

## EFFECT OF TOPICAL 10% PHENYLEPHRINE ON BLOOD PRESSURE AND HEART RATE DURING PHACOEMULSIFICATION UNDER LOCAL ANESTHESIA

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**SUMMARY** – Due to its alpha-adrenergic action, a topical mydriatic phenylephrine may alter blood pressure during cataract surgery. The aim of the study was to evaluate the effect of topically administered 10% phenylephrine on perioperative blood pressure (BP) and heart rate (hr) during phacoemulsification. This prospective, randomized, double-blind study included 49 patients who underwent phacoemulsification under local anesthesia. Patients were divided into two groups. The experimental group patients were administered 1% tropicamide and 10% phenylephrine. In the control group, 0.9% saline solution was administered instead of 10% phenylephrine. Blood pressure and heart rate were measured at preoperative assessment, at admission prior to instillation of mydriatics, prior to giving peribulbar anesthesia, during surgery, and one hour postoperatively. All patients were partially sedated with midazolam *per os*. Statistical analysis of collected data was performed. There was a small but statistically nonsignificant increase in the mean blood pressure (BP) and heart rate (hr) in experimental group as compared to control group:  $p(\text{BP})=0.841$ ,  $p(\text{hr})=0.636$  at preoperative assessment;  $p(\text{BP})=0.968$ ,  $p(\text{hr})=0.561$  prior to instillation of mydriatics;  $p(\text{BP})=0.279$ ,  $p(\text{hr})=0.554$  prior to giving peribulbar anesthesia;  $p(\text{BP})=0.094$ ,  $p(\text{hr})=0.645$  during surgery; and  $p(\text{BP})=0.823$ ,  $p(\text{hr})=0.732$  one hour postoperatively. There were no systemic side effects or intraoperative and postoperative complications. In conclusion, there was no statistically significant difference (although there was an increase in the mean blood pressure in experimental group with 10% phenylephrine) between the experimental and control group in the measurement of either blood pressure or heart rate. According to our results, 10% phenylephrine is safe for topical application in ophthalmology in adults. For definitive conclusion about the effect of 10% phenylephrine on perioperative blood pressure and heart rate, a larger study with standardized preoperative and intraoperative procedure should be performed.

**Key words:** *topical mydriatic, 10% phenylephrine, cataract surgery, local anesthesia, blood pressure, heart rate*

### Introduction

Phenylephrine hydrochloride is a sympathomimetic with mainly direct effect on alpha adrenergic receptors. Phenylephrine solution is used in local ocular disorders and in ophthalmic surgery because of its vasoconstrictor, decongestive and mydriatic (without cycloplegia) ac-

tion. It is used as a mydriatic in concentrations of up to 10%; generally, solutions containing 2.5% or 10% are employed but systemic absorption can occur and 10% strength in particular should be used with caution<sup>1-3</sup>. Systemic complications of topical phenylephrine applied to the eye are those common to sympathomimetics. Side effects in adults include hypertension, tachycardia, arrhythmias, sweating, headaches, faintness, trembling and pallor<sup>4,5</sup>.

The aim of the study was to evaluate the effect of topically administered 10% phenylephrine on blood pressure (BP) and heart rate (hr) during cataract surgery.

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## Patients and Methods

Forty-nine patients (27 men and 22 women) were included in our prospective, randomized, double-blind study conducted at University Department of Ophthalmology, Sestre milosrdnice University Hospital, between December 2004 and February 2005. There were 25 patients in experimental group and 24 patients in control group. Each patient underwent uncomplicated phacemulsification under peribulbar anesthesia (2 mL 2% lidocaine; 2 mL levobupivacaine). There was no history of cardiovascular disease. Patients were divided into two groups. The experimental group patients received one drop of 1% tropicamide, 4 times over 1 hour preceding surgery and one drop of 10% phenylephrine, once, 30 minutes prior to surgery. In the control group, 0.9% saline solution was administered instead of 10% phenylephrine. Blood pressure and heart rate were measured at preoperative assessment, at admission prior to instillation of mydriatics, prior to giving peribulbar anesthesia, during surgery, and one hour postoperatively. All patients were partially sedated with midazolam *per os*.

