

The effect of sevoflurane anesthesia on the corneal endothel

Nihat Polat¹, Ahmet Selim Ozkan², Abuzer Gunduz¹, Pamuk Betul Ulucan¹, Cemil Colak³

¹Inonu University Faculty of Medicine Department of Ophthalmology, Malatya, Turkey

²Inonu University Faculty of Medicine Department of Anesthesiology, Malatya, Turkey

³Inonu University Faculty of Medicine Department of Biostatistics, Malatya, Turkey

Abstract

Aim: To evaluate the mean changes in corneal endothelial cells in eyes that operated under sevoflurane general anesthesia.

Material and Methods: 32 eyes of 32 patients who had extraocular surgery under general anesthesia included in this prospective study. Cell density (CD), Coefficient of Variation (CV) and Hexagonality rate (Hex) specular microscopy results at before surgery and 1 week and 1 month after surgery were analyzed.

Results: The mean age of the patients was 15 ± 10 (min 4- max 36). The mean operation time of the patients was 90 ± 15 minutes. The mean preoperative CD value of the study subjects was 3097 ± 15 cell/mm². The mean postoperative CD value was 3119 ± 194 cell/mm² at the 1. week and 3120 ± 207 cell/mm² at the 1. month ($p=0.678$). The mean preoperative CV was 0.27 ± 0.4 while the postoperative 1. week value was 0.27 ± 0.4 , and the postoperative 1st month value was 0.27 ± 0.5 ($p=0.319$). The mean preoperative Hex value of the study subjects was $53 \pm 10\%$. The mean postoperative Hex value was $54 \pm 11\%$ at the 1. week and $55 \pm 10\%$ at the 1. month ($p=0.992$). No significant difference was present between the periods in terms of CD, CV and Hex.

Conclusion: There is no change in the corneal endothel in patients who suffered general anesthesia with sevoflurane.

Keywords: General Anesthesia; Corneal Endothel; Sevoflurane.

INTRODUCTION

The corneal endothelium is composed of single-layer hexagonal cells and that is placed on the descemet membrane. Age-related endothelial cell loss is about 0.5% per year (1). Hexagonal cell percentage is also gradually decreasing from 75% (2). Trauma, intraocular surgeries and intraocular implants, intraocular inflammations such as chronic uveitis, acute angle closure glaucoma attacks, laser applications may endothelial damage and cause the number of cells to fall below normal limits for age (2). The endothelium, pumps the fluid back that entering the cornea by endothelium pump and so keeping the corneal water level constant. Na⁺, K⁺ -ATPase, which is abundant in the lateral wall of the endothelial cells, transports Na to the intercellular space and K into the cells. Passive water flow from the endothelial cells to the anterior chamber is achieved by creating an osmotic difference resulting from the low concentration of Na in the stroma (3,4). As the ability of the endothelial cells to proliferate is very limited, when the number of cells in the endothelium decreases for anyreason, the size and shape of the neighboring endothelial cells change and thus the water content of the cornea is tried to kept constant (5). This causes appeararent of different sizes of cells (polymegathism), a decrease in the ratio of hexagonal cells (pleomorphism)

and increase of different geometric shaped cells (6). Polymegathism and pleomorphism should be evaluated together with the endothelial cell density in order to estimate the healthy cell reserve.

Sevoflurane is currently the most commonly used general anesthetic agent. Studies have shown that sevoflurane and its metabolites may damage renal tubule cells during renal excretion, depending on the duration of anesthesia and the toxicity ratings of degradation products. As a result of these damages, changes from in the ability of reabsorbing in the proximal tubules as far as necrosis may occur (7-9). Therefore, during anesthesia, this agent is also likely to cause toxic effects on the corneal endothelium. In our study, we aimed to evaluate the effect of sevoflurane on corneal endothelium using specular microscopy data.

