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ORIGINAL ARTICLE

Dexmedetomidine for Controlled Hypotension In Middle Ear Surgery with Low-Flow Anesthesia Controlled Hypotension with Low-Flow Anesthesia

Bayazit Dikmen, Fazilet Sahin, Dilsen Ornek, Yasar Pala, Oya Kilci, Eyup Horasanli, Mehmet Canturk

Chief of Anesthesiology and Reanimation Clinic, Ankara Training & Research Hospital, Ankara-TURKEY, (BD)
Niğde State Hospital, Niğde – TURKEY, (FS)
Ankara Numune Training & Research Hospital, Ankara - TURKEY, (DO, OK, EH)
Çerkezköy OptimedGüven Hospital, Tekirdağ - TURKEY, (YP)
Yozgat State Hospital, Yozgat - TURKEY, (MC)

Objectives: Controlled hypotension is commonly used to achieve a bloodless operative field which is needed for successful middle ear surgery. Dexmedetomidine can be a potential agent in controlled hypotension. In this study we investigated efficacy of dexmedetomidine as an adjunct to induce controlled hypotension in tympanoplasty with low-flow anesthesia.

Materials and Methods: Forty patients undergoing middle ear surgery were studied. Anesthesia was induced with thiopental and vecuronium bromide. Maintenance of anesthesia was achieved by 1.5 % isoflurane delivered in mixture of O2 and N2O, 4.4 L.per minute for 10 min and then flow rate was reduced to 1 L.min-1 and isoflurane concentration increased 2 %. Group Dexmedetomidine (In Group D, n=20), Dexmedetomidine (0,1μg.kg-1.min-1 for 10 minutes) was administered before induction and continued with a rate between 0,2-0,7 μg.kg-1.h-1 and Group Saline (Group S, n=20) received normal saline with a rate of 50 ml.h-1. Infusions were stopped with the end of microsurgery. Twenty minutes before the replacement of tympanic membrane greft, N2O was discontinued and then the patients were extubated. Hemodynamic parameters, quality of the surgical field and surgeon's satisfaction were evaluated.

Results: Demographic and hemodynamic data, the quality of the surgical field and surgeon's satisfaction were similar in both groups. Desired level of hypotension was achieved at the 5 th minute in group D, but in group S it couldn't be achieved until the 30th minute.

Conclusion: Dexmedetomidine was effective in inducing consistent and sustained controlled hypotension in low-flow anesthesia during middle ear microsurgery.

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Introduction

During the past 10 years, it has became a current issue interest in low-flow anesthesia in adult practice. This appears to reflect a desire to minimize wastage of expensive volatile anesthetic agents and reduce atmospheric pollution [1]. Isoflurane is suitable anesthetic agent to be used in this technic. Furthermore, isoflurane causes a dose-dependent decrease of mean arterial pressure (MAP) due to peripheral vasodilatation, whereas cardiac output is unaffected by concentrations up to 2 minimum alveolar concentration (MAC) [2]. However, isoflurane may cause rebound hypertension and reflex tachycardia. This rebound sympathetic stimulation may cause a difficult or impossible attainment of the desired level of hypotension.

Controlled hypotension is commonly used to achieve a bloodless operative field which is needed for successful middle ear microsurgery [3,4]. Although the primary premise for the use of controlled hypotension is to limit intraoperative blood loss, an additional benefit may be improved visualization of the surgical field [4]. With its pharmacological effects as reduction in heart rate and MAP, dexmedetomidine can be a potential agent in controlled hypotension. Dexmedetomidine can limit rebound hypertension and diminish both sympathetic outflow and reflex tachycardia.

The rationale for performing the study in patients undergoing middle ear microsurgery with low-flow anesthesia is that, to our knowledge, no similar study design in low-flow anesthesia in adult patients exists in the literature.

