

ORIGINAL ARTICLE

Controlled Hypotension: Remifentanyl or Esmolol during Tympanoplasty

Gözde Bumin Aydın, Onur Özlü, Hale Alacakır, Mustafa Aksoy

Ministry of Health Diskapi
Education and Research Hospital
II. Anesthesiology and
Reanimation Clinic
ANKARA / TURKEY

Corresponding author:
Gozde Bumin Aydın

Adress: Mustafa Kemal Mah.
Baris Sitesi 59 sokak No:4
(Eskisehir Yolu) Ankara, Turkey

Tel: +90 312 284 10 16
Fax: +90 312 2157597
E-mail: drgozdeaydin@yahoo.com

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OBJECTIVE: Controlled hypotension is used to improve surgical conditions during middle ear surgery. New short acting drugs allow control of intraoperative blood pressure and improve surgical field for the surgeon. Our purpose is to determine whether remifentanyl or esmolol could induce controlled hypotension, provide a dry operative field.

MATERIAL AND METHODS: Thirty six adult patients undergoing tympanoplasty had an induction with propofol 2 mg/kg, fentanyl 1 (g/kg and vecuronium 0.1mg/kg were randomly assigned in two groups to receive either 1 (g/kg remifentanyl iv in 30-60 seconds, followed by a continuous infusion of 0.25-0.50 (g/kg/min, or 500 (g/kg esmolol iv in 30 seconds, followed by a continuous infusion of 100-300 (g/kg/min.

RESULTS: Controlled hypotension was achieved at the target systolic arterial blood pressure of 80 mmHg in the groups, within $222,00 \pm 79,65$ sec in remifentanyl group and $658,94 \pm 176,64$ sec in Esmolol group. The duration of hypotension was $100,33 \pm 7,79$ minutes in remifentanyl group and $64 \pm 4,37$ minutes in esmolol group. There were no difference in the mean arterial blood pressure (mmHg) values at sistolic arterial pressure of 80 mmHg between the groups. Heart rate was lower in Remifentanyl group (Group R) than Esmolol group ($p<0.05$). Mean arterial blood pressure was lower in Remifentanyl group than Esmolol group ($p<0.05$). There was significant decrease in Surgical Field Rating in Esmolol group for the first 20 minutes, but the maximum bleeding scores in Esmolol group was higher than Group R for the first 60 minutes.

CONCLUSION: Our study showed that remifentanyl was preferable in providing good, stable and reliable surgical conditions in terms of quality of operative field and provided convenient induced hypotension for tympanoplasty.

Controlled hypotension is commonly used as a means of limiting intraoperative blood losses or avoiding the need for homologous blood transfusions; it is also used to achieve a bloodless operative field which is needed for successful middle ear microsurgery^[1]. In middle ear surgery, even minor bleeding impairs the surgeon's ability to operate under an optical microscope^[2]. For this reason, arterial blood pressure must be decreased to achieve a bloodless cavity in the middle ear^[2]. In spite of the arterial pressure being reduced to very low values in many instances, there was no morbidity or mortality which could be ascribed to the technique^[3]. Various drugs have been used to facilitate the induction of controlled hypotension for middle ear surgery including vasodilators such as sodium nitroprusside^[4-7], nicardipine^[5], nitroglycerin^[5], beta-adrenergic antagonists such as propranolol^[5], esmolol^[8], alpha and beta-adrenergic antagonist such as labetalol^[9], and high doses of potent inhaled anesthetics such as halotane^[4-6]. Some disadvantages have been reported for this techniques including long postanesthetic recovery for halotane^[4], resistance to vasodilators^[4], tachyphylaxis^[10], and cyanide toxicity^[11] for nitroprusside, or possibility of myocardial depression for esmolol^[12].

Remifentanyl hydrochloride, a ultra-short acting μ -opioid receptor agonist, is now currently used to induce hypotension. Compared with fentanyl and alfentanil, remifentanyl appears to offer a superior intraoperative hemodynamic stability during stressful surgical events and maintains intact cerebral blood flow reactivity^[13-15]. Meanwhile, it appears to provoke moderate to mild hypotension^[16-17]. One advantage of remifentanyl in this indication could be its short duration of action.

Esmolol is an ultra short acting intravenous cardioselective beta-antagonist. It has an extremely short elimination half life (mean:9 minutes; range 4-16 minutes) and a total body clearance approaching 3 times of cardiac output and 14 times of hepatic blood flow^[18]. With careful titration and monitoring of the patient, esmolol is relatively safe in the management of hypertension^[19].

We designed this prospective study a) to determine whether remifentanyl or esmolol could induce controlled hypotension at a target systolic arterial blood pressure of 80 mmHg b) to determine the time to achieve this arterial pressure c) to evaluate the quality on the dryness of the operative field.

