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RESEARCH ARTICLE

A RANDOMIZED CONTROLLED SINGLE BLIND CROSS-SECTIONAL STUDY OF THE EFFECT OF DEXMEDETOMIDINE VERSUS ESMOLOL FOR CONTROLLED HYPOTENSIVE ANAESTHESIA IN PATIENTS UNDERGOING MIDDLE EAR SURGERY

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ABSTRACT

Aims and Objectives: Our aim of the study is to compare dexmedetomidine and esmolol as a hypotensive agent in patients posted for middle ear surgery.

Material and Methods: 60 patients (ASA physical status I–II), age group of 18–55 years scheduled for middle ear surgery were recruited for study. 30 patients to group *E* to have Esmolol whereas remaining patients were named "*D*" have Dexmedetomidin. Group D (n=30) were pre-loaded with Inj. Dexmedetomidine 1 μg/kg over 10 minutes followed by maintenance with 0.4-0.7 μg/kg/hr. Group E (n=30) received Inj. Esmolol 1 mg/kg pre-loading followed by maintenance with 0.4-0.7 mg/kg/hr as per hemodynamics. patients' cardio-respiratory parameter were continuously observed and recorded. They were also observed for surgical field, time to eye-opening and requirement of another hypotensive agent.

Observation and Results: We have observed stable hemodynamics in group D as compare to group E. We have also observed significant less time for eye opening, less requirement of muscle relaxants and inhalational agent and other hypotensive agent.

Conclusion: Dexmedetomidine is better option with good stability of hemodynamics and lesser requirements of inhalational and neuromuscular blocking anaesthetic drugs with better post operative outcome.

INTRODUCTION

Controlled hypotensive anaesthesia is deliberate and reversible lowering and maintaining of the arterial blood pressure below 50% of normal values or to a mean blood pressure of 50-65 mmHg (Kayhan Z. Klinik Anestezi, 1997). Controlled hypotension is commonly used in middle ear surgery to decrease intraoperative bleeding and to improve visualization of the operative field (Boezaart *et al*., 1995 and Cincikas and Ivaskevicius, 2003). Intraoperative bleeding impairs surgical field conditions and increase the risk of complications (Shander, 2003 and Davies, 2002). It has been suggested that Esmolol and Dexmedetomidine influence core components of an anaesthetic regimen, such as analgesia, hypnosis, and memory function and have the ability to reduce both the anaesthetic and opioid analgesic requirements during the perioperative period (Chiia *et al*., 2004 and Davidson *et al*., 2001). Laryngoscopy and tracheal intubation are associated with a sympathetically mediated increase in blood pressure by 40-50% and heart rate by 20% that may be deleterious in patients with underlying cardiovascular and cerebrovascular disease (Shribman *et al*., 1987 and Bruder *et al*., 1992).

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to ameliorate this press or response, various interventions have been tried including adrenergic blockers, vasodilators, calcium channel blockers, alpha 2 agonists, narcotics and inhalation anaesthetics. Drugs used to induce controlled hypotensive anaesthesia can provide better hemodynamic conditions during anaesthesia induction, maintenance and extubation periods by suppressing the sympathoadrenal response (Karaören *et al*., 2008). Dexmedetomidine, although does not have a direct effect on neuromuscular block, has been reported to increase plasma Rocuronium concentration, and Esmolol, by decreasing cardiac output prolongs onset time of rocuronium (Talke *et al*., 1999 and Szmuk *et al*., 2000). Less number of comparative studies are available on comparative effectiveness between Dexmedetomidine and Esmolol in controlled hypotension. The primary objective of our study was to determine effect of Dexmedetomidine in improving surgical field visibility. The secondary objectives of this study were effect of Dexmedetomidine in reduction of anaesthetics consumption, intra-operative hemodynamic changes and early recovery of patients undergone middle ear surgery from anesthesia.

MATERIALS AND METHODS

This randomized controlled trial was conducted in our hospital between February 2013 to December 2013.