Corresponding address:
Eyup HORASANLI
Guclukaya mah.Kalan sk. No:5/10, 06310 Kecioren
Ankara-TURKEY
Phone:+ 90 312 5084229, Fax:+ 90 312 3103460, E-mail: eyuphorasanli@yahoo.com

The aim of this double-blind, controlled , prospective study was to determine the efficacy of dexmedetomidine usage as an adjunct to induce controlled hypotension in middle ear microsurgery with low-flow anesthesia .

Materials and Methods

After obtaining Ankara Numune Research and Training Hospital ethical committee approval and patient consent, we enrolled into the study 40 ASA physical status I and II patients, aged 18 to 65 years, 40 patients of whom were to undergo elective middle ear microsurgery under general anesthesia. It was performed in Ankara Numune Research and Training Hospital Anesthesia Department May 2005 and July 2005. No patient had concomitant cardiac, liver, respiratory, hematological or renal diseases, psychiatric disorders, or drug and alcohol abuse. Patients receiving monoamine oxidase inhibitors, nonsteroidal anti-inflammatory and anticoagulant drugs were excluded from the study. Other exclusion criteria included hypertension (systolic BP > 160 mmHg) and bradycardia (HR < 50 beats per min).

No preanesthetic medication was prescribed, and the patients were fasted from midnight before the operation Intraoperative fluid and blood loss were adequately compensated with Lactated Ringer's solution infusion of at 4 to 5 mL kg per hour with an infusion pump throughout the study. Arterial blood pressure (systolic, SAP, mean, MAP) and heart rate (HR) were monitored in all patients.

Patients were randomly assigned, using computer-generated random numbers and concealed envelops for dexmedetomidine (Group=D, n=20) and saline (Group=S, n=20) groups. The 20 patients per group were chosen by prospective power analysis based on data from previous studies. In our study 20 patients per group would give 80% power with α= 0.05 to detect 30% difference in MAP between groups. Study drugs were prepared by an independent anesthesiologist. All operating room anesthesiologists, surgeons, and nurses were blinded to the study protocol. Solution of infusion in Group D was prepared as 2µg.ml-1 dexmedetomidine in normal saline(49ml saline+1ml dexmedetomidine). The dexmedetomidine solution was administered to patients in Group D at a rate 0,1µg.kg per minute. for 10 minutes and the infusion was continued after induction with a rate between 0,2-0,7 µg.kg per hour.hand Group S received normal saline with a rate of 50 ml. per hour via an enjector type infusion pump. Infusion of solutions were stopped with the termination of microsurgery and infused dose of dexmedetomidine was recorded.

Patients were monitored with electrocardiography, a pulse oximeter (SpO2), end-tidal carbon dioxide tension (EtCO2) and inhalational agent monitor(Datex-Ohmeda ADU S/5, Finland). Inspired O2 concentrations (FiO2),EtCO2, SpO2, MAC of isoflurane were recorded during the anesthesia.. Approximately 3 minutes before induction of anesthesia 1.5 mg.kg-1 lidocaine was administered intravenously. Anesthesia was induced initially with 2 mg. per kg thiopental supplemented with 25mg i.v. boluses at every 15 s until loss of eyelash reflex. Vecorunium bromide (0.1 mg.per kg i.v.) was administered to facilitate endotracheal intubation. Maintenance of anesthesia was achieved by 1.5 % isoflurane delivered in mixture of 35 % O2 and 65 % N2O , 4.4 L per min for 10 minutes with a fresh gas flow and then flow rate was reduced to 1 L per min with 2 % isoflurane in mixture of 50 % O2 and 50 % N2O. 20 minutes before the replacement of tympanic membrane greft, N2O was stopped and switched to medical air. During the N2O free period, if SAP and HR were measured 20 % higher than the value when N2O was stopped, fentanyl citrate 50µg was administered intraveously for analgesia. Isoflurane was stopped and comsumption of isoflurane was recorded. The patients were started to be ventilated by SIMV during 10 min before the end of the surgery. Flow rate was increased to high-flow during 5 min before the end of the surgery. Then the patients were exubated and extubation and operation time were recorded.