MATERIALS AND METHODS

Patients:

36 normotensive ASA physical status I-II patients aged between 18-65 undergoing tympanoplasty for tympanic membran perforation were included in the present study. Each signed consent forms were approved by the Institutional Ethics Comitee. All patients have normal middle ear mucosa, were in good physical conditon, and had good nutritional status. No neurological or psychiatric disorders were clinically detected in these patients, and none of the patients were taking any long-term medications. Patients were randomly assigned to receive either remifentanyl or esmolol infusion. All patients were fasted at least 8 hours before surgery. All patients received 3 mg midazolam im 30 minutes before operation for sedation.

Hemodynamic measurements:

After induction of anesthesia, a 22-gauge catheter was inserted into a radial artery for direct determination of arterial blood pressure systolic arterial pressure (SABP), mean arterial pressure (MABP) and heart rate (HR), which were continuously measured and recorded every five minutes from T0 until extubation. An 18-gauge catheter was inserted into a forearm vein and used for fluid and drug administration, and %0.09 NaCl was administired continuously at a rate of 5 ml/kg/hr.

Quality of the surgical field:

The quality of the surgical field in terms of blood loss and dryness, was rated every 20 minutes by the same attending surgeon who was unaware of the pharmacological treatments, using a six point scale (0 = no bleeding, virtually bloodless field, 5 = uncontrolled bleeding)^[19-20].

Surgical Field Rating (SFR)

0 = No bleeding

1 = Slight bleeding, no suction 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 suctioning 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.

Anesthesia:

Patients had propofol 2 mg/kg, fentanyl 1 (g/kg and vecuronium 0.1 mg/kg during induction, and all the patients were intubated. The anesthesia was maintained with 40 % O₂ and 60 % N₂O, 2 % sevoflurane. Controlled ventilation was adjusted to an end tidal CO₂ concentration of 35 mmHg and to insure SpO₂ > 97%.

Procedures:

After induction of anesthesia and insertion of endotracheal tube, a five minute quiet rest period was observed, then at T0 hemodynamic measurements (baseline values) were measured, and patients underwent the treatment protocol; drugs were delivered to induce controlled hypotension that was considered effective when SABP reached the target pressure of 80 mmHg. Infusion rate was adapted in order to maintain hypotension, and infusion rate was increased or decreased when SABP deviated from 80 mmHg. The time to achieve 80 mmHg SABP was recorded. When SABP>100mmHg, 50 µgr fentanyl was added intravenously, and when SABP < 80 mmHg, patients received a single bolus of 500 ml of %0.09 NaCl if unresponsive efedrine 5 mg by single intravenous bolus enjection.

Patients assigned to the remifentanyl group (Group R) received 1 µg/kg remifentanyl iv in 30-60 seconds, followed by a continuous infusion of 0.25-0.50 µg/kg/min until SABP of 80 mmHg was achieved; then infusion rate was adapted to maintain hypotension at this level.

Patients assigned to the esmolol group (Group E) received 500 µg/kg esmolol iv in 30 seconds, followed by a continuous infusion of 100-300 µg/kg/min until SABP of 80 mmHg was achieved; then infusion rate was adapted to maintain hypotension at this level. Delay in onset of hypotension was measured from T0.

Direct visual analysis of the surgical field was performed from T0 until end of surgery every 20 minutes. To obtain a fast recovery, all drugs were discontinued at least 10 minutes before end of surgery.

Statistics:

For each patient, descriptive data was expressed as mean ± SD. Comparison of groups are expressed as Mann Whitney-U test. Analyzes were performed by using SPSS software (Statistical Package for the Social Sciences, version 11.2 SPSS Inc, Chicago, IL, USA). P value <0.05 is accepted as statistically significant

RESULTS

Demographic data, duration of anesthesia, baseline hemodynamic data did not differ among groups (Table 1).

When surgical stress was avoided, controlled hypotension was achieved at the target systolic arterial blood pressure of 80 mmHg in the groups, within 222,00 ± 79,65 sec in Group R, 658,94 ± 176,64 sec in Group E. Delay in onset of hypotension was significantly lower in Group R than Group E (p<0.05). The duration of hypotension was 100,33 ± 7,79 minutes in Group R and 64 ± 4,37 minutes in Group E. There were a significant difference between duration of hypotension between groups (p<0.05). There were no difference between the MABP (mmHg) values at SABP 80 mmHg between the groups (p>0.05). Infusion rate, total dose, duration of hypotension,

delay in onset of hypotension and MABP (mmHg) at SABP 80 mmHg are shown in Table 2.