After obtaining institute review board approval and written informed consent from patients, 60 patients (ASA physical status I–II), age group of 18–55 years scheduled for middle ear surgery were recruited for study. Patients with pre-existing systemic diseases (cardiovascular, respiratory, hepatic and renal diseases), known allergy to study drugs, patients on anti-hypertensives or anti-anginals were excluded from our study. 30 patients were randomized to group named " *E*" to have Esmolol along with conventional anaesthetic drugs whereas remaining patients were assigned to group named "*D*" have Dexmedetomidine in similar manner with help of computer generated block randomization sequences. Either Dexmedetomidine (4 µg/cc) or Esmolol (4mg/cc) was filled in identical syringe for infusion pump as per assignment by the anaesthesiologist who was not part of the study. This syringe was then loaded in infusion pump by another anaesthesiologist providing anaesthesia. Before induction of anaesthesia, baseline vital parameters- heart rate (HR), blood pressure, oxygen saturation and electrocardiogram (ECG) of patients were observed.

Group D (n=30) patients were administered with pre-loading dose of Inj. Dexmedetomidine 1 µg/kg over 10 minutes followed by maintenance dose with 0.4-0.7 µg/kg/hr corresponding to instantaneous hemodynamic response. Group E (n=30) patients were given Inj. Esmolol 1 mg/kg pre-loading dose over 10 min followed by maintenance dose with 0.4-0.7 mg/kg/hr corresponding to instantaneous hemodynamic response. All patients were intravenously induced with Inj. Thiopentone 5-7 mg/kg followed Inj. Succinylcholine 1-2 mg/kg. Endotracheal intubation with suitable sized Portex® cuffed oral endotracheal tube was then accomplished with direct laryngoscopy using standard Macintosh blade. Patients were maintained with O_2(40%)/N_2O(60%), Isoflurane and Inj. Vecuronium 0.1 mg/kg loading dose followed by 0.02 mg/kg maintenance dose.

During on-going surgery, patients' cardio-respiratory parameters (such as Heart rate, systolic and diastolic blood pressure, SpO_2) were continuously observed and recorded for analysis. If occurred, Intraoperative significant bradycardia (<40 HR) was treated with Inj. Atropine and significant hypotension (MAP <50 mmHg) were treated with vasopressors. At the end of surgery, patients were reversed using Inj. Neostigmine 50-70 µg/kg and Glycopyrrolate 10-15 µg/kg intravenously and were extubated.

The surgeon estimated the quality of the surgical field using a predefined category scale adopted from that of Fromme *et al*. (1986) and Shams *et al*. (2013). Average category scale for assessment of intraoperative surgical field:

0 - No bleeding
1 - Slight bleeding – no suctioning of blood required
2 - Slight bleeding – occasional suctioning required. Surgical field not threatened
3 - Slight-bleeding – frequent suctioning required. Bleeding threatens surgical field a few seconds after suction is removed
4 - Moderate bleeding – frequent suctioning required. Bleeding threatens surgical field directly after suction is removed
5 - Severe bleeding – constant suctioning required Bleeding appears faster than can be removed by suction. Surgical field severely threatened and surgery not possible.

Comparative Analysis

Intraoperative changes in systolic and diastolic blood pressure, heart rate and SpO_2 were compared in both the groups. End tidal Isoflurane concentrations were also compared in both the groups along with intermittent requirement of Vecuronium. Data were analyzed by the Graphpad Prism V.6.0 statistical software. Unpaired t-test and chi-square test were performed where appropriate. Sample size of 60 with 30 in each group was determined with statistical study power of 80%.. Data were presented in terms of mean ± SD. Standard tests of significance were applied to determine the P value. P<0.05 was considered significant.

RESULTS

A total of 60 patients were recruited for the study. No significant differences were found between the two groups in demographic data and duration of surgery (Table 1).

Table 1. Demographic Profile

Parameters	Group D n=30	Group E n=30	P VALUE	
Mean Age (years)	38.6 ± 11.9	36.06 ± 10.9	P>0.05	NS
Sex (M/F)	14/11	13/12		
Heart Rate (HR) (bpm)	84 ± 9.7	83 ± 8.6	P>0.05	NS
Systolic Blood pressure (SBP)(mmHg)	132 ± 13.4	129 ± 11.7	P>0.05	NS
Diastolic Blood pressure (DBP)(mmHg)	88 ± 9.6	87 ± 8.9	P>0.05	NS
Duration of surgery (min)	152.6 ± 27.2	158.6 ± 23.4	P>0.05	NS

