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ORIGINAL PAPER

Ophthalmic artery resistance index after peribulbar block in the presence of epinephrine

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Abstract

Purpose There are controversies regarding ophthalmic artery (OA) flow after peribulbar block in the presence of epinephrine. Therefore, we aimed to evaluate OA flow via echo-Doppler before and after peribulbar block with lidocaine in the presence or absence of epinephrine.

Methods Fifty-six patients who had an American Society of Anesthesiologists (ASA) classification of I, II or III and were eligible for cataract phacoemulsification surgery were selected. Patients with other eye diseases were excluded. Patients were divided into two groups: group 1—peribulbar block with lidocaine and 1/200,000 epinephrine; group 2—peribulbar block with lidocaine in the absence of epinephrine. The resistance index (RI), peak systolic velocity (PSV), end diastolic velocity (EDV) of the OA were evaluated using echo-Doppler before and 10 min after the peribulbar block.

Results No differences between groups were observed in the RI before the peribulbar block as well regarding the presence of hypertension and the age or gender of the patient. After the peribulbar block, we observed a decrease in the RI in group 1 ($p = 0.038$, Cohen's $d = 0.336$) and no difference in the RI in group 2 ($p = 0.109$, Cohen's $d = 0.172$). When comparing group 1 and group 2, we observed a decrease in the RI in group 1 ($p = 0.028$, Cohen's $d = 0{,}583$). There was no difference between groups regarding the PSV and EDV after the peribulbar block.

Conclusions A decrease in RI was observed in the OA after peribulbar block with a vasoconstrictor, an effect that could be a benefit in some ocular surgeries.

Keywords Ocular flow · Cataract surgery · Peribulbar block · Ocular Doppler

Introduction

Cataract surgery is the most common surgical procedure in ophthalmology, and the choice of anesthetic technique has a significant effect both economically and in terms of patient health. Since the 1990s,

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anesthetic blocks have become the technique of choice in ophthalmology [1]. Peribulbar block was first described by Davis and Mandel in 1986 as an effective and safe technique and an alternative to retrobulbar anesthesia [2]. In a study analyzing 16,224 blocks, the peribulbar technique proved effective in terms of anesthesia and akinesia, with low complication rates [3]. In a study comparing 1084 cataract cases with topical anesthesia to 1121 cases with peribulbar and retrobulbar anesthesia, peribulbar block was found to be a superior analgesic technique than topical anesthesia [4].

However, local hemodynamic changes after peribulbar and retrobulbar anesthesia measured by tonometry have been described, including increased intraocular pressure and decreased pulsatile ocular flow [5]. Ocular echo-Doppler evaluations after retrobulbar anesthesia with 2 ml of anesthetic solution have shown a decrease in flow velocity in the ophthalmic artery (OA), the central retinal artery (CRA) and the central retinal vein (CRV), and this effect is more pronounced when anesthetics are used with vasoconstrictors [6]. Echo-Doppler evaluations after peribulbar anesthesia without the use of a vasoconstrictor have shown decreased flow in the CRA with an increased resistance index (RI) and no changes in OA flow [7]. A study of cataract patients showed a reduction in ocular flow after retrobulbar blocks with epinephrine, with no changes in intraocular pressure, indicating drug-induced vasoconstriction [8].

Color Doppler is a good technique for evaluation of ocular hemodynamics. It is safe, noninvasive, reproducible, commonly used to investigate the circulatory parameters of retrobulbar vessels [9–11] and the standard for diagnosis of carotid artery stenosis [12]. The parameters evaluated by Doppler include peak systolic velocity (PSV), end diastolic velocity (EDV), average velocity (AV) and RI [10]. It is possible to evaluate the hemodynamic parameters of OA and CRA; however, CRA presents large diameter variability throughout its course, which leads to large changes in blood flow velocity [10, 11, 13]. Because of those variations, measurements can substantially change depending on the position of the probe, causing considerable variation in the data obtained. Thus, we choose OA for assessment of hemodynamic parameters after peribulbar block since previous studies [5, 7, 14, 15] have demonstrated that ocular blocks can cause changes in retrobulbar vessel flow, with possible negative effects, particularly in patients with glaucoma and diabetic retinopathy. Therefore, evaluation of the effect of peribulbar block with and without epinephrine on OA flow is important. The objective of this study was to detect changes in the RI, PSV and EDV of the OA using echo-Doppler after peribulbar block in the presence or absence of epinephrine.

Methods

The Ethics Committee of our Institution approved this prospective, randomized and double-blind clinical trial, which was registered in Clinicaltrials.gov, number NCT 04153123. Patients were selected at the preanesthetic visit on the day of the surgery. The patients who agreed to participate received instructions about the study and signed an informed consent form. The patient inclusion criteria were age between 50 and 85 years, American Society of Anesthesiologists (ASA) I, II or III and selection for phacoemulsification cataract surgery; patients of both genders were enrolled. The exclusion criteria were the presence of other eye diseases, such as glaucoma or diabetic retinopathy; a previous history of eye surgery in the same eye; a history of ocular trauma; allergies to any protocol medication; uncooperative patients and/or those with cognitive difficulties; smokers; patients refusing to participate; and patients with an axial eye diameter of less than 21.0 mm or greater than 25.5 mm.

