Comparison Of Dexmedetomidine, Remifentanil And Esmolol In Controlled Hypotensive Anaesthesia

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Citation

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Abstract

We aimed at comparing dexmedetomidine, remifentanil, esmolol in controlled hypotension application during tympanoplasty for intraoperative bleeding, preoperative hemodynamics, recovery and adverse effects.
70 patients, undergoing tympanoplasty operation, were included in the study. For hypotension, the target SAP was calculated as 40 % below the basal value.
Group D (n=26) Dexmedetomidine 1 μg kg^{-1} (10 min), 0.2-0.7 μg $kg^{-1}h^{-1}$
Group R (n=21) Remifentanil 0.2-0.5 μg $kg^{-1}min^{-1}$
Group E (n=23) Esmolol 500 μg kg^{-1}(1 min), 50-300 μg $kg^{-1}min^{-1}$
The same surgeon performed all the operations to ensure consistency in the estimation of the surgical field. Spontaneous eye open, extubation, verbal response, cooperation and orientation time were recorded.
Groups did not differ in surgical area bleeding assessment scores. No statistically significant difference was found between postoperative recovery features. Dexmedetomidine, remifentanil and esmolol may be advisable used for controlled hypotension during tympanoplasty in respect of intraoperative bleeding, recovery and adverse effects.

INTRODUCTION

Controlled hypotension involves reducing arterial blood pressure 40-50 % below its normal range or reducing mean arterial pressure to 60 mmHg intentionally and recoverably and maintaining it at this level throughout the operation process ([1]).

Controlled hypotension is intended for reducing blood loss, thereby minimising blood transfusion requirement. Surgeries during which controlled hypotension is preferred are mostly brain surgery, ear nose and throat, orthopaedics and plastic surgery. Middle ear surgeries involve utilisation of a microscope in a small area. During these surgeries, a slightest bleeding at the surgical area would look larger due to the magnifying effect of the microscope, which could upset the surgical comfort. Controlled hypotension is employed to provide an bloodless, readily visible surgical area in middle ear surgeries ([2], [3]).

There is a variety of methods and medications administered for controlled hypotension. The ideal medication for controlled hypotension should be non-toxic, maintain cerebrovascular auto-regulation, not change cardiac performance, have short-term effect and be easily titrated ([4],[5]).

With this study we aimed at comparing dexmedetomidine, remifentanil and esmolol in controlled hypotension application during tympanoplasty operations for intraoperative bleeding, preoperative hemodynamics, recovery and adverse effects.

METHODS

70 ASA I-II patients, aged between 18-60, undergoing tympanoplasty operation, were included in the study upon consent of the hospital's ethical committee (Ref. No: 06-15) and written consents of the patients. Patients with dysrhythmia and with arterial pressure of 60 mmHg or lower were not included in the study. As a premedication 10 mg Diazepam (IM) was administered 30 minutes preoperatively. After written consents of the patients were taken, they were randomised through computer-generated method and taken in the operating room. Although 70 patients were randomised, 10 were excluded from the study. Electrocardiography and peripheral oxygen saturation (SPO_2) monitoring was performed, and peripheral vascular access was obtained. Through Allen test and local anaesthesia administered at the area, invasive arterial

monitoring was achieved through right arteria radials cannulation. Basal blood gas sample was collected. Basal systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial pressure (MAP) and heart rate (HR) values were recorded. For hypotension, the target SAP was calculated as 40 % below the basal value. In attaining the target SAP, MAP value of 60 mmHg was taken as the threshold value. In anaesthetic induction to patients, fentanyl 1 μg kg^{-1} , propofol 2.5-3 mg kg^{-1} , vecuronium 0.1mg kg^{-1} was administered. Anaesthetic maintenance was ensured through 50 % O_2-N_2 O and 3-6 % desflurane. End-tidal CO_2 ($EtCO_2$) monitoring for the patients were performed within a pressure range of 32-35 mmHg. Before surgery commenced, the skin behind the ear was infiltrated with 10 ml of 2 % prilocaine, containing 1:300 000 epinephrine. All patients were positioned with the head tilted up 20 . At the beginning of the surgery, a surgical area bleeding assessment was made by the surgical team ($_6$).

0: No bleeding- a virtually bloodless field.
1: Bleeding-so mild that it was not a surgical nuisance.
2: Moderate bleeding- a nuisance but without interference with accurate dissection
3: Moderate bleeding- which moderately compromised surgical dissection
4: Bleeding- heavy but controllable, and which significantly interfered with surgical dissection

MASSIVE UNCONTROLLABLE BLEEDING.