MATERIALS and METHODS

The study was conducted at Inonu University Medical Faculty Ophthalmology Department according to Helsinki declaration. Approval of the ethics committee for the study (Reference Number: 2015/92) was obtained. Informed consent was obtained from all patients. This prospective study involved 32 eyes of 32 patients who underwent strabismus surgery. 26 of all were operated because of esotropia, 6 of all were operated because of exotropia and

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Corresponding Author: Nihat Polat, Inonu University Faculty of Medicine Department of Ophthalmology, Malatya, Turkey
E-mail: drnihatpolat@gmail.com

at most two muscle surgeries were performed. Patients who had any intraocular surgery, refractive surgery, uveitis, glaucoma, retinopathy, corneal dystrophy, globe trauma history and any systemic chronic disease, long term topical or systemic drug use were excluded. Patients who developed any complications during or after surgery were also excluded from the study. All patients best corrected visual acuity (BCVA) with Snellen chart, intraocular pressure (IOP) measurement with applanation tonometry, and fundus examinations was done at preoperatively, and at the first week and the first month postoperatively. Specular microscopy and pachymetry was done by Konan specular microscopy (Konan Medical Inc. Nishinomiya, Japan) at preoperatively, and at the first week and the first month postoperatively. Cell density (CD), Coefficient of Variation (CV) and Hexagonality rate (Hex) values were used for endothelial cell investigations.

Statistical analysis

The data were analyzed in a computer program using SPSS 22.0 (Microsoft Inc., Chicago, IL, USA). Preoperative and postoperative values were compared using the Friedman test. A p value of less than 0.05 was considered statistically significant.

RESULTS

Of the patients participating in the study, 21 were male and 11 were female. The mean age of the patients was 15 ± 10 (min 4- max 36). The mean operation time of the patients was 90 ± 15 minutes. There was no statistically significant difference between the preoperative and postoperative periods in the BCVA and IOP measurements of the patients ($p > 0.05$). The mean preoperative CD value of the study subjects was 3097 ± 15 cell/mm². The mean postoperative CD value was 3119 ± 194 cell/mm² at the 1. week and 3120 ± 207 cell/mm² at the 1. month ($p=0.678$). The mean preoperative CV was 0.27 ± 0.4 while the postoperative 1. week value was 0.27 ± 0.4 , and the postoperative 1st month value was 0.27 ± 0.5 ($p=0.319$). The mean preoperative Hex value of the study subjects was 53 ± 10 %. The mean postoperative Hex value was 54 ± 11 % at the 1. week and 55 ± 10 % at the 1. month ($p=0.992$). No significant difference was present between the periods in terms of CD, CV and Hex. The mean preoperative pachymetry was 566 ± 33 μ m while 570 ± 33 μ m in the first postoperative week and 561 ± 38 μ m in the first postoperative month. There was no significant difference between pre- and postoperative corneal thicknesses ($p= 0.421$) (Table 1).

Table 1. Changes of corneal endothelial specular microscopy values according to periods.

Variables	Preoperative values (Mean \pm SD)	Postoperative first week values (Mean \pm SD)	Postoperative first month values (Mean \pm SD)	p
CD (cell/mm ²)	3097 \pm 15	3119 \pm 194	3120 \pm 207	0.678
CV	0.27 \pm 0.4	0.27 \pm 0.4	0.27 \pm 0.5	0.319
Hex (%)	53 \pm 10	54 \pm 11	55 \pm 10	0.992
Pachymetry (μ m)	566 \pm 33	570 \pm 33	561 \pm 38	0.421

CD: Cell density, CV: Coefficient of Variation, Hex: Hexagonality rate

DISCUSSION

Eye surgeries are mostly performed under local anesthesia, but general anesthesia is preferred especially in patients who have undergone previous complicated eye surgery or who need a long operation time. In such cases, if there is corneal endothelial damage due to previous complicated surgery, the extra damage and toxicity that may be to corneal endothelium becomes much more important. Based on this, we showed the effect of sevoflurane which that the most preferred agent for general anesthesia on corneal endothelium, in our study. Mean operating time and sevoflurane exposure times in our study patients were approximately 1.5 hours. We think that this period of time is generally close to the duration of ophthalmic surgeries and may allow a general evaluation.

