Investigation of the Acute Effects of Captopril Usage on Intraocular Pressure Before Cataract Surgery

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ABSTRACT

Purpose: In this study, our aim was to investigate the acute effects of captopril on intraocular pressure (IOP) in patients who received captopril preoperatively due to high systemic arterial blood pressure (SABP) before cataract surgery.

Material and Methods: This prospective and cross-sectional study included 28 eyes of 28 patients, who presented for cataract surgery and preoperatively received captopril (25 mg, sublingual) due to detection of high SABP between December, 2019 and April, 2020. The IOP and anterior chamber depth (ACD) measurements were performed by Goldmann applanation tonometry and ocular biometry (Lenstar LS 900, Haag-Streit, USA) immediately before and 30 minutes after the drug intake. Wilcoxon test was used for statistical analysis.

Results: The study included 28 patients (18 female, 10 male) mean age was 64.9±10.7 (49-85). Significant decreases were observed in systolic blood pressure and mean arterial blood pressure after the drug intake (P<0.001 and P=0.001, respectively). No significant difference was found in diastolic blood pressure, ACD, and IOP parameters (P>0.05 for all).

Conclusion: This study concluded that the preoperative usage of captopril to lower the SABP in cataract cases had no acute effects on IOP; thus it can be safely used before the operation.

Keywords: Captopril, Cataract Surgery, Hypertension, Intraocular pressure**.**

INTRODUCTION

It is well-known that renin-angiotensin-aldosterone system (RAAS) plays an important role in the pathophysiology of systemic hypertension, congestive heart failure and diabetic nephropathy.[1-3] The RAAS blockade decreases blood pressure; thus, agents blocking RAAS system can be used in the treatment of hypertension. The RAAS blockers include angiotensin converting enzyme (ACE) inhibitors, angiotensin II receptor blockers and aldosterone inhibitors. ACE inhibitors exert their systemic arterial blood pressure (SABP) lowering effect via factors such as decreased norepinephrine release, increased vasodilator mediators such as bradykinin and reduction in aldosterone release.

Besides systemic effects, it is though that the RAAS has an important role in ocular tissues. In previous studies, it was shown that RAAS components are present at retinal, uveal, corneal and conjunctival tissues at varying amounts.[4] In addition, it has been suggested that the RAAS system is affected in diseases such as glaucoma, uveitis and diabetic retinopathy.[5] In animal models of glaucoma, it was found that neuroprotection was achieved by RASS inhibition.[6] Moreover, IOP reduction was observed in patients on ACE inhibitors.[7]

In our study, it was aimed to investigate acute effects of sublingual captopril use before cataract surgery on IOP.

MATERIAL AND METHOD

This prospective, cross-sectional study was conducted at SBU Ulucanlar Training and Research Hospital of Eye Disorders between December, 2020 and April, 2020. The study included 28 eyes of 28 patients who presented for cataract surgery and had preoperative SABP elevation. The study was approved by Ethics Committee of Ankara Training and Research Hospital. All patients gave written

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informed consent. The study was conducted in accordance to tenets of Helsinki Declaration.

In patients given sublingual captopril (25 mg; Kapril®) under supervision of anesthesiologists, IOP (using Goldmann applanation tonometry) and anterior chamber depth (ACD) measurements (using ocular biometry; Lenstar LS 900, Haag-Streit, USA) were performed without pupil dilatation before and 30 minutes after drug use. After measurements, the patients without contraindication underwent surgery.

The study included patients (aged≥40 years) with presenile and senile cataract. The patients with previous diagnosis of glaucoma or IOP elevation, those with history of ocular trauma, uveitis or surgery and those on systemic drug therapy with history of systemic diseases such as hypertension, diabetes mellitus, metabolic disorders and cardiovascular disorders were excluded. In addition, patients diagnosed with any corneal disease (keratoconus, nephelion, corneal degeneration or dystrophy etc.), pseudo-exfoliation, pigment dispersion, lens subluxation or phacodonesis were also excluded. The patients with axial length 23.0-25.0 mm as measured by ocular biometry (Lenstar LS 900, Haag-Streit, ABD) were included in the study. Data from single eye eligible to study inclusion was analyzed in each patient.

Statistical analysis

Data analysis was performed using SPSS (Statistical Package for Social Sciences) for Windows 24.0 (SPSS Inc, Chicago, IL). Descriptive statistics are presented as mean±standard deviation (min-max). The normal distribution of data was tested using visual (histogram and probability graphics) and analytic methods (Kolmogorov-Smirnov/Shapiro Wilk test). Paired samples t test was used in variables with normal distribution while Wilcoxon test was used in variables with skewed distribution. A p value<0.05 was considered as statistically significant.

RESULTS

Overall, 28 patients including 18 women and 10 men were recruited to the study. Mean age was 64.9±10.7 (49-85) years. Before drug intake, mean SABP (systolic/diastolic) was 183.0±11.0/ 101.0±20.0 (170.0-200.0/ 90.0-170.0) mmHg while mean IOP was 18.4±4.1 (13.0-25.0) mmHg. 30 minutes after captopril intake, mean SABP was 163.0±19.0/95.0±15.0 (130.0-205.0/70.0-130.0) mmHg while mean IOP was 18.5±5.2 (12.0-26.0) mmHg. Mean arterial blood pressure (MABP) was calculated as 128.0±15.0 (116.0-180.0) mmHg and 117.0±13.0 (96.0-140.0) mmHg before and on minute 30 after captopril intake. Mean ACD was 2.87±0.31 (2.25-3.54) mm before drug intake whereas 2.88±0.34 (2.26-3.34) mm after drug intake. A significant reduction was detected in systolic blood pressure (SBP) and MABP after drug intake while no significant difference was detected in diastolic blood pressure (DBP), ACD and IOP ($p > 0.05$ for all) (Table 1).

