Esmolol and Dexmedetomidine for Controlled Hypotension in Middle Ear Surgeries - A Prospective, Open-Labeled, Single-Center Study

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Abstract

Backgroundand Aims: Controlled hypotension has been used to reduce bleeding, the need for blood transfusions and provide a satisfactory bloodless surgical field. Esmolol, a short-acting cardioselective beta-blocker and dexmedetomidine, a central α-2 adrenergic agonist both cause controlled hypotension. The aim was to study the effect of dexmedetomidine and compare it to esmolol for controlled hypotension, surgical field, dose requirement of induction agent, requirement of inhalational agent, and muscle relaxant in middle ear surgeries.

Method: This study is a prospective, open-labeled, and single-center study. 100 patients of American Society of Anesthesiologists physical Status I and IIscheduled for middle ear surgeries lasting for 2–3 hunder general anesthesiawere included. Patients were divided into two groups of 50 each by computer-generated random numbers.Group E (n=50) patients esmolol infusion and Group D patients received dexmedetomidine infusion.

Results: The two groups were comparable in terms ofhemodynamic parameters and surgical field assessment. The thiopentone dose requirement was 494 ± 12.93 mginGroup E and 354.50 ± 17.26 mg in Group D (P-0.022). The mean isoflurane concentration used in GroupsE andD was 45.30 ± 5.85 mland 13.79 ± 4.51 ml, respectively (P-0.002).The requirement of vecuronium was 11.19 ± 0.71mg in Group E and 4.58 ± 0.46 mg in Group D (P-0.009).

Conclusion: The drugs provide controlled hypotension, good surgical field and reduce pressor response equally. In addition, dexmedetomidine reduces the dose requirement of induction agent, inhalational agent, and skeletal muscle relaxant.

Keywords: Controlled hypotension, esmolol, dexmedetomidine, middle ear surgery.

Introduction

Controlled hypotension has been used to reduce bleeding, the need for blood transfusions, and provide a satisfactory bloodless surgical field for half a century [1].Ear surgeries under the microscope warrant a bloodless clear field for appropriate visualization. Esmolol, a cardioselective beta-blocker is devoid of partial agonistic or membrane stabilizing action. It can be titrated easily with its short duration of action and has been found to be useful for controlled hypotension[2].Dexmedetomidine, a central α-2 adrenergic agonist, provides controlled hypotension and gives a satisfactory operative field by reducing intraoperative bleeding in middle ear surgeries[2,3]. Thus, the two drugs were compared.

Methods

The study was conducted in collaboration with a tertiary care level institute. A synopsis of the study protocol was submitted to the Institutional Ethics Committee,andapproval was obtained. Before inclusion in the study, subjects were given all information and details about the surgical procedure, technique of anesthesia and drugs used. A written informed consent was obtained from each subject. All patients received glycopyrrolate 5mcg/kg intramuscular, ondansetron 0.08 mg/kg, midazolam 0.03 mg/kg, and pentazocine 0.3 mg/kg intravenously as premedication 15–20 minbefore induction of anaesthesia. In addition, patients in Group E received esmolol 1mcg/kg intravenous over 10 min as aloading dose and Group D received intravenous dexmedetomidine as loading dose 500 mcg/kg/min over 10 min.

Preoxygenationwas done with 100% oxygen for 3 min. Inductionwas done with injection thiopentone (5–7 mg/kg) till the loss of eyelash reflex and injection succinylcholine (2mg/kg) as a muscle relaxant. After laryngoscopy, the patient was intubated with appropriate sized endotracheal tube and maintained on 50:50 O2:N2O, inhalational isoflurane and injection vecuronium as a skeletal muscle relaxant. In addition, Group E received injection esmolol(50mcg/kg/h) and Group D received injection dexmedetomidine infusion (0.1–0.5 mcg/kg/h). The infusion was continued up to 15–20 minbefore the end of surgery. Skeletal muscle relaxant was administered as per the train of four (TOF) ratio.At the end of surgery, reversal with glycopyrrolate 10mcg/kg and neostigmine 0.04 mg/kg intravenous was done once spontaneous respiratory attempts and eye-opening were present. The patient was extubated once respiration was spontaneous and adequate,the patient was obeying commands and had good muscle tone and power. We monitored heart rate(HR) and systolic blood pressure