Statistical analysis was performed with SPSS 8.0 statistical package for Windows (SPSS Inc., Chicago, IL, USA). Data were compared with Mann-Whitney U-test. A value of  $p > 0.05$  was considered statistically nonsignificant.

## Results

We analyzed 27 men and 22 female patients (49 eyes), mean age 64 years in both experimental and control group (experimental 29-81 and control 29-86 years). In experimental group there were ten men and 15 women, whereas in control group there were 17 men and seven women. In experimental group, the mean blood pressure (heart rate) was 105 mm Hg (80/min) at preoperative assessment, 108 mm Hg (77/min) at admission prior to instillation of mydriatics, 107 mm Hg (78/min) prior to giving peribulbar anesthesia, 108 mm Hg (76/min) during surgery, and 100 mm Hg (71/min) one hour postoperatively. In control group, the mean blood pressure (heart rate) was 103 mm Hg (78/min) at preoperative assessment, 107 mm Hg (75/min) at admission prior to instillation of mydriatics, 103 mm Hg (75/min) prior to giving peribulbar anesthesia, 101 mm Hg (73/min) during surgery, and 99 mm Hg (70/min) one hour postoperatively. There was a small but statistically nonsignificant increase in the mean blood pressure (BP) and heart

rate (hr) in experimental group compared to control group:  $p(\text{BP})=0.841$ ,  $p(\text{hr})=0.636$  at preoperative assessment;  $p(\text{BP})=0.968$ ,  $p(\text{hr})=0.561$  prior to instillation of mydriatics;  $p(\text{BP})=0.279$ ,  $p(\text{hr})=0.554$  prior to giving peribulbar anesthesia;  $p(\text{BP})=0.094$ ,  $p(\text{hr})=0.645$  during surgery; and  $p(\text{BP})=0.823$ ,  $p(\text{hr})=0.732$  one hour postoperatively. An hour postoperatively, a small decrease in blood pressure and heart rate was recorded in both experimental and control group. In control group, a decrease in blood pressure and heart rate was also recorded prior to peribulbar anesthesia and during surgery, however, not reaching statistical significance either. None of the patients required i.v. hypotensive agent to control blood pressure. There were no arrhythmias, ischemic changes or oxygen desaturation episodes observed intraoperatively. None of the patients complained of palpitation, headache or chest discomfort.

According to the measurements and statistical analysis, we concluded that there was no statistically significant difference between the experimental and control group with respect to the drug effect on either mean blood pressure or heart rate.

## Discussion

Phenylephrine is a selective  $\alpha$ -1 agonist, with  $\alpha$  activation only at very high doses<sup>4,5</sup>. The onset of action occurs 30-90 minutes after instillation, and the effects last for 6-7 hours<sup>4,6</sup>. Solutions stronger than 2% may cause intense irritation. Ocular solutions containing lower concentrations (usually 0.12% phenylephrine hydrochloride) are used as a conjunctival decongestant<sup>1</sup>.

Phenylephrine HCl (2.5%) is used for pupillary dilation in uveitis, for many ophthalmic surgical procedures, and for refraction without cycloplegia. It may be used with miotics in patients with open angle glaucoma in lowering the intraocular pressure<sup>3</sup>.

In our study, we used only 10% phenylephrine as a mydriatic prior to cataract surgery. We did not observe any local side effects.

Ophthalmic solutions of phenylephrine HCl are contraindicated in patients with anatomical narrow angles or narrow angle glaucoma. It may be contraindicated in low birth weight infants and in some adults with arteriosclerotic and cerebrovascular disease, hypertension and hyperthyroidism<sup>3,7,8</sup>.