NS – Non Significant S- Significant

Table 2. Intra-operative and Post-operative parameters

	Group D (n=30)	Group E (n=30)	P value
Total duration of Infusion (min)	135.6 ± 8.7	144.9 ± 9.4	P<0.05
Total Vecuronium Consumption (mg)	8.5 ± 1.5	11.0 ± 2.0	P<0.05
End tidal Isoflurane Concentration (%Iso)	0.85 ± 0.12	1.35 ± 0.14	P<0.05
Time to eye-opening(min)	3 ± 1.2	9 ± 1.7	P<0.05
Requirement of Atropine or Vasopressors	9/30 (30%)	8/30 (26.67%)	
Requirement of another hypotensive agent (Propofol/NTG)	0/30	2/30 (6.67%)	

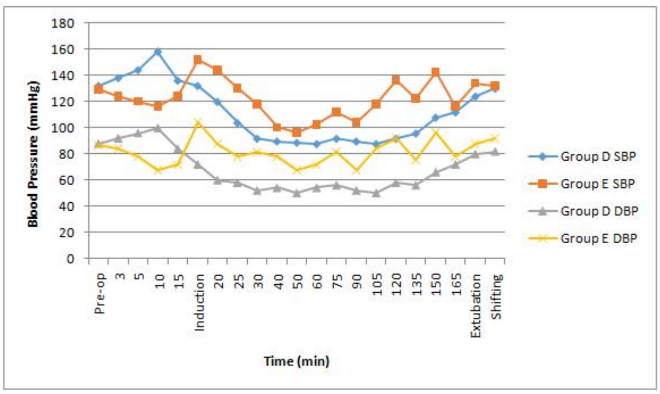

Figure 1. Change in Systolic and Diastolic Blood Pressure

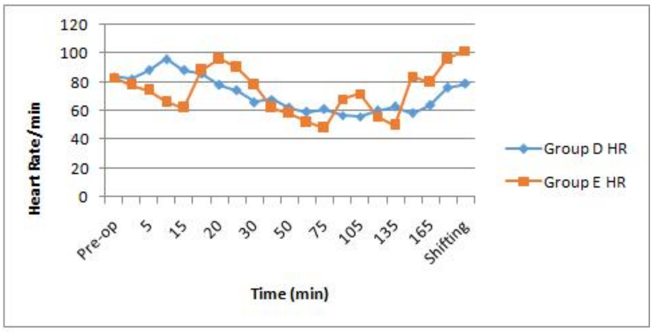

Figure 2. Change in Heart Rate

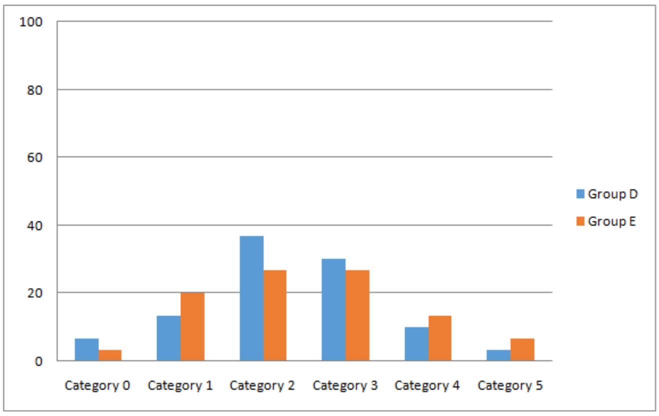

Figure 3 Comparison of surgeons' opinion regarding surgical field

We have also compared hemodynamic parameters (Fig.1 & 2) and surgeons' opinion regarding surgical field.