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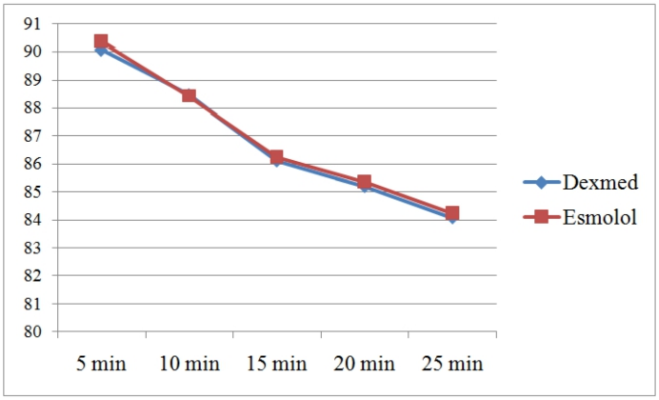

Figure 1: Comparison of systolic blood pressure in the two groups

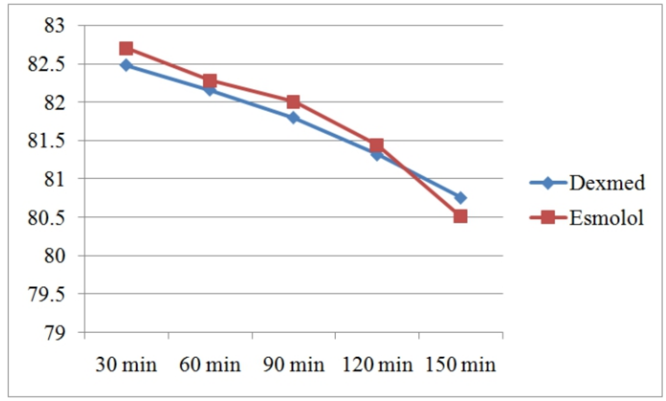

Figure 2: Comparison of systolic blood pressure in the two groups

(BP) every minute initially till loading dose of dexmedetomidine and esmolol was being administered, every minute during induction, and every minute till 5 minafter intubation followed by every 5 minfor the next 30min.Then, it was measured every 15minthroughout surgery. The amount of induction agent required was calculated, and response to laryngoscopy and intubation was noted. TOF ratio was evaluated every 30min. The amount of inhalational agent and skeletal muscle relaxant required was noted. The Dions formula was used to calculate the amount of isoflurane required. The surgical field was assessed by the surgeon using the surgical field assessment score. It was scored as;0-no bleeding,1-bleeding so mild that there was no surgical nuisance,2-bleeding a nuisance, but no interference with appropriate dissection,3-moderate bleeding, moderate compromise of surgical dissection,4-bleeding heavily, compromising with dissection but controllable,5-uncontrolled bleeding. The primary objective was to compare the two drugs in terms of fall in BP, surgical field, dose requirement of induction agent, requirement of inhalational agent and muscle relaxant. The secondary objective was to note side effects if any. The data wereanalyzed using SPSS®Version 17. All means were expressed as the mean ± standard deviation. Two independent sample t-testwas used for quantitative data, and the $\chi 2$was used for qualitative data. A difference was regarded as significant at $P< 0.05$. Preliminary sample size estimation showed that approximately 50patients should be included in each group considering the power of 80% and alpha error of 5%(95% confidence interval).

Result

We found that the two groups were comparable with regard to mean age (years), sex (male/female) and weight (kilograms) using two independent sample t-test ($P> 0.05$). Mean baseline BP in Group E it was 123.56 ± 6.81 and in Group D was 124.12 ± 7.76 (P-0.237). Similarly, during induction mean HR was 77.60 ± 5.74 in Group E (P-0.790) and inGroup D was 78.24 ± 5.98. Mean BP in Group E was 101.32 ± 3.55 (P-0.603) and in Group D it was 101.44 ± 3.25 during induction. During intubation mean HR in Group E was 75.52 ± 4.45 and in Group D was 73.76 ± 4.09 (P-0.317). At 2min following intubation, the mean HR in Group E it was 75.04 ± 5.71 and in Group D was 74.96 ± 4.73 (P-0.255). During intubation mean BP in Group E it was 95.12 ± 5.17 and in Group D was 94.88 ± 4.96 (P-0.524). At 2min following intubation mean BP in Group E was 95.56 ± (5.50) and in Group D was 95.12 ± (4.55) (P-0.251). Thus, the mean baseline BP and HR, BP, and HR at induction, during and after intubation did not show any statistical significance between the two groups. During the intraoperative period there was a fall in BP in both the groups (Fig.1 and 2) but with $P<0.05$ which shows that there is no significant difference between these study groups. The thiopentone dose requirement was 494 ± 12.93mg in Group E and 354.50 ± 17.26 mg in Group D with P = 0.022) which was statistically significant (Table2). Similarly, the mean isoflurane required in Group E and Group D was 45.30(±5.85) ml and 13.79 (±4.51) ml, respectively, with $P<0.002$ which was statistically significant (Table2).The requirement of vecuronium in milligrams was 11.19 ± 0.71 in Group E and 4.58± 0.46 in Group D. P = 0.009thus making it significant(Table2). There was no statistically significant difference in the adequacy of the surgical field between the two groups(P-0.091).