Hypotension was induced by increasing the inspired concentration of isoflurane until the desired MAP 50-65 mmHg was achieved. If MAC of isoflurane exceeded 2.5 and desired level couldn't be achieved, fentanyl citrate 50µg was given intravenously.

The quality of the surgical field in terms of blood loss and dryness, was rated every 10 min 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). Surgeon's satisfaction was rated with a four-point scala (0= unsuccessful, 3= very good)[3].

The data (FiO2,SpO2,ETCO2,SAP,MAP,HR,MAC) that was used for statistical analysis included the values obtained at the beginning of the infusion, before

induction, after induction, immediately after intubation, 5 , 10 min after intubation, after the skin incision, 30 , 45 , 60 , 90 , 120 , 150 min before and after extubation. Microsurgery was started at the 30 min of entubation.

The comparison of groups was carried out with mean and standard deviation values by SPSS 11.0 package program. Demographic paramaters were compared with Mann-Whitney U test and Chi Square test with Fisher's exact correction when appropriate. Comparisons of the data within a measurement period between two groups were performed by the Mann-Whitney U test. Friedmann two-way analysis of variance was used for comparisons of measurement periods within each group. Where statistical significance was found, the Wilcoxon signed rank test with Bonferroni's modification was used to deliniate the difference. For comparison of 30% decrease in basal MAP measurement periods within each group the Chi Square test with Fisher's exact correction were used. P value of the less than 0.05 was considered significant

Results

Patient's demographic data (Table 1), FiO2, SpO2, ETCO2 and preoperative hemodynamic parameters, the quality of the surgical field and surgeon's satisfaction were similar in two groups ($p>0.05$) (Table 2).

After intubation, SAP and MAP increased in the group S, SAP and MAP were similar compared with baseline measurements in the group D (Figure 1, 2). Although desired level of hypotension was achieved at the 5 th min in the group D, in the group S it couldn't be achieved until the 30th min ($p<0.05$). 30 % decrease in basal MAP in the Group D was 80 % at the 30th min, it was 22 % in the Group S and the difference between two groups was significant ($p<0.05$). HR in the Group S was higher than in the Group D ($p<0.05$) (Figure 3).

