**                       | **Group L** |
| Time for target MAP (min)         | 39.82±6.2 | 33.67±7.1 | 0.000 |
| Time for return to baseline MAP (min) | 28.57±5.2 | 31.50±3.8 | 0.03 |
| Emergence time (min)              | 3.27±0.8 | 1.30±0.5 | 0.000 |

\( \text{MAP} = \text{Mean arterial pressure}, \text{SD} = \text{Standard deviation} \)
halothane to induce hypotension without any compensatory rise in HR. Combination of labetalol with halothane, enfurane, or isoflurane was found to result in a stable HR during induced hypotension.

The target MAP of 55–65 mmHg was achieved in both the groups, though two patients in the desflurane group required nitroglycerine infusion to achieve the target MAP. However, there was no significant difference in the use of nitroglycerine, atropine, and ephedrine between the groups. Both desflurane and labetalol have been successfully used to attain the desired MAP for providing hypotensive anesthesia. In fact, combining labetalol with inhalational agents produces a remarkable hypotensive synergism; labetalol is less potent in this regard when combined with intravenous anesthetics.

Mean time taken to achieve the target MAP was significantly shorter with the combination of labetalol and desflurane, as compared to when desflurane was used alone. Also found more rapid induction of hypotension when labetalol was combined with isoflurane as compared to when the latter was used alone. Mean time taken to return to baseline MAP after cessation of induced hypotension was significantly less in the desflurane group as compared to the labetalol group. A faster return to baseline blood pressure with desflurane has been observed as compared to sevoflurane and propofol. Desflurane has a low blood-gas solubility which allows for its rapid elimination and thus, a rapid reversal of induced hypotension. On the other hand, labetalol has a long elimination half-life of 5–8 h which explains the longer time taken to return to baseline MAP.

The mean emergence time was found to be statistically significantly longer with desflurane (3.3 ± 0.8 min) as compared to labetalol (1.3 ± 0.5 min). Delayed recovery in the desflurane group could be attributed to the higher concentration of desflurane required to produce deliberate hypotension (6%–9%), as compared to when it was used with labetalol (3%). In the immediate postoperative period, all patients were awake and alert in the labetalol group, as compared to only three in the desflurane group. This difference was clinically significant. Patients in both groups were, however, awake and alert at 1, 2, and 4 h postoperatively.

Recovery time was found to be longer when isoflurane alone (1.4%) was used to induce hypotension, as compared to when it was used with labetalol (0.7%). Balanced anesthesia using high dose desflurane offers significant advantages with respect to dryness of the operating site, as compared to an opioid-based anesthesia, but at the cost of a delayed immediate recovery.

Clear visibility of the operative field and satisfactory operating conditions were achieved in both groups. Kaygusuz et al. were able to provide excellent surgical conditions during middle ear microsurgery using remifentanil with desflurane or isoflurane for hypotensive anesthesia. Both esmolol and dexmedetomidine in combination with desflurane have been found to provide a clear operative field in patients undergoing tympanoplasty.

There was no significant difference in the mean PaO₂ during and after the end of the hypotensive period between the groups. This finding supports the fact that hypotension induced with labetalol produces only a minimal increase in intrapulmonary shunting and thus an insignificant decrease in PaO₂.

Postoperatively, all the patients had a stable HR, and there was no incidence of persistent hypotension or rebound hypertension. Among the postoperative side effects, nausea and vomiting were observed (attributed to middle ear surgery) and the incidence was comparable between the groups.

This study has limitations. desflurane concentration and FGF could not be kept constant between the groups till the onset of hypotension (due to the study design). Though arterial blood pressure monitoring and arterial blood gas analysis added to the cost, monitoring of these parameters was considered essential only for the purpose of the study. In clinical practice, noninvasive blood pressure monitoring can be used safely when using desflurane or labetalol for hypotensive anesthesia. Bispectral index monitoring should have ideally been used, since beta blockers may mask the clinical signs of awareness. However, it was not available to us at the time of the study.

Conclusion

We conclude that desflurane is an effective agent both with and without labetalol for inducing deliberate hypotension in middle ear microsurgery. However, the combination of desflurane with labetalol offers certain advantages over desflurane alone, due to the decreased requirement of desflurane, absence of reflex tachycardia, faster induction of hypotension, faster recovery from anesthesia, and less postoperative sedation.

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Conflicts of interest

There are no conflicts of interest.
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