Since phenylephrine is absorbed through the mucosa, systemic effects may follow application to the eyes. Systemic complications of topical phenylephrine include

tachycardia, hypertension, arrhythmias, sweating, headaches, faintness, trembling and pallor<sup>4,5</sup>. Great care needs to be taken in local application of these drugs. Phenylephrine should be used with caution in patients with cardiac disease, and in those on concomitant medications (tricyclic antidepressants, atropine, sodium bisulfate, beta adrenergic blocking agents), which can compound its pharmacodynamic effects<sup>4,9</sup>.

Our study did not show any of the above mentioned systemic complications. We did not have patients with cardiac disease. Knowing the pharmacological activity of 10% phenylephrine, we expected a significant increase in the mean blood pressure and heart rate, which did not happen. Furthermore, 10% phenylephrine used for pupillary dilatation prior to phacoemulsification did not show statistically significant alteration in the mean blood pressure or heart rate, although there was a small rise in experimental group compared to control group. A major but statistically nonsignificant ( $p=0.094$ ) increase in the mean blood pressure was recorded during intraoperative measurement in experimental group compared to control group. How could we explain this? Maybe surgical procedure had an effect on blood pressure and heart rate. Two different persons measured blood pressure and heart rate. One measured blood pressure and pulse rate at preoperative assessment and one hour postoperatively, and another one measured these parameters prior to instillation of mydriatics, prior to giving peribulbar anesthesia and during surgery.

According to our results, we could say that 10% phenylephrine is safe for topical application before cataract surgery in adults. We can ask ourselves whether there may have been any effect of midazolam or anxiety on blood pressure and heart rate that could have masked our results? Was our study too small for statistical analysis? We did not analyze difference between sexes. Perhaps the results would be different if we had analyzed systolic and diastolic blood pressure separately. What would have happened if we had closed the lacrimal sac after the application of 10% phenylephrine? Maybe the mean blood pressure and heart rate would have been even lower.

There is a controversy about the concentration of topical phenylephrine recommended for diagnostic or therapeutic mydriasis. Kumar *et al.* concluded that the mean blood pressure was higher with 10% phenylephrine<sup>10,14</sup>. Chin *et al.* in their study concluded that significant hypertensive effects could arise after topical phenylephrine with no significant difference between

2.5% phenylephrine and 10% phenylephrine<sup>11,14</sup>. Symons *et al.* report no significant change in the mean systolic and diastolic blood pressure in patients receiving 10% phenylephrine<sup>12,14</sup>. Malhorta *et al.* showed no difference in systemic cardiovascular effects of either 2.5% or 10% concentration<sup>13,14</sup>. Kenawy *et al.* showed a statistically significant rise in systolic blood pressure in the 10% group<sup>14</sup>. Brown *et al.* report the lack of side effects from topically administered 10% phenylephrine on blood pressure or heart rate<sup>15</sup>. Lam *et al.* showed no untoward cardiovascular effects in 2.5% and 0.5% phenylephrine group<sup>16</sup>. Schlichtenbrede *et al.* monitored biochemical stress parameters during cataract surgery and showed no changes in serum catecholamines between 10% and 5% phenylephrine. They recommend the use of 10% phenylephrine as a routine medication for cataract surgery<sup>17</sup>. Mathew *et al.* concluded that 10% phenylephrine significantly altered perioperative blood pressure<sup>18</sup>. Jennings *et al.* report no significant change in systolic or diastolic blood pressure for any of the treatment groups (2.5% phenylephrine, 1% tropicamide, and placebo)<sup>19</sup>.

Some case series revealed systemic side effects in neonates and children<sup>4</sup>. In our study, we did not have any experience with children, as all study subjects were adults. In other studies, there are two case reports of hypertension, acute left ventricular failure and pulmonary edema with ocular phenylephrine given intraoperatively<sup>4,20,21</sup>. There are isolated case reports of paralytic ileus, necrotizing enterocolitis, and acute gastric dilatation in neonates in the 24-hour period after ROP screening<sup>4,22-24</sup>. With regard to the above mentioned side effects, caution is required in the application of phenylephrine in children, especially infants.