Table 1: Requirement of induction agent, inhalational agent and muscle relaxant in the two groups

Requirement of	Study group		P value
	Esmolol	Dexmed	
Induction agent (mg)	494.00 ± 12.93	354.50 ± 17.26	0.022**
Inhalational agent (ml)	45.30 ± 5.85	13.79 ± 4.51	0.002**
Skeletal muscle relaxant (mg)	11.19 ± 0.71	4.58 ± 0.46	0.009**

*Data presented as Mean ± SD. **P value < 0.05 considered significant

Disucssion

Controlled hypotension has been used to reduce bleeding and the need for blood transfusions, and provide a satisfactory bloodless surgical field. It is defined as a reduction of the systolic BP to 80–90 mmHg, a reduction of mean arterial pressure (MAP) to 50–65 mmHg or a 30%

reduction of baseline MAP[1, 2]. Middle ear surgeries require good surgical field visibility. Oozing blood obscures vision during ear microsurgery and can make correct graft placement difficult. The primary methods to minimize blood loss during middle ear surgery included mild head elevation of 15°, and infiltration, or topical application of epinephrine[3, 4]. Pharmacological agents used for controlled hypotension include those agents that can be used successfully alone and those that are used adjunctively to limit dosage requirements and, therefore, the adverse effects of the other agents. Agents used alone include inhalation anesthetics, sodium nitroprusside, nitroglycerin, trimethaphancamsylate, alprostadil (prostaglandin E1), adenosine, remifentanil, and agents used in spinal anesthesia [2]. Agents that can be used alone or in combination include calcium channel antagonists and beta-adrenoceptor antagonists. Agents that are mainly used adjunctively include angiotensin-converting enzyme inhibitors and clonidine. New agents and techniques have been recently evaluated for their ability to induce effective hypotension without impairing the perfusion of vital organs. Esmolol is a cardioselective beta-blocker which can be titrated easily with its short duration of action and has been found to be useful for controlled hypotension with an effect of capillary vasoconstriction due to unopposed alpha-adrenergic action on the mucous membrane vasculature [5]. Dexmedetomidine is a central α-2 adrenergic agonist with sedative, analgesic, and hypnotic properties maintaining respiratory stability. It provides controlled hypotension which gives the satisfactory operative field by reducing intraoperative bleeding in middle ear surgeries. Dexmedetomidine has been shown to decrease the induction dose of intravenous anesthetics, decrease intraoperative opioid, muscle relaxant, and volatile anesthetic requirements[6]. With an emphasis on multidimensional features of dexmedetomidine, the present study was designed to compare the effect of this drug and compare it to esmolol in middle ear surgeries in context with its effect to provide controlled hypotension, pressor response, hemodynamic changes, effect on the requirement of anesthetic agent, opioids, and skeletal muscle relaxant. The two groups were comparable with regard to age, sex, and weight of the patients. Our results showed that both esmolol and dexmedetomidine decreases the mean HR and mean BP and prevent the hemodynamic and sympathoadrenal responses to laryngoscopy and tracheal intubation. The results of our study are consistent with the results obtained in other studies[7, 8]. Similarly, in the intraoperative period, the BP remained at a lower level with a systolic BP between 80 and 90mmHg.Thus, it is clear that esmolol and dexmedetomidine provide controlled hypotension in middle ear surgeries of 2–3 h duration. However, the difference between the two groups was statistically not significant(Fig. 1 and 2). The results of our study are consistent with the results obtained in another study[9]. In modern anesthetic practice, we are using a variety of agents with different pharmacokinetic and pharmacodynamic profiles to maximize their benefits and minimize their adverse effects. Thus, it would be desirable to use an adjuvant which would reduce the requirement of the anesthetic agents and thus reduce the resultant side effects. By reducing the requirement of induction agent, inhalational agent, skeletal muscle relaxant and opioids, dexmedetomidine decreases the total dose of drugs that the patient is subjected to and thus decreases the risk of dose-related adverse effects. In the present study, the thiopentone dose requirement in Group E was 494 ± 12.93 and in Group D was 354.50 ± 17.26 mg with $P = 0.022$ which was statistically significant(Table2). Our results are in accordance with previous studies who observed a similar reduction in the dose requirement of thiopentone[7]. The mean amount of isoflurane used in Group E and Group D was 45.30 ml (±5.85) and 13.79 ml (±4.51) which is a 71.12% difference with $P<0.002$ which was statistically significant (Table2). We used the Dions formula for calculation of the amount of isoflurane used in milliliter[10, 11]. Isoflurane