Patients were randomized into two groups using computer-generated random number tables: group 1: peribulbar block with 6 ml of 2% lidocaine with epinephrine 1/200,000; group 2: peribulbar block with 6 ml of 2% lidocaine without epinephrine. Hyaluronidase 25 IU/mL was added to both solutions. Patients were monitored through electrocardiogram, mean arterial pressure (MAP), heart rate (HR) and oxygen saturation (SpO_2) assessments. Peripheral venous access with a 22G intravenous catheter was performed on the upper limb for infusion of 0.9% sodium chloride solution. The preparation of the syringes was performed by one of the researchers not involved in execution of the blockades. The same anesthesiologist performed all the blocks, and the same person performed the echo-Doppler evaluation.

The following variables were analyzed: demographic data (age, sex and weight), presence of comorbidities and use of medication. The preoperative and postoperative variables evaluated by Doppler were the RI, PSV and EDV.

The surgeries were performed in the morning with patients having fasted in order to mitigate the effects of external influences, such as coffee intake, food intake, alcohol use, intense exercise and time of day, on ocular flow [10, 16, 17]. No patient received preanesthetic medication. Patients were asked to rest for 10 min prior to the echo-Doppler. The examination was performed with the patient in a supine position considered comfortable by the patient and that avoided factors that could compromise venous return (tight clothes, a cross-legged position and/or a position that would provoke the Valsalva maneuver). Patients were asked to keep their eyes closed and fixed on one point. The examiner sat behind the patient's head without exerting pressure on the eye; the examiner supported the probe cable to avoid examiner fatigue and strain on the eye. All examinations were performed using Sonosite equipment, the Titan model, with a linear transducer of 7.5 MHz. The anterior segment of the OA was studied from the nasal to the optic nerve, approximately 10 mm from the posterior scleral wall. The angle of incidence was corrected when it was greater than 20 degrees. Three measurements were obtained based on regular spectral curves.

After the examination, the patient underwent peribulbar anesthesia with a single inferolateral injection. A fine needle (25 G $^1/_2$ × 0,45 × 13 mm, BD) was introduced through the skin immediately above the orbital rim along the floor, with care taken to keep the needle out of the muscle cone. Ten minutes after anesthesia, the same examiner performed echo-Doppler measurements. The examiner did not know which solution was being used to perform the peribulbar block.

The methodology proposed by Fleiss [18] was used to calculate the sample size. For a 5% significance level, minimum power of 80% and effect size of 0.80, each group needed to include at least 26 subjects. An effect size of 0.80 indicates that the test will detect a significant difference of 0.80 deviations between groups. Marginal linear regression was used to compare the RI in each group before and after the peribulbar block. This analysis was controlled for age, gender and presence of hypertension. Therefore, it was possible to verify the effects of age, gender and hypertension on the RI. The same analysis was used for PSV and EDV. The software used for data analysis was R version 3.1.3. $p < 0.05$ was considered statistically significant.

Results

Table 1 describes the patient profile in terms of age, gender, hypertension and echobiometry. No significant differences were observed in any of these variables between the groups. Similarly, there were no differences between the groups regarding the presence of other comorbidities and/or use of medications (data not shown).

According to the data in Table 2, which presents the RI controlled for gender, hypertension and age, there were no significant differences between groups in terms of the RI in the preblock condition. In group 1, there was a significant decrease ($p = 0.038$, Cohen's $d = 0.336$) in the RI in the postblock condition (Fig. 1), and the mean RI value was 0.048 lower than the initial RI value. In group 2, no significant difference was observed in the RI in the postblock condition ($p = 0.109$, Cohen's $d = 0.172$). When comparing group 1 and group 2, after the block, there was a decrease in the RI in group 1 ($p = 0.028$, Cohen's $d = 0.583$) (Fig. 2). According to the data presented in Table 3, which presents the PSV controlled for gender, hypertension and age, there were no significant differences between groups in terms of the PSV in the postblock condition. In Table 4, which presents the EDV controlled for the same factors as in Table 3, there were no significant differences between groups in terms of the EDV in the postblock condition.