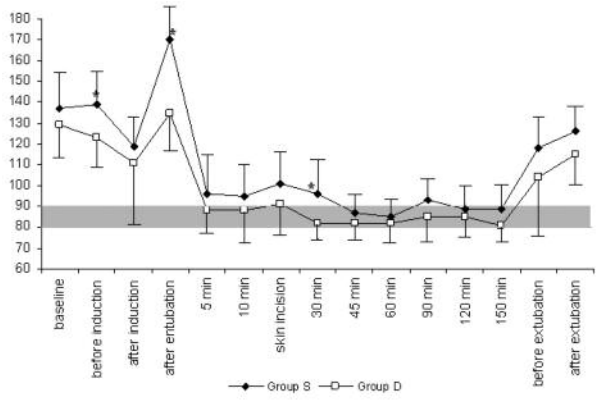

Figure 1. Systolic arterial pressure

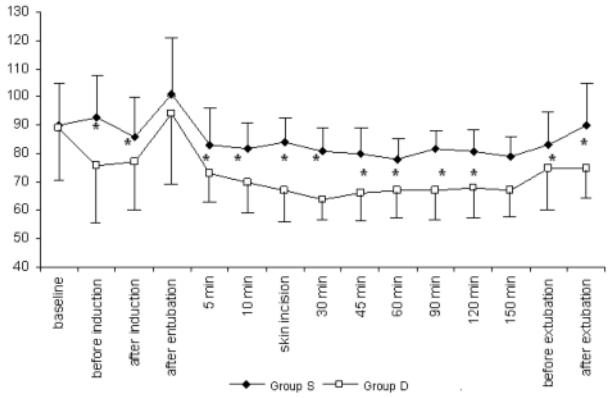

Figure 3. Heart rate

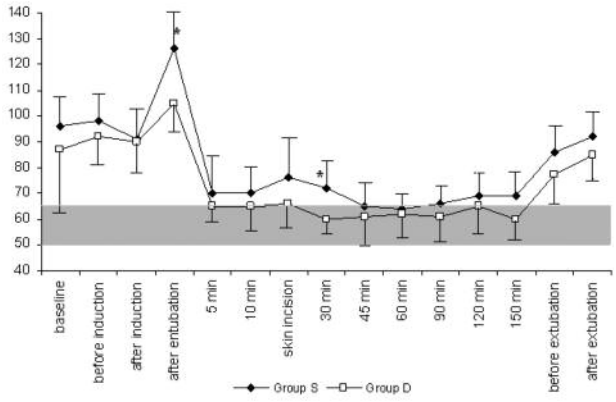

Figure 2. Mean arterial pressure

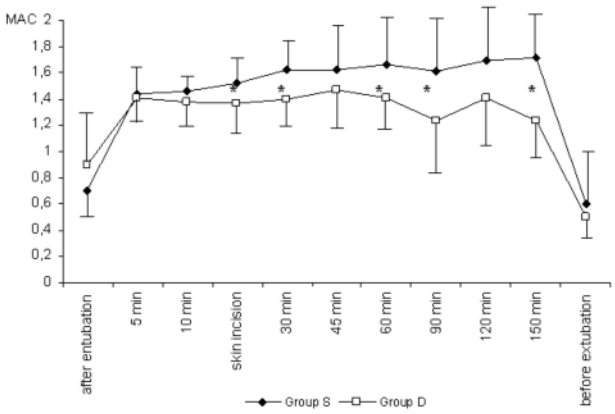

Figure 4. Minimum alveolar concendration

Bradycardia, as defined by fewer than 50 bpm, were not observed in any of the dexmedetomidine or control group patients. Hypotension, as defined by MAP levels less than 50 mmHg during surgery were only one patient in the Group D . MAC of isoflurane in the Group D was less than in the Group S, but this difference was not statistically significant ($p>0.05$) (Figure 4).

Discussion

In the present study, we found that dexmedetomidine, decreased induction dose of thiopental, reduced hemodynamic reaction to intubation and extubation, maintained controlled hypotension and decreased consumption of isoflurane in low- flow anesthesia.

Controlled hypotension has been defined as a reduction of systolic blood pressure to 80 to 90 mmHg or a 30 % reduction of baseline MAP. It has been used to limit intraoperative blood loss and it may improve visualization of the surgical field. Advances in drug therapy have provided the clinician with several options for controlled hypotension.

Dexmedetomidine is an imidazole compound [5]. It displays specific and selective α2- adrenoceptor agonism. For α2- adrenoceptor, dexmedetomidine is 8 times more specific than clonidine [6]. Drugs acting as agonists at α2- adrenoceptors may enhance anesthesia by providing dose-related sedation, anxiolysis, decreased upper airway secretions, peroperative hemodynamic stability and analgesia [6,7]. There is substantial evidence that the α2-agonists also exert an anesthetic-sparing effect mediated in part through a decrease in central noradrenergic activity, but mainly through a direct effect on central α2- adrenoceptors in the locus coeruleus and other sites [8,9]. The pharmacologic profile of dexmedetomidine indicates that this drug has potential in controlled hypotension and clinical data are needed to define its role [10].

There are several potentional benefits of using the inhalational anesthetic agents for controlled hypotension, including their ease of titration, ease of administration (without the need for infusion pumps etc), ready availability in every operating room, combined hypotension and anesthetic action, and rapid reversal of the effect with discontinuation. Due to its specific pharmacokinetic and pharmacodynamic properties, isoflurane is suitable anesthetic agent to be used in low-flow anesthesia. Based on its pharmacologic actions, including a decrease in heart rate and MAP, it may be useful agent for controlled hypotension. Both sudden and gradual increase of the inspiratory concentration of isoflurane to 3 % elicit the same speed of induction of hypotension in man [11]. The desired level of MAP was obtained in 10 -14 min [11,12]. In our study, the desired level of MAP in the control group was achieved in 30 min. We think that this situation can arise from low-flow anesthesia. Dexmedetomidine administration can be a useful adjuvant for controlled hypotension in middle ear microsurgery because it facilitates the speed of induction of hypotension in low-flow anesthesia.