At the 15 th minute following the anaesthetic induction, a second blood gas sample was taken, which was recorded as the normotensive period blood gas.

Hypotensive agent was started in groups 5 minutes before the exposure of the operative field by the microscope

Group D (n=26) Dexmedetomidine 1 μg kg^{-1} (10 min) loading, 0.2-0.7 μg kg^{-1} h^{-1} infusion Group R (n=21) Remifentanil 0.2-0.5 μg kg^{-1} min^{-1} Group E (n=23) Esmolol 500 μg kg^{-1} (1 min) loading, 50-300 μg kg^{-1} min^{-1} infusion

Hypotensive agent infusions were started from the lower limit and titration was achieved with dosage increments every five minutes. Time of attaining the target SAP was recorded for each patient. The lowest MAP value was allowed to be 60 mmHg. Once the target SAP was achieved, hypotensive agent infusion was continued to maintain such value. The same surgeon performed all the operations to ensure consistency in the estimation of the surgical area (every 10 min). He was blinded to the hypotensive agent used, as well as to the monitor recording the hemodynamic variables. The ORS beep of the monitor was silenced to the surgeon could not judge the heart rate. At the 15 th minute after the target SAP is achieved, a blood gas sample was collected, which was recorded as the hypotensive period blood gas value. Where the target SAP could not be achieved although maximum infusion dose of the hypotensive agent was continued for 5 minutes, 0.1 mg nitro-glycerine bolus was administered; and it was our intention that patients who did not respond to administration of nitro-glycerine bolus for twice would be excluded. When hypotension occurred (MAP< 60 mmHg) ephedrine 10 mg (IV) was applied and hypotensive agent infusion was stopped. This patient were excluded. Bradycardia (HR < 50 beats min^{-1}) was treated atropine 0.01 mg kg^{-1} and hypotensive agent infusion was stopped. This patient were excluded.

All of the drugs were discontinued by the end of the operation. Spontaneous eye opening time, extubation time, verbal response time, cooperation and orientation time were recorded. Side effect such as nausea, vomiting, hypotension and hypertension were recorded.

STATISTICAL ANALYSIS

SPSS (Statistical Package for social Sciences) for Windows 10,0 was used for the analysis of the recorded data. The sample number of the groups were found n=13 for Power 0,80, :0,20 and :0,05 when : 0.80, SD: 0.70 was accepted for surgical area bleeding score parameter.

Additional to the descriptive statistical methods (Mean, Standard deviation), Student t test was used for the comparison of quantity of the parameters among groups. Normality of the data was tested by Kolomogorov – Smirnov method. Repeated measures data were analysed by ANOVA (analysis of variance); differences from the basal values were analysed by Bonferroni method, paired sample t test. Chi square test was used for the quality parameters. During the analysis of the results p<0,05 was accepted significant in the 95 % confidence interval.

RESULTS

No statistically significant difference was found between demographic properties of the subjects (Table 1).

Figure 1

Table 1: Patients characteristics (Mean ± SD)

	Group D (n=26)	Group R (n=21)	Group E (n=23)	P
Age (Year)	30.8 ± 8.8	29.9 ± 9.5	34.7 ± 11.4	0.279
Weight (Kg)	64.5 ± 12.1	69 ± 15.8	73.25 ± 12	0.127
Height (cm)	165.7 ± 8.8	170 ± 10.2	166.25 ± 7.6	0.266
Gender(M/F)	12 / 14	10 / 11	9 / 14	0.435

No difference was found between groups in terms of duration of anaesthesia, duration of surgery, duration of hypotensive agent infusion, starting times of hypotensive agent infusions, time of achieving the target SAP, controlled hypotension times (Table 2).

Figure 2

Table 2: Intraoperative data (Mean ± SD)

	Group D	Group R	Group E	P
Duration of surgery (min)	131.6 ± 36	130.9 ± 36.3	145 ± 37.5	0.410
Duration of anaesthesia (min)	150.7 ± 38.4	153.1 ± 36.3	159.3 ± 39.8	0.279
Duration of infusion (min)	87.05 ± 38.9	103.45 ± 33.2	92.9 ± 35.8	0.353
Time to start infusion (min)	58.3 ± 25.8	51.1 ± 20.4	55.4 ± 23.5	0.620
Time to reach target SAP (min)	15.5 ± 8.4	12.2 ± 8.3	13.75 ± 6.2	0.410
Duration of hypotensive anaesthesia (min)	71.2 ± 39.2	91.2 ± 35	79.3 ± 37.5	0.240

Groups did not differ in surgical area bleeding assessment scores. Regarding recovery features, no difference was found between groups as to spontaneous eye opening, extubation, verbal response time, cooperation time and orientation time (Table 3). None of the patients showed postoperative adverse effects.