has been found to be a good agent for ear surgeries. We observed a significant reduction in isoflurane use in the dexmedetomidine group as compared to esmolol group[7, 12]. Dexmedetomidine produces a decrease in activity of the projections of the locus coeruleus to the ventrolateral preoptic nucleus. Thisincreases gamma-aminobutyric acid and galanin release in the tuberomammillary nucleus, producing a decrease in histamine release in cortical and subcortical projections. The α2agonists seem to inhibition conductance through L-type or P-type calcium channels and facilitate conductance through voltage-gated calcium-activated potassium channels. It, thus, produces subcortical depression which reduces the requirement of maintenance agent. A 62.5% reduction in the induction dose of propofol, with a 30% less end-tidal concentration of isoflurane requirement for maintenance of anesthesia was noted in other studies[13, 14, 15]. Similarly, there was a definite decrease in the requirement of vecuronium in the dexmedetomidine group than esmolol group, and the difference was statistically significant(Table2). There is no direct interaction of dexmedetomidine with the neuromuscular junction, but it is a known fact that deepening the plane of anesthesia reduces the requirement of muscle relaxant. It suggests a cortical action as cortical depression promotes unconsciousness, leading to immobility, which is opposed by ambient stimulation and the excitatory effects of pain projected on the cortex. Dexmedetomidine provides both hypnosis and analgesia. Thus, the cortical stimulation for purposeful movement is suppressed. The drug provides a more stable anesthetic plane by attenuation of the stress response. This could explain the reduced requirement of the neuromuscular blocking agent (NMBA). However,the fact that we have observed a reduced requirement of non-depolarizing NMBAs by monitoring the TOF ratio shows that there should be some other explanation for the prolongation of the duration of the NMBA like postsynaptic augmentation. Further studies are required to draw a definitive conclusion. In addition to this pharmacodynamic interaction which we assume to be present, there could be an explanation in relation to the pharmacokinetic interaction. The effect of dexmedetomidine on neuromuscular blockade with rocuronium was studied. It was concluded that the change in twitch tension was the result of the increased rocuronium concentration.The reason for the increase in plasma rocuronium concentration in the presence of dexmedetomidine was not clear. That dexmedetomidine may have altered the biodisposition of rocuronium was proposed. The clearance of rocuronium decreased by 6% over the course of dexmedetomidine infusion, which suggests that dexmedetomidine influences the pharmacokinetics of rocuronium. The above studies suggest that there could possibly be a pharmacokinetic interaction between dexmedetomidine and NMBA[16]. Adequacy of surgical field in terms of pulsatility and oozing was noted by the surgeon in both the groups. By improving the surgical field esmolol as well as dexmedetomidine provides better operating conditions for the surgeon and reduces the blood loss, thus decreasing the requirement of blood transfusion and its attending risks. We have carried out a subjective assessment by the surgeon (who was blinded) of adequacy of the surgical field[17]. However, there was no statistically significant difference between the two groups. The possible explanation could be that dexmedetomidine reduces the amount of circulating catecholamines and thus reduces the pulsatility and oozing from the surgical field. This effect could be attributed to the sympatholytic effect and hypotension and bradycardia associated with the use of dexmedetomidine[18, 19, 20]. A possible limitation of our study may have been the use of subjective criteria to determine the dose of thiopentone and isoflurane for each patient. Estimating anesthesia depth by changes mediated by the autonomic nervous system is difficult during dexmedetomidine infusion as it increases the hemodynamic stability. Intraoperative bispectral index monitoring would have been definitely more objective in deciding the depth of anesthesia and the requirement of anesthetic agent. It was not done because of practical difficulty. Measurement of the end-tidal isoflurane concentration would have been ideal to indicate the depth and for quantifying the decrease in utilization between the groups.

Conclusion

Both the drugs esmolol and dexmedetomidine provide controlled hypotension in middle ear surgery, reduce the stress response associated with intubation and surgical stimulation and minimize the intraoperative hemodynamic alterations. However,in addition, as compared to esmolol, dexmedetomidine had an advantage in terms of decrease in the dose of induction agent and intraoperative requirement of the inhalational agent as well as a muscle relaxant.