DISCUSSION

Previously many studies were performed related to hypotensive technique or deliberate hypotension intra-operative in different types of surgeries (Osama *et al*., 2013). Various interventions are identified to achieve controlled hypotension for reducing bleeding and thereby improving the visibility of surgical field in middle ear surgery, which is prime requirement due to microscopic nature of surgery. They are also aimed at shortening the duration of surgery by decreasing the number of manipulations and also lessening extent of microtrauma in the tissues (Newton *et al*., 1996 and Kayhan Z. Kan, 2005). In our study, we aimed to achieve optimal field by mean arterial blood pressure around 50-60 mmHg with help of a cardio-selective β blocker, Esmolol and a α2 receptor agonist, Dexmedetomidine. Pre-loading with Dexmedetomidine 1 µg/kg before induction led to transient hypertension resulted from initial peripheral vasoconstrictive effects of the drug followed by hypotension, which is result of known sympatholytic effect of α2 receptor agonist in form of inhibition of norepinehrine release (Langer, 1980) in a dose dependent manner. However, transient hypertension is self-limiting and doesn't require treatment (Yildiz *et al*., 2006). It also led to decreased requirement of Thiopentone during induction as compared to that of Esmolol due to sedative effect produced by Dexmedetomidine by activation of α2-adrenoceptors (Montazeri *et al*., 2011 and Aantaa *et al*., 1990). Dexmedetomidine obtunds the stress response in relation to laryngoscopy and intubation .Suparto *et al*. (2010) has also shown that Dexmedetomidine causes less change in mean arterial blood pressure during tracheal intubation in comparison with Esmolol and control (Tirelli *et al*., 2004). Esmolol 's similar sympatholytic effect but of less magnitude was found due to its activity through β receptors (Coloma *et al*., 2001 and Karaören *et al*., 2008). Due to hemodynamic stability in terms of blood pressure in group D, requirement of isoflurane was less compared to that of Esmolol. The requirement and duration for intermittent muscle relaxant administration was also less compared to group E. In this study, thiopental dose for induction of anaesthesia was significantly reduced in patients receiving Dexmedetomidine compared to those under Esmolol . Our findings correspond with the previous reports demonstrating anaesthesia to potentiate the effects of the drug. Aantaa *et al*. showed that preanaesthetic medication with Dexmedetomidine reduced thiopental dose for induction of anaesthesia (Aantaa *et al*., 1990 and Bloor and Flacke, 1982) Similarly, Basar *et al*. reported a decrease in thiopental dose in patients receiving Dexmedetomidine with a single dose of 0.5 µg/kg preoperatively (Basar *et al*., 2008). Dexmedetomidine produces sedation by activation of alpha-2-adrenoceptors located in the locus cerulous (Bloor and Flacke, 1982).

The reduced anaesthetic requirements, reported in the studies mentioned above and also observed in this study, seem to be related to this effect of Dexmedetomidine on the central nervous system. Previous study mentioned that time to spontaneous eye opening in group D was more. This can be accounted for by the sedative effect of the drug as it acts on the locus ceruleus. This is a small neuronal nucleus in the upper brainstem which is an important modulator of wakefulness. In our study, Time to spontaneous eye-opening after withdrawal of anaesthetics was significantly less in Group D. As less amount of isoflurane was consumed in group D, patient outcome and post-operative sedation was less in comparison with group E. (Superto *et al*., 2010 and Aantaa *et al*., 1997) has also shown similar results in their study. Depth of anaesthesia was maintained in both the groups. Superiority of Dexmedetomidine was inferred in context of improvement in operative field visibility when surgeons' opinions were mapped to interventions. Whereas hypotensive field was also maintained with Esmolol either by giving frequent muscle relaxants, higher concentrations of isoflurane or by adding other hypotensive agent.

Tanskanen *et al.* demonstrated that Dexmedetomidine plasma target doses of 0.2 and 0.4µg/mL decreased the haemodynamic responses caused by stimuli during anaesthesia14. Others noted that hypotension and bradycardia are the main side effects associated with Dexmedetomidine, in our study lowest level of mean arterial pressure was 63 mmHg(88/50 mmHg) which was maintained by reducing and manipulating the infusion doses (Lawrence and De Lange, 1997 and Guler *et al*., 2005). Guven *et al.* (2011) and Goksu *et al.* (2008) reported better hemodynamic stability, visual analog scale for pain and clear surgical field with less side effects in DEX group than placebo group. Similarly in our study we have also observed stable hemodynamics with dexmedetomidine. Esmolol associated with reduction of mean arterial pressure with bradycardia. Only side effects were observed in form of significant bradycardia with associated hypotension, which was more common (30% cases in Group E) in Esmolol group, was counteracted by Atropine and vasopressors. Unlike previous similar studies, No excessive reduction in HR or blood pressure values in the Dexmedetomidine group was seen which required treatment as compared to other groups.

Conclusion

Principles of hypotensive technique mainly includes adequate efficacy, easy-to-use and lack of toxicity at clinical concentrations . Both Dexmedetomidine and Esmolol in combination with anaesthetic regimen are well-tolerated and have shown potential to provide controlled hypotension to have better surgical field with reduction in bleeding in middle ear surgery. But, Dexmedetomidine is still better option with stability of hemodynamics and lesser requirements of inhalational and neuromuscular blocking anaesthetic drugs with better post operative outcome.

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Conflicts of interest: None

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