Figure 3

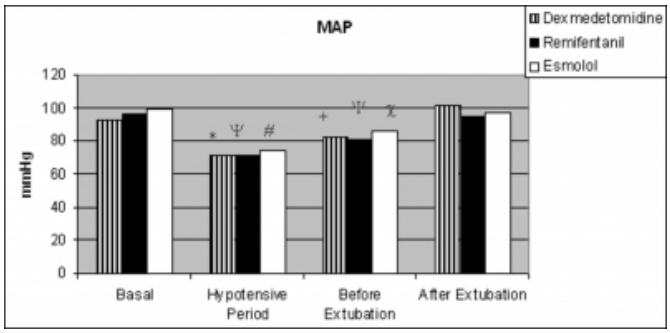
Table 3: Bleeding score and recovery times (Mean ± SD)

	Group D	Group R	Group E	P
Surgery area bleeding score	1.6 ± 1	1.7 ± 0.6	1.8 ± 0.4	0.794
Extubation time (min)	4.9 ± 2.8	6.8 ± 4.4	4.9 ± 2.6	0.126
Spontenous eye open (min)	5.9 ± 3.9	7 ± 3	4.7± 2.8	0.106
Verbal response time (min)	7.4 ± 3.4	7.9 ± 3	6.5 ± 2.8	0.364
Cooperation time (min)	6 ± 2.9	8.4 ± 3.4	7 ± 3.1	0.066
Orientation time (min)	7.9 ± 3.7	9.6 ± 4.6	8 ± 3.7	0.323

Given MAPs and HRs, no difference was found between groups, while intra-group assessments revealed statistically significant differences between basal measurements and hypotensive period and pre- and post-extubation period; however, values of the hypotensive period were within the targeted physiological limits. (Figure 1,2)

Figure 4

Figure 1: Mean arterial pressure (Mean ± SD)



* p<0.001 Hypotensive period MAPs were significantly decreased in dexmedetomidine group when compared to basal values

+ p<0.05 Before extubation MAPs were significantly decreased in dexmedetomidine group when compared to basal values

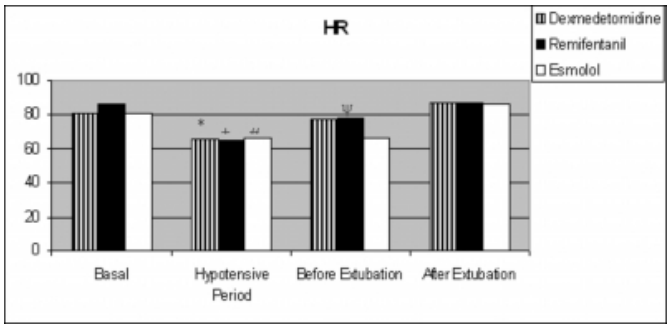
 p<0.001 Hypotensive period and before extubation MAPs were significantly decreased in remifentanil group when compared to basal values

p< 0.001 Hypotensive period MAPs were significantly

decreased in esmolol group when compared to basal values
 p< 0.01 Before extubation MAPs were significantly decreased in esmolol group when compared to basal values

Figure 5

Figure 2: Heart rate (Mean ± SD)



* p<0.001 Hypotensive period HRs were significantly decreased in dexmedetomidine group when compared to basal values
+ p<0.001 Hypotensive period HRs were significantly decreased in dexmedetomidine group when compared to basal values
 p<0.05 Before extubation HRs were significantly decreased in remifentanil group when compared to basal values
p< 0.001 Hypotensive period HRs were significantly decreased in esmolol group when compared to basal values

10 out of 70 randomised patients were excluded from the study. 1 patient of Group E and 3 patients of Group D were excluded from the study due to hypotension; 3 patients of Group D and 1 patient of Group E were excluded due to hypertension; 1 patient of Group R and 1 patient of Group E were excluded due to bradycardia. These patients were dismissed from the study.