DISCUSSION

The RAAS system has a particular role in the regulation of SABP. The ACE inhibitors blocks the RAAS enzyme that regulates conversion of angiotensin I to angiotensin II.[4] In animal studies, the ACE was shown in the retina, ciliary body and vitreous in pig eye which has similar features with human eye.[8] In addition, ocular hypotensive effect was also detected by topical use of ACE inhibitors.[9,10] On contrary, in a study, Kotikoski et al.[11] administered captopril to anterior chamber of rabbit eye and found that captopril did not change humor aqueous efflux. It is known that angiotensin 2 has pro-inflammatory, mitogenic and vasoconstrictor effects which exacerbate vascular and inflammatory disorders by leading capillary endothelial dysfunctionr.[12-14] Based on these data, in some studies, it was advocated that RAAS inhibition has neuroprotective features in addition to hypotensive effect in animal models

Table 1: *Changes in systemic blood pressure and ocular parameters before and after captopril intake.*

	Before captopril intake (n = 28) Mean±SD (min-max)	After captopril intake (n =28) Mean±SD (min-max)	*P* [a]
SBP (mmHg)	183.0±11.0 (170.0-200.0)	163.0±19.0 (130.0-205.0)	**<0.001**
DBP (mmHg)	101.0±20.0 (90.0-170.0)	95.0±15.0 (70.0-130.0)	0.201
MABP (mmHg)	128.0±15.0 (116.0-180.0)	117.0±13.0 (96.0-140.0)	**0.001**
IOP (mmHg)	18.4±4.1 (13.0-25.0)	18.5±5.2 (12.0-26.0)	0.975
ACD (mm)	2.87±0.31 (2.25-3.54)	2.88±0.34 (2.26-3.34)	0.150

SBP, systolic blood pressure; DBP, diastolic blood pressure; MABP, mean arterial blood pressure; *ACD*, anterior chamber depth; *IOP*, intraocular pressure; *SS*, standard deviation, [a] Wilcoxon test

of glaucoma.[6] Moreover, it has been suggested that RAAS activation leads neuronal dysfunction; thus, the balance in the RAAS system is important in several diseases such as diabetic retinopathy, age-related macular degeneration and glaucoma.[5] Yıldız et al.[15] found higher renin level in humor aqueous in eyes with exfoliation syndrome when compared to controls, suggesting that RAAS may be involved in glaucoma pathogenesis.

In addition, in the postmortem studies on enucleated human eye, it was shown that RAAS is present in retinal and uveal tissues.[4] Costagliola et al.[7] evaluated effects of captopril on IOP and found that there was reduction in IOP in addition to reduction in systemic blood pressure in patients with hypertension. Moreover, in a study using topical solution of captopril, it was shown that topical captopril decreased IOP in both glaucoma and control groups.[16] Iskedjian et al.[17] reported that the need for topical anti-glaucomatous treatment was lower in glaucoma patients using systemic ACE inhibitor. On contrary, in a large, epidemiological series, it was reported that IOP was significantly higher in cases using ACE inhibitor when compared to those not.[18] In our study, no acute change was observed in IOP and ACD in patients received captopril.

In the literature, there are several studies about relationship between hypertension and IOP. In a retrospective study on hypertensive patients, Rim et al.[19] found that primary open-angle glaucoma development was more common in hypertensive patients with increased risk in patients with SBP≥120 mmHg and DBP≥90 mmHg. In a large cohort, it was suggested that presence of diabetes mellitus and hypertension contributed to POAG development.[20] In a meta-analysis by Zhao et al.[21] it was concluded that hypertension is associated with IOP elevation. Again, it was reported that each 10 mmHg increase in SBP was associated with 0.26 mmHg IOP elevation while each 5 mmHg increase in DBP is associated with 0.18 mmHg IOP elevation. It is though that hypertension causes glaucoma by increasing humor aqueous production or decreasing humor aqueous efflux.[22,23] However, Wu et al.[24] and McLeod et al.[25] found no significant correlation between hypertension and IOP.

Although there are contradictory outcomes regarding hypertension and IOP change, it is well-known that uncontrolled hypertension is a risk factor for suprachoroidal hemorrhage.[26-28] In addition, ocular risk factors including acute IOP reduction during surgery, prolonged and complicated surgery, high myopia and history of glaucoma also play role in the development of suprachoroidal hemorrhage.[29,30] Thus, IOP reduction during surgery and elevated SABP seem to be involved in suprachoroidal hemorrhage.

In our study, we evaluated acute effect of captopril on SABP and IOP and found a significant decrease in SBP and MAPB values ($p<0.001$ and $p=0.001$, respectively) but no significant change in DBP, IOP and ACD measurements ($p>0.05$ for all). These results showed that preoperative captopril use had SABP lowering effect without IOP reduction.

This study has some limitation including relatively small sample size and measurements in acute period. The measurements were performed on minute 30; thus, no assessment was performed in earlier or later periods; however, it was reported that captopril exerts its effects within 30 minutes in most patients with maximum effect on minute 30.[31,32]

In conclusion, it was found that there was a reduction in SBP and MAPB but not in IOP by captopril use during acute phase despite contradictory outcomes about ACE inhibitor use and IOP alteration in the literature. The finding that no change was detected in IOP by sublingual captopril use indicates that it can be used safely before surgery.

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