According to our knowledge, it will be the first study done on this subject. According to our results, we found that the average 1.5 hour exposure of sevoflurane was not toxic to corneal endothelium. In our specular microscopy investigation, the cells maintained regular hexagonal patterns. The cells maintained clear and sharp borders. In order to be able to detect the possible toxic effect of the

drug in our study in the late period and to make changes in the endothelium become obvious, we followed up the patients until the first postoperative month (Figure 1-3).

We used pachymetry as a marker of acute changes in corneal endothelium and we have not found any change in the pachymetry values. This result may be indicative of the absence of acute toxicity of sevoflurane. In other words, we can say that there is no disruption in endothelial function. There are several risk factors that explain the susceptibility of anesthetics to some patients being more susceptible to toxicity. Female gender, age, obesity, and drug use are associated with high incidence of toxic reactions (10,11). The fact that our patients are young and that there are no weight problems can be the reason why we can not show the toxic effect. There are studies that show that sevoflurane does not produce oxidative stress on the body, even shows antioxidant properties (12,13). Our results may be based in part on these antioxidant properties of sevoflurane, but this should be confirmed by laboratory studies. CV and Hex ratios (pleomorphism and polymegatism) in the endothelium are remodeling indicators (5,6). Remodeling after corneal endothelial damage can last up to 3 months (14). Our work is limited to

one month, which is one of our limitations but the fact that the cell density has not declined at any time suggests that there is no cell loss here that would require remodeling

and therefore suggests that these results will not change in later periods. In a similar study done in the literature, the duration is also limited to 1 month (15).

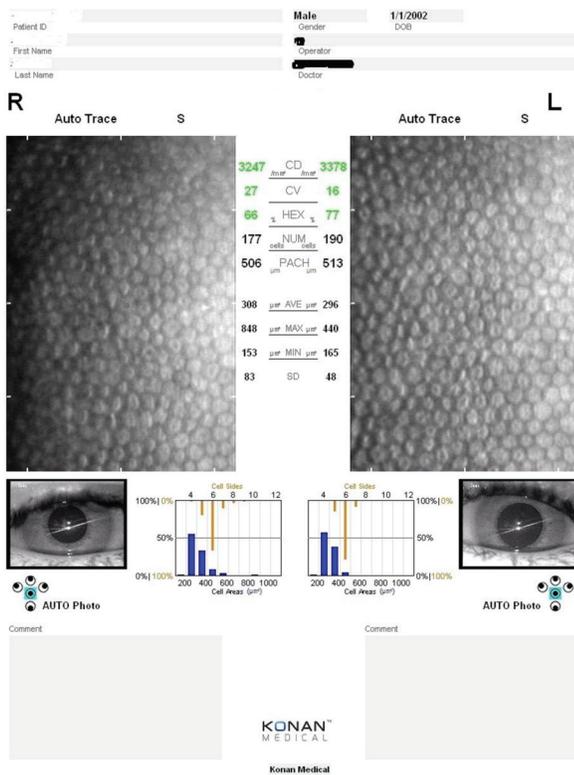


Figure 1. Preoperative corneal endothelial specular microscopy image of a patient.