Arterial blood gas results in pH measurements and measurements after extubation were observed to be significantly lower in Group E as compared to Group D (p< 0.01). An intra-group comparison suggested that post-extubation values in Group R and E were at physiological limits and significantly lower as compared to those of hypotensive period (p<0.05, p<0.01). Lactate levels did not differ between groups. Intra-group assessments showed that post-extubation values in Group R and E were higher than basal ones, though within normal limits (p<0.01, p<0.05)

DISCUSSION

Tympanoplasty surgeries involve various methods and agents administered to minimise bleeding at the surgical area. If inhaled anaesthetics are used to decrease blood pressure, larger inspired concentrations are used than required to provide surgical anaesthesia and it can cause more bleeding because of their peripheral vasodilator effects ([7]). Accordingly, using additional medications with hypotensive effects is more appropriate. Dexmedetomidine creates hypotensive effect with its sympatholytic effect. This agent can be applied in hypotensive anaesthetic applications. ([8], [9]). Remifentanil is an opioid with a very short lasting effect, provides stable hemodynamics in intraoperative application as compared to opioids such as alfentanil, and its effect disappears soon after the infusion is stopped ([10], [11]). Esmolol, a cardioselective blocker, can be titrated easily with its short duration of effect ([12]). There are studies investigating hypotensive anaesthetic effects and recovery properties of Dexmedetomidine, remifentanil or esmolol with different volatile anaesthetics. Dal et al. ([13]) studied on remifentanil in tympanoplasty surgeries with the doses used in our study, investigated into its hypotensive effectiveness under desflurane, isoflurane and sevoflurane anaesthetics and obtained similar hypotensive effectiveness and surgical conditions for the three inhaled anaesthetics with their use in conjunction with remifentanil.

Degoute et al. ([6]) combined remifentanil with propofol infusion which they administered in doses 0,25-0,5 μ kg $^{-1}$ min $^{-1}$ following 1 μ kg $^{-1}$ bolus in tympanoplasty surgery; they measured middle ear blood flow with laser-Doppler flow meter and found a significant decrease, and consequently a good surgical area. Our study did not use remifentanil bolus dose; however, our remifentanil infusion was not started at the beginning of the surgery but a short time after the study with the microscope. Since the patient was at a certain anaesthetic level, we did not require remifentanil bolus dose administration. Surgical area assessment in our study was not conducted with the use of subjective measurement parameters, as was the case with the study of Degoute et al. but appropriate conditions were found for all patients based on the surgical area assessment score.

Lim et al. ([14]) used esmolol for controlled hypotension in patients undergoing spinal surgery, in the same doses used in our study, by bolus and infusion later, with or without administration of acute normovolemic hemodilution. They reported that esmolol was an appropriate agent for controlled hypotension in acute normovolemic hemodilution for the prevention of blood loss in patients except those who do not have cardiovascular problems.

For the use of esmolol for controlled hypotension in tympanoplasty surgeries, Pilli et al. ([15]) reported that the achievement of the target was successful but late. Achievement of the target value later than our study's results may be attributed to the fact that they started application of esmolol directly in the lowest dose of 50 μ kg^{-1} infusion without administering bolus dose. On the other hand, we started with the loading dose prior to esmolol infusion, which suits nature of the use of the agent better. Patients who are treated with the loading dose did not report any adverse effects such as bradycardia or hypotension. Although Pilli et al. increased maximum dose up to 500 μ kg^{-1} min^{-1} as different from our study, they were late in attaining the target value.

Lawrence et al ([16]) showed that dexmedetomidine decreases skin bleeding in an animal experiment. Durmus et al.([17]) used dexmedetomidine 10 minutes preoperatively in doses of 1 μg kg^{-1} and later 0,5 μg kg^{-1} h^{-1} in tympanoplasty and septoplasty surgeries, assessed the bleeding score, and reported that dexmedetomidine decreased bleeding and facilitated earlier recovery within the framework of hemodynamic stability. They did not observe hypertension, hypotension, bradycardia or tachycardia in any of the patients. Unlike our study, dexmedetomidine loading and infusion dose was started prior to the operation. We observed hypotension in 3 patients treated with the loading dose under general anaesthesia, which required intervention. We attributed this condition to general anaesthesia volatile anaesthetic additive. Loading dose is not necessarily recommended for dexmedetomidine, and it is reported that the treatment can be started with a direct infusion dose. While hypotension may be observed after the loading dose, it may be observed after the temporary hypertension period ([18], [19]). Thus, we observed hypertension in 3 patients following loading dose. During the planning phase of our study, we had some drawbacks regarding the loading dose of dexmedetomidine, particularly in relation to hypotension as it concurred with the stable general anaesthesia period; consequently, we did not administer loading dose to 5 patients for experimental purposes, for whom we did not attain the target blood pressure and surgical bleeding was assessed to be more than usual. In light of these observations, we judged that dexmedetomidine loading dose should be administered. Given the advantage that dexmedetomidine treatment does not lead to respiratory depression, we think that using it at the very beginning of the surgery and even prior to the preoperative induction would be more appropriate.

Dexmedetomidine, remifentanil and esmolol may be advisable used for controlled hypotension during tympanoplasty operations in respect of intraoperative bleeding, recovery and adverse effects.

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