Heart rate at 45, 50, 55, 60, 65, 70 and 90 minutes decreased significantly in Group R than Group E (Figure 1) ($p<0.05$), MABP at 30, 35, 40 and 100 minutes decreased significantly in Group R compared to Group E (Figure 2) ($p<0.05$). SABP decreased significantly at 100 minutes (Figure 3) ($p<0.05$) in Group R and diastolic arterial pressure (DABP) decreased significantly at 40 and 100 minutes in Group R (Figure 4) ($p<0.05$) compared to Group E.

There were a significant decrease in Surgical Field Rating scores in Group E for the first 20 minutes than Group R (Figure 5) ($p<0.05$) but the maximum bleeding scores in Group E was higher than Group R and Group E was not a homogenous group in surgical field rating as seen in Figure 6.

There were no differences between the groups in terms of using additional drugs ($p>0.05$).

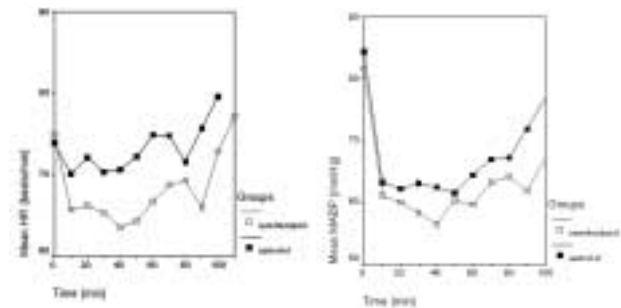


Figure-1: Heart rate changes between the groups.

Figure-2: Mean MABP differences between the groups.

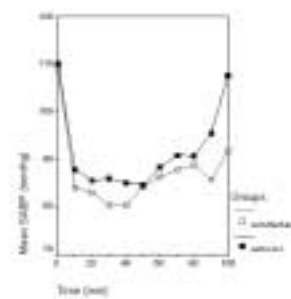


Figure-3: Mean SABP differences between the groups.

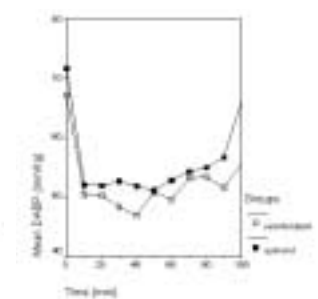


Figure-4: Mean DABP differences between the groups.

Table-1: Demographic data, duration of anesthesia, baseline hemodynamic data.

		Group R (mean \pm SD)	Group E (mean \pm SD)
Patients	Gender F/M	11/7	12/6
	Age (year)	31,89 \pm 2,19	29,94 \pm 2,14
	Weight (kg)	66,83 \pm 2,29	61,17 \pm 2,19
Duration of anesthesia (min)		123 \pm 8,5	101 \pm 3,83
Baseline SABP (mmHg)		109 \pm 2,51	110 \pm 3,22
Baseline MABP(mmHg)		81,67 \pm 2,73	84,44 \pm 3,03
Baseline HR (beats/min)		75 \pm 2,38	74 \pm 3,52

$p>0.05$

Table-2: Doses, duration of hypotension and time delay for hemodynamic effects of drugs used for controlled hypotension in the groups.

	Group R (mean \pm SD)	Group E (mean \pm SD)
Infusion rate (μ g/kg/min)	0,20 \pm 0,02	166,66 \pm 18,07
Total dose (μ g)	1,32 \pm 0,21	587,70 \pm 66,06
Delay in onset of hypotension (sec)	222,00 \pm 79,65*	658,94 \pm 176,64
Duration of hypotension (min)	100,33 \pm 7,79*	64 \pm 4,37
MABP (mmHg) at SABP 80 mmHg	61,72 \pm 1,29	60,71 \pm 1,39

$p>0.05$

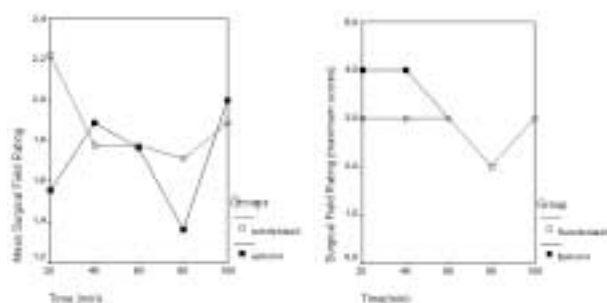


Figure-5: Mean surgical field rating.

Figure-6: Maximum scores at surgical field rating between the groups.

DISCUSSION

In the present study remifentanyl hydrochloride a) was effective in inducing consistent and sustained controlled hypotension b) was effective in providing a dry surgical field during tympanoplasty. Controlled hypotension with either remifentanyl or esmolol ensured good operative conditions. The present study shows using remifentanyl or esmolol anesthesia, moderate controlled hypotension could be achieved without administering additional antihypertensive agents in 90 % of the patients. This result is in accordance with a study comparing the use of remifentanyl, esmolol and sodium nitroprusside during tympanoplasty ^[3].