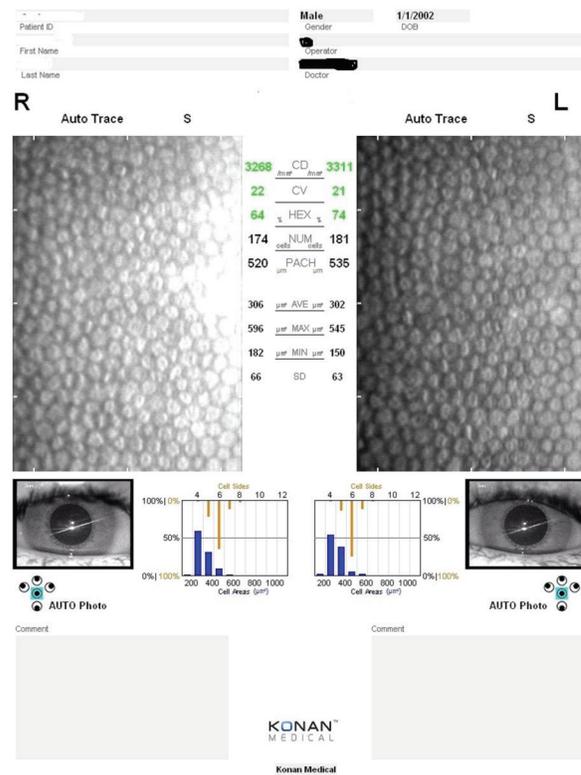


Figure 2. Corneal endothelial specular microscopy image of the same patient at postoperative 1. week.

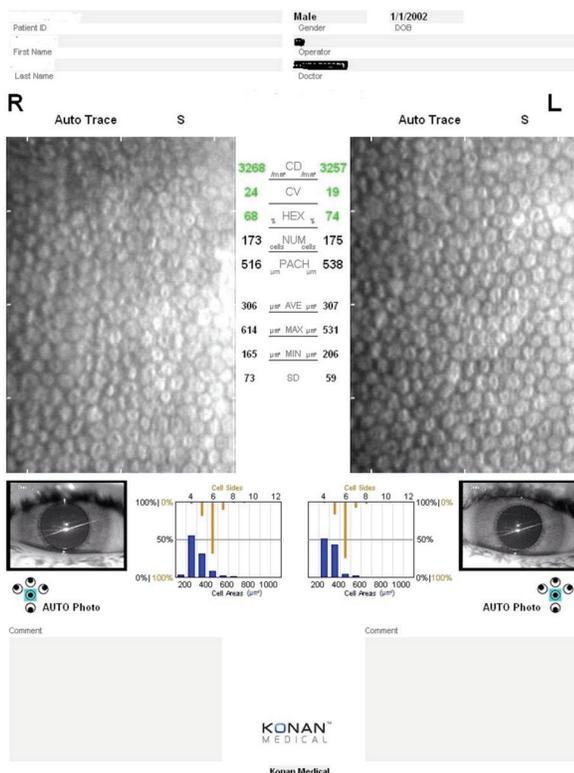


Figure 3. Corneal endothelial specular microscopy image of the same patient at postoperative 1. month

Toxic products resulting from the disruption of sevoflurane by soda lime both as direct effects of sevoflurane can cause toxic effects in repeated applications. In an experimental study conducted, it has been shown that sodalime, which is frequently used in anesthesia practice, is toxic to kidney tissue in repeated applications of sevoflurane anesthesia (16). Nitrous oxide that the only inorganic gas commonly used in anesthesia practice for human anesthesia affects DNA synthesis in a negative way and has toxic effects on bone marrow (17). There is also need studies related to the effects of nitric oxide on corneal endothelium. Repeated applications of inhaled anesthetics may also increase the toxic effects, so careful attention may also be needed in this regard. Furthermore, there is a need to study the effect of low-flow anesthesia on corneal endothelium, which has been used for more than 1 hour.

The period during which patients are exposed to general anesthesia is one of the limitations of our study. Sevoflurane has been shown to exhibit toxic effects in the kidney during operations that last 3 hours or more (18). Therefore, there is a possibility of corneal endothelial toxicity during such long operations which last more than 3 hours. Extensive studies are needed to determine changes in exposures for longer periods. The absence of histopathologic examination and confocal microscopic examination are the limitations of our study. The comparative studies of commonly used general anesthetics may provide more detailed information.

In conclusion, we showed that the general anesthesia of sevoflurane was not a toxic effect at least during this time because it did not change the cell number and cell morphology in the corneal endothelium.

This study was presented as a poster at the 34. ESCRS congress (Copenhagen/Denmark-2016).

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