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The effect of propofol infusion with topical epinephrine on cochlear blood flow and hearing: An experimental study

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ABSTRACT

Background and objective: Propofol is the most commonly used intravenous (IV) anesthetic agent and is associated with hypotension upon induction of anesthesia. Intravenous propofol infusion has several properties that may be beneficial to patients undergoing middle ear surgery. Topical application of concentrated epinephrine is a valuable tool for achieving hemostasis in the middle ear and during mastoid surgery. The purpose of the present study was to determine the effects of propofol infusion with topical epinephrine on cochlear blood flow (CBF) and hearing in rats.

Materials and methods: Twenty one male Sprague-Dawley rats were divided into three groups. The rate of intravenous infusion of propofol was 4–6 ml/kg/hour. The first group (control group, n = 7) was given IV infusion of phosphate buffered saline (PBS) with topical application of PBS in the round window. In study group A (n = 7), the effect of topical phosphate buffered saline with IV infusion of propofol on CBF and hearing was evaluated. In study group B (n = 7), additional effects of topical epinephrine with IV infusion of propofol on CBF and hearing were evaluated. The laser Doppler blood flowmeter, CBF, and the mean arterial blood pressure (MAP) were measured and analyzed. Additionally, hearing test using auditory brainstem response (ABR) was performed in both groups.

Results: In both groups, infusion of propofol induced a time-dependent decrease in MAP. Approximately 30 min after the start of the propofol infusion, the CBF started to decrease slowly. The decrease in CBF was significantly greater in the study group compared to the control group. The threshold was elevated in the study group relative to the control group.

Conclusion: During middle ear surgery, use of IV infusion of propofol with topical epinephrine cotton ball or cottonoid application is not recommended.

1. Introduction

Tympanoplasty or tympanomastoidectomy may be performed under local or general anesthesia [1,2]. Recently, common middle ear surgeries, including tympanoplasty and mastoidectomy are being performed under local anesthesia with sedation [3–5].

Propofol is an emulsive form of diisopropylphenol developed initially as an intravenous (IV) general anesthetic. The advantages of propofol use during outpatient surgical procedures include its minimal side effects, controllable anesthetic state, rapid onset of action, complete and clear-headed recovery of consciousness, and the rapid recovery of psychomotor and cognitive function [6]. The IV propofol infusion has several properties that may benefit patients undergoing middle ear surgery. For instance, a bloodless surgical field is ideal, as even small amounts of blood will obscure the surgeon's view during microsurgery. Furthermore, controlled hypotension technique has often been used in anesthesia procedure during surgery and propofol provides.

induced hypotension with no need for additional hypotensive drugs [4–6]. Use of a controlled hypotension is helpful for bloodless

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surgical field, but it is often accompanied by side effects [7–9].

The cochlear microcirculation is considered to be a key factor contributing towards cochlear fluid homeostasis which is similar to the cerebral blood flow regulation system. It is sensitive to both systemic arterial pressure and local factors [10]. To date, there are only two clinical articles and one research paper on the relationship between propofol and cochlear blood flow (CBF) that have been published [11–13]. These two clinical trials on the effects of propofol on CBF changes with patients who underwent middle ear surgery did not provide consistent conclusion. No previous study has assessed the effect of propofol induced hypotension. Systemic hypotension must be considered as the potential cause responsible for the development of sudden sensorineural hearing loss in young, healthy individuals due to cochlear ischemia [14].

Clinically, topical application of concentrated epinephrine is a valuable tool for achieving hemostasis during middle ear and mastoid surgery. Cotton ball or gelatin sponge soaked in 1:10,000 epinephrine solution is helpful, when resecting the diseased middle ear mucosa or granulation tissue [15]. However, epinephrine can penetrate the round window membrane and act as a vasoconstrictor for the cochlear vasculature. Therefore, we speculate that IV infusion of propofol combined with topical application of epinephrine in the middle ear might accelerate cochlear ischemia.

The purpose of the present study was to assess the combined effects of propofol infusion with topical epinephrine on CBF and hearing changes in rats.