Remifentanyl is a fentanyl derivative with an ester linkage that can be broken down by nonspecific plasma esterase, making clearance independent of hepatic or renal diseases, gender, age and body weight. Even after infusion for several hours, time to recover from respiratory depression by %50 is only 6 minutes ^[18]. The hemodynamic data for esmolol is in agreement with those previous studies reported in middle ear surgery ^[4,6,8]. Esmolol induced hypotension was considered safer and more effective than nitroprusside ^[12]. Advantages of remifentanyl for controlled hypotension, shown by the present study, include a short delay of action, an ability to ensure a satisfactory operative field, hemodynamic stability and safe anesthesia by limiting surgical stress and pain. This result is in accordance with the study comparing the

use of remifentanyl, esmolol and sodium nitroprusside during tympanoplasty operations ^[3]. The evident benefit of remifentanyl for middle ear surgery shown by the present study was the dryness of the operative field by reduction in heart rate and blood pressure. In our study, decrease in baseline heart rate was more in Group R like Degoute et al's study ^[3]. Also hemodynamic variations decreased more in Group R in our study. In our study, surgical field rating in the Group E was significantly lower for the first 20 minutes. In Degoute et al's study, decrease in middle ear blood flow from baseline (recorded by laser-Doppler) was lower in the esmolol group than remifentanyl and nitroprusside groups. In our study although esmolol induced low Surgical Field Rating (SFR) in the first 20 minutes, in the view of the fact regarding maximum bleeding scores, Group R seems to be more stable and safer while Group E have some high maximum bleeding scores. Low SFR while having high hemodynamic variations can be explained by the mechanism responsible for the control of middle ear blood flow which acts by modulating vessel tone via extrinsic (blood pressure, autonomic nervous system) or local factors (autoregulation) ^[3]. Autoregulation refers to the ability of an organ to maintain flow delivery relatively constant despite variations in blood pressure ^[3]. In another study, autoregulation was defined as the relative stability of blood flow during alteration in arterial pressure ^[2]. An autoregulatory mechanism presumably exists for the control of middle ear blood flow and was not fully suppressed by remifentanyl as the non-linearity of the blood pressure - SFR relationship. Techniques that reduce blood flow and induce a dry operative field must take into account mechanisms of control of the microcirculation. Autoregulation may act as a local protective mechanism to ensure minimal tissue metabolism and so, may act against excessive and deleterious reduction of blood flow. In the esmolol group, autoregulation was not easy to interpret, decrease in SFR in the first 20 minutes was accompanied by small variations in blood pressure.

Also there was some high and some low SFR values in esmolol group. In other studies performed on skin blood flow, it is found to be relatively independent from blood pressure and heart rate ^[20-22].

In our study, SABP of 80 mmHg was chosen to define in order to preserve 'protective' autoregulatory mechanism of cochlear blood flow that exists above this value ^[23,24]. The blood flow correlates with the arterial blood pressure below SABP of 80 mmHg ^[24]. The hypotensive effect of esmolol and remifentanyl was a balanced result between their direct cardiac effect and/or vasomotor effect and the vasomotor drives originating from the counter-regulatory responses. The hypotensive effect of esmolol is due to a profound decrease in cardiac output, but in our study, the hypotensive mechanism of remifentanyl resembles esmolol by means of reduction in heart rate ^[11,19]. In our study, remifentanyl induced a decrease in heart rate which resembles the study comparing remifentanyl with nitroprusside in children during middle ear surgery ^[11].

Some studies ^[7,12] have shown that induced hypotension with a beta blocking agent enhanced norepinephrine, endocrine and metabolic responses of small magnitude during middle ear surgery; this attested that there was an increase of the sympathetic tone ^[5, 25] leading to vasoconstriction of arterioles and precapillary sphincters that resulted unopposed alpha-adrenergic effects during esmolol or remifentanyl hypotension. Lack of relationships between hypotension, heart rate and SFR observed in our study, and in Degoute's study could be explained by autoregulation, altered baroreceptor activation, enhanced sympathetic nerve activity, and/or renin angiotensin secretion ^[4,6,7,23,26].

Hemodynamic stability during hypotension and stability in SFR which was caused by remifentanyl can obviate arterial catheterization with its constraints and its risks for this specific indication.

In conclusion, our study showed that although esmolol induced low SFR scores for the first minutes,

remifentanyl was preferable in providing good, stable and reliable surgical conditions in terms of quality of operative field and provided convenient induced hypotension for tympanoplasty.

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