There is no uniform attitude about phenylephrine dosage and concentration. The 2.5% phenylephrine eye drops are licensed for use in all age groups, whereas the 10% eye drops are unlicensed in children and not recommended in this age group<sup>4,6</sup>. The New York State Guidelines recommend 0.25% phenylephrine with the initial dose in adults of up to 0.5 mg. In children (up to 25 kg), the initial dose should not exceed 20  $\mu\text{g}/\text{kg}$ <sup>25,26</sup>. The lacrimal sac should be compressed by digital pressure for two to three minutes after instillation to avoid excessive systemic absorption<sup>27</sup>.

In conclusion, our experimental group with 10% phenylephrine compared to control group showed a small perioperative rise in the mean blood pressure and heart rate, which was not statistically significant. We recorded no side effects or intraoperative and postoperative

complications. Accordingly, to reach a uniform approach, we need a larger study with standardized perioperative procedure and monitoring.

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## Sažetak

## UTJECAJ TOPIČKI PRIMIJENJENOG 10% FENILEFRINA NA KRVNI TLAK I PULS TIJEKOM FAKOEMULZIFIKACIJE U LOKALNOJ ANESTEZIJI

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Za vrijeme ultrazvučne operacije sive mreže moguće je utjecaj midrijatika, fenilefrina, na krvni tlak i puls zbog njegovog alfa-adrenergičnog djelovanja. Cilj rada bio je ispitati učinak lokalno primijenjenog 10%-tnog fenilefrina na perioperacijski krvni tlak i puls tijekom fakoemulzifikacije. Ovim prospektivnim, randomiziranim, dvostruko slijepim istraživanjem obuhvaćeno je 49 bolesnika koji su podvrgnuti operaciji sive mreže u lokalnoj anesteziji. Bolesnici su podijeljeni u dvije skupine. U eksperimentalnoj skupini bolesnicima se je ukapavao 1%-tni tropikamid i 10%-tni fenilefrin. U kontrolnoj skupini se je umjesto 10%-tnog fenilefrina ukapavala 0,9%-tna fiziološka otopina. Krvni tlak i puls mjereni su prilikom prijeoperacijskog pregleda na odjelu, kod pripreme za operaciju prije ukapavanja midrijatika, prije peribulbarne anestezije, za vrijeme operacije i jedan sat nakon operacije. Svi bolesnici bili su djelomice sedirani midazolamom (*per os*). Prikupljeni podaci statistički su obrađeni. Usporedba eksperimentalne i kontrolne skupine pokazala je mali, statistički neznatčan porast prosječnog krvnog tlaka i pulsa u eksperimentalnoj skupini:  $p(\text{BP})=0,841$ ,  $p(\text{hr})=0,636$  kod prijeoperacijskog pregleda;  $p(\text{BP})=0,968$ ,  $p(\text{hr})=0,561$  kod pripreme za operaciju prije ukapavanja midrijatika;  $p(\text{BP})=0,279$ ,  $p(\text{hr})=0,554$  prije peribulbarne anestezije;  $p(\text{BP})=0,094$ ,  $p(\text{hr})=0,645$  za vrijeme operacije;  $p(\text{BP})=0,823$ ,  $p(\text{hr})=0,732$  jedan sat nakon operacije. Nisu nađene sistemske nuspojave, kao niti intraoperacijske ili poslijeoperacijske komplikacije. Na temelju iznesenih rezultata zaključeno je kako nije bilo statistički značajne razlike (iako je zabilježen porast prosječnog krvnog tlaka u eksperimentalnoj skupini uz 10%-tni fenilefrin) između eksperimentalne i kontrolne skupine u vrijednostima prosječnog krvnog tlaka i pulsa. Prema našim rezultatima sigurna je lokalna uporaba 10%-tnog fenilefrina kod odraslih u oftalmologiji. U zaključku ističemo potrebu provedbe istraživanja na velikom broju bolesnika, s unaprijed standardiziranim perioperacijskim postupkom i motrenjem parametara radi postizanja što točnijih rezultata.

Ključne riječi: *topički midrijatik, 10% fenilefrin, operacija sive mreže, lokalna anestezija, krvni tlak, puls*