2. Materials and methods

Twenty one male Sprague-Dawley rats (mass: 300–350 g) with normal tympanic membranes and Preyer reflexes were tested. They were housed separately in sterile cages in rooms with a constant temperature of 22 °C, humidity of 50%, and an ambient noise level <40 dB. All animal experiments followed a protocol approved by the Committee for Animal Experimentation at Chonnam National University, Korea (CNU IACUC-H-2016-31). The animals were anesthetized in order to expose the cochlea, with an intraperitoneal injection of a mixture of Zoletil 1 (a 1:1 combination of tiletamine/zolazepam; Virbac, Carros, France) and xylazine hydrochloride. The animals were randomly divided into three groups which consist of 7 animals each. The first group (control group) was given IV infusion of phosphate buffered saline (PBS) with topical application of PBS in the round window. The second group (study group A) was infused with propofol with topical application of PBS in the round window. Anmials in the third group (study group B) were given the propofol infusion with topical epinephrine in the round window. The CBF was measured in each animal, according to a method previously described [16]. In brief, the right femoral artery was cannulated and connected to a pressure transducer (AD Instruments, Castle Hill, Australia) for measurement of arterial blood pressure. The right femoral vein was cannulated as well for propofol infusion, using an infusion pump. A ventral approach was used to expose the right tympanic bulla and it was opened by drilling. After the middle ear mucosa over the bony wall of the cochlea was removed, a 1.0 mm needle probe of a laser Doppler blood flow meter (moorLAB, Moor Instruments, Axminster, Devon, UK) with a cotton pledget was placed on the lateral wall of the basal turn of the cochlea (Fig. 1). The CBF output and systemic blood pressure (SBP) data were sampled every 20 s, and were analyzed by a computer that was equipped with a data acquisition program (PowerLab, AD Instruments). Immediately following baseline measurements, IV propofol infusion was titrated. Fixed doses used in the current study were derived from Brammer et al. [17]. The IV infusion rate was set at 4–6 ml/kg/hour. For both the control and group A, 10 μL of PBS soaked in gelfoam was placed in the round window niche for 10 min. For group B, 10 μL of epinephrine 1:10,000 (Bosmin, Solution 1 mg/ml, Je Il Pharm, Seoul, Korea) soaked in gelfoam was placed at the same point and for the same duration as the control and group A. Gelfoam was then removed gently by suction through a cotton wick from the niche. All parameters of the measurement were recorded on PowerLab. The data were displaced, using Sigmaplot software. All data were expressed as a mean value. The three groups were compared with each other, using an analysis of variance (ANOVA) and Wilcoxon paired matching test with P values of <0.05 to be considered as statistically significant.

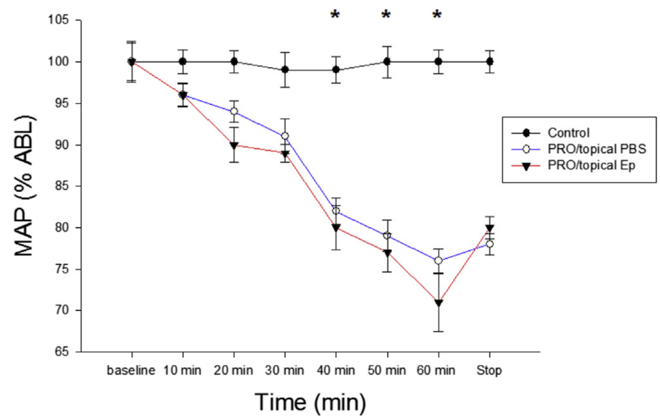

Fig. 1. Intravenous infusion of propofol produced a significant time-dependent decrease in the mean arterial pressure (MAP) of both experimental group compared to control group (Asterisk, $p < 0.05$). There was no significant difference between experimental group A and B.

Auditory brainstem response (ABR) was recorded using an evoked potential system (Tucker-Davis Technologies, Alachua, FL, USA). Acoustic stimuli consisting of an auditory click (low frequencies less than 4 kHz) and tone burst stimuli at 4, 8, 16, and 32 kHz were produced. The stimulus was presented at 90 dB sound pressure level (dB SPL) and progressively stepped in a downward direction by 10 dB until no response was identifiable. Auditory brainstem responses were assessed preoperatively, 30 min and 1 day after the treatment. ANOVA was used to test for differences in the ABR thresholds among three groups. A separate model was used for each frequency. Pairwise contrasts were used to determine if the effect of topical treatment with epinephrine inhibitor was statistically significant ($P < 0.05$).

3. Results

In both study groups, MAP decreased in a time-dependent manner after 10 min (Fig. 1). Compared to the control group, the study groups showed a significant reduction in MAP in a time-dependent manner after 30 min, but baseline values were restored after propofol infusion was discontinued. However, there was no significant difference between the study groups A and B ($P > 0.05$). Compared with the control group, the study groups showed a reduction in CBF in a time-dependent manner. The maximal reductions in CBF were observed in both study groups at 60 min after the start of propofol infusion. The maximal decrease in CBF was 85.1% in group A and 58.9% in group B. However, CBF was restored after infusion of propofol was discontinued in both study groups. The reduction pattern in CBF was quite different between the two study groups. In group A, CBF showed no significant reduction compared to the control group, except only after 60 min. In this instance, the CBF was not influenced significantly by a reduction in MAP until only after 50 min from the titration point of