Low-flow anesthesia may reduce amount of anesthetic. Isoflurane uptake is large in the first few minutes, requiring high flow and concentration to deliver sufficient anesthetic to the circuit and alveoli, and blood and vessel-rich compartment concentrations soon increase. As the blood concentration increases, uptake progressively decreases. If higher maintenance gas flow rates are used, uptake remains the same but more isoflurane is wasted. However, if the carrier gas flow is reduced after the 10-15 min, uptake is the same but wastage is reduced [1].

Madsen et al [12] reported rebound hypertension after discontinuation of isoflurane, suggesting that isoflurane does not entirely prevent reflex sympathetic stimulation. Resistance to the hypotensive effects of isoflurane may occur in a significant percentage of patients. Isoflurane has prominent vasodilatory properties and therefore reflex tachycardia is commonly encountered, especially in younger patients. Recent studies in animals and patients showed that combining isoflurane with different drugs, which were used for controlled hypotension attenuated the negative effects of isoflurane [13,14].

Tobias et al were used dexmedetomidine for controlled hypotension in spinal surgery and found that dexmedetomidine could be titrated to achieve the desired MAP without reflex tachycardia [15]. We preferred dexmetetomidine as an adjuvant for controlled hypotension in the middle ear microsurgery with low-flow anesthesia. Our data showed that infusion of dexmedetomidine was effective in inducing consistent and sustained controlled hypotension in low-flow anesthesia.

Previous studies have reported attenuation of hypertension and tachycardia in response to laryngoscopy and intubation by dexmedetomidine [16-18]. Studies in healty surgical patients and volunteers have shown that dexmedetomidine has centrally mediated

sympatholytic effects [18-,20]. Our data consistent with those of others, which show that dexmedetomidine attenuated hypertension and tachycardia in response to laryngoscopy and intubation, skin incision and extubation[17-19].

Furthermore, we found that dexmedetomidine in low flow-anesthesia decreased consumption of isoflurane from 28.4±11 ml to 21.2±14 ml in the Group D. Dexmedetomidine has been shown to reduce peri-operative dose requirements for thiopental [21], propofol [22], fentanyl [23] and isoflurane [24, 25]. Kahn et al [26]showed a left shift in isoflurane dose-response curves in volunteers receiving an infusion of dexmedetomidine. Dexmedetomidine 0.35 ng.ml-1 decreased isoflurane requirements to prevent movement in response to a noxious stimulus by 35 %; dexmedetomidine 0.75 ng.ml-1 decreased isoflurane requirements by approximately 50 % 26 [16]. Our data are consistent with those of others. Aantaa et al [16] showed that clinically relevant doses of dexmedetomidine induced a dose-dependent and significant reduction of isoflurane MAC in persons having surgery. We found that MAC of isoflurane in the Group D was less than in the Group S, but there was no statistical difference.

There are some limitations in our study, that we couldn't measure middle ear blood flow and depth of anesthesia. However we assessed the quality of the surgical field in terms of blood loss, dryness and surgeon satisfaction by the same attending surgeon who was unaware of the pharmacological treatments. We found that infusion of dexmedetomidine achieved clear surgical field during middle ear surgery In conclusion, present study showed that dexmedetomidine was effective in inducing consistent and sustained controlled hypotension, and achieved clear surgical field during middle ear surgery with no need for additional use of a potent hypotensive agent in low-flow anesthesia. Dexmedetomidine also reduced isoflurane and fentanyl requirements for deliberate hypotension and attenuated cardiovascular responses perioperatively.

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