Discussion

In the present study, we observed a decrease in the RI when we performed peribulbar anesthesia with epinephrine (group 1) and no difference in the RI when we performed the block without epinephrine (group 2). Because there were no differences between groups regarding comorbidities, echobiometry and RI before the blockade, a comparison between group 1

Table 1 Description of patients overall and by group

	Gender *N* (%)		Hypertension *N* (%)		Age mean (SD)	Echobiometry (mm) mean (SD)
	Female	Male	No	Yes		
Overall	34	22	21	35	67.02	22.94
	(60.71)	(39.29)	(37.50)	(62.50)	(12.16)	(0.86)
Group 1	20	12	14	18	66.90	22.89
	(62.50)	(37.50)	(43.80)	(56.20)	(13.41)	(0.92)
Group 2	14	10	7	17	67.10	23.00
	(58.30)	(41.70)	(29.20)	(70.80)	(10.54)	(0.78)
p value	0.778[a]		0.403[a]		0.875[b]	0.312[b]

[a] Fisher's exact test

[b] Mann–Whitney test

Table 2 Generalized estimating equation linear regression for the resistance index (RI)

	ß	S.E. (*ß*)	CI 95%	*p* value	Cohen's d
Category					
Before PBB, group 1 versus group 2	0.021	0.033	[− 0.04; 009]	0.532	0.074
After PBB, group 1 versus group 2	0.065	0.030	[− 0.12; − 0.01]	0.028	0.583
Group 1 after versus before PBB	− 0.048	0.023	[-0.09; 0.00]	0.038	0.336
Group 2 after versus before PBB	0.038	0.024	[− 0.01; 0.08]	0.109	0.172
Control variables					
Gender (male or female)	0.004	0.026	[− 0.05; 0.06]	0.870	
Hypertension (presence)	0.026	0.044	[− 0.06; 0.11]	0.559	
Age	0.001	0.001	[0.00; 0.00]	0.286	

PBB peribulbar block

and group 2 was possible and indicated a decrease in the RI in group 1 after peribulbar anesthesia.

A previous study [7] showed that pulsatile choroidal blood flow and retinal blood flow velocity decreased after peribulbar anesthesia with lidocaine without epinephrine. This reduction was still present 5 min after peribulbar anesthesia when intraocular pressure had returned to baseline. This variation supports the theory of drug-induced vasoconstriction after peribulbar anesthesia, where vasoconstriction could trigger self-regulatory mechanisms that function to maintain perfusion and meet metabolic demands [19, 20]. Self-regulation can be defined as the ability to maintain relatively constant blood flow despite changes in perfusion pressure. Self-regulation is a complex phenomenon that may involve metabolic, neurogenic, myogenic and endothelial mechanisms [20]. Ocular blood flow is regulated by the sympathetic and parasympathetic systems through receptors, and α-adrenergic and ß-adrenergic receptors are present in ocular tissue [21–24]. One possibility explored by this study involves direct action of adrenaline on the α-adrenergic and ß-adrenergic receptors. The effect of adrenaline on those receptors might be dependent on the concentration of adrenaline, the localization and the amount of the receptor. At smaller doses, the action of adrenaline on ß-2 receptors could lead to vasodilation. This is clearly just a hypothesis because we are unable to verify whether the alterations in blood flow are due to this effect considering the complexity of the mechanisms involved in the control of the ocular blood flow.

Different flow rate responses have been observed in the OA and the middle cerebral artery (MCA) after

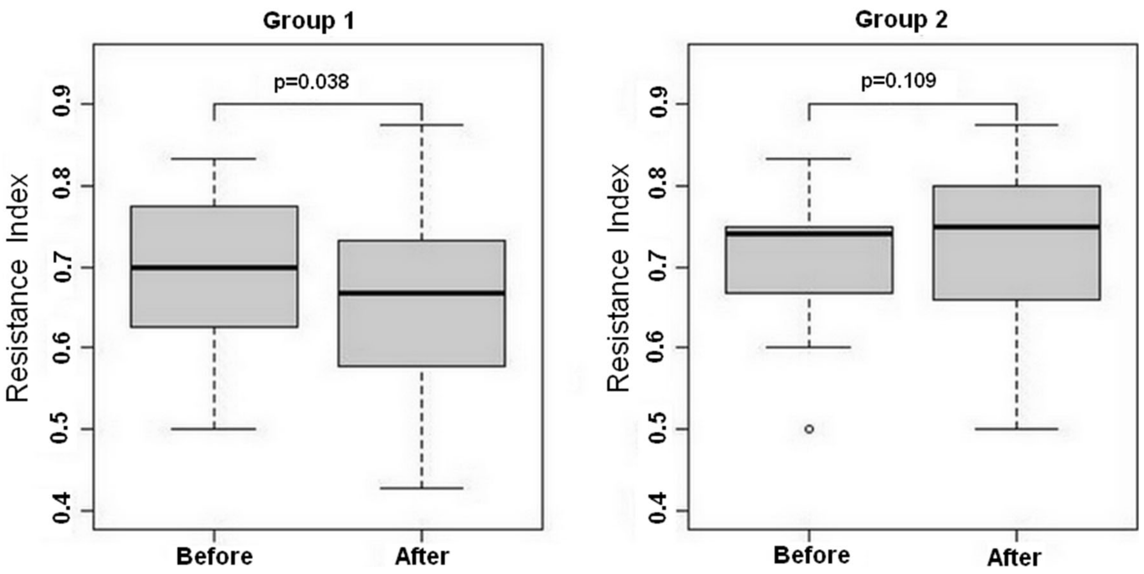

Fig. 1 Comparison of the resistance index before and after the block