References

1. Michal B, Leiser Y, Imad A.Hypotensive anesthesia versus normotensive anesthesia during major maxillofacial surgery: A review of the literature. Sci World J 2015;2015:1-7.

2. Nasreen F, Bano S, Khan RM, Hasan SA. Dexmedetomidine used to provide hypotensive anesthesia during middle ear surgery. Indian J Otolaryngol Head Neck Surg 2009;61:205-7.

3. Degoute CS. Controlled hypotension: A guide to drug choice. Drugs 2007;67:1053-76.

4. Ryu JH, SohnSI .Controlled hypotension for middle ear surgery: A comparison between remifentanil and magnesium sulphate. Br J Anaesth 2009;103:490-5.

5. Guney A, Kaya FN, Yavascaoglu B, Gurbet A, Selmi H, Kaya S, et al. Comparison of esmolol to nitroglycerine in controlling hypotension during nasal surgery. Eurasian J of Med 2012;44:99-105.

6. Paris A, Tonner PH. Dexmedetomidine in anaesthesia. CurrOpinAnaesthesiol 2005;18:412-8.

7. Bajwa SS, Kaur J, Singh A, Parmar SS, Singh G, Kulshrestha A, et al. Attenuation of pressor response and dose sparing of opioids and anaesthetics with pre-operative dexmedetomidine. Indian J Anaesth 2012;56:123-8.

8. Shroff PP, Mohite SM, Panchal ID. Bolus administration of esmolol in controlling the haemodynamic response to tracheal intubation. J AnaesthClinPharmacol 2004;43:69-72.

9. GuptaK, Bansal M, Prashant K, Gupta P, PandeyM, Agarwal S. Dexmedetomidine infusion during middle ear surgery under general anaesthesia to provide oligaemic surgical field: A prospective study. Indian J Anaesth 2015;59:26-30.

10. Dion P. The cost of anaestheticvapours. Can J Anaesth 1992;39:633.

11. Ryksen E. Calculation of comparative utilisation and cost: Intravenous vs. inhalational anaesthesia. South Afr J AnaesthAnalg 2012;18:310-17.

12. Turan G, Dincer E, Ozgultekin A, Uslu C, Ormanci F, Akgun N. Comparison of dexmedetomidine, remifentanil and esmolol in controlled hypotensive anaesthesia. Internet J Anesth 2008;17:1-7.

13. Ghodki PS, Thombre SK, Sardesai SP, Harnagle KD. Dexmedetomidine as an anesthetic adjuvant in laparoscopic surgery: An observational study using entropy monitoring. J AnesthesiolClinPharmacol 2012;28:334-8.

14. Shams E, Bahnasawe NS, Abu-Samra M, El-Masry R. Induced hypotension for functional endoscopic sinus surgery: A comparative study of dexmedetomidine versus esmolol.Saudi J Anaesth2013;7:175-80.

15. Turan G, Ozgultekin A, Turan C, Dincer E, Yuksel G. Advantageous effects of dexmedetomidine on haemodynamic and recovery responses during extubation for intracranial surgery.Eur J Anaesthesiol2008;25:816-20.

16. Ahmad El-Awady A, Abdelhalim JM, Azer AS. Effect of dexmedetomidine on neuromuscular blockade in patients undergoing complex major abdominal or pelvic surgery. J Egypt Nat Cancer Inst 2003;15:227-33.

17. Fromme GA, MacKenzie RA, Gould AB Jr. Lund BA, Offord KP. Controlled hypotension for orthognathic surgery. AnesthAnalg 1986;65:683-6.

18. Ayoglu H, Yapakci O, Ugur MB, Uzeen L, Altunkaya H, Ozer Y, et al. Effectiveness of dexmedetomidine in reducing bleeding during septoplasty and tympanoplasty operations.J

ClinAnaesth2006;53:646-52.

19. Kol IC, Kaygusuz K, Yildirim A, Dogan M, Gursoy S, Yucel E, et al. Controlled hypotension with desflurane combined with esmolol or dexmedetomidine during tympanoplasty in adults: A double-blind, randomized, controlled trial. CurrTher Res 2009;70:197-208.

20. Guven DG, Demiraran Y, Sezen G, Kepek O, Iskender A. Evaluation of outcomes in patients given dexmedetomidine in functional endoscopic sinus surgery. Ann OtolRhinolLaryngol 2011;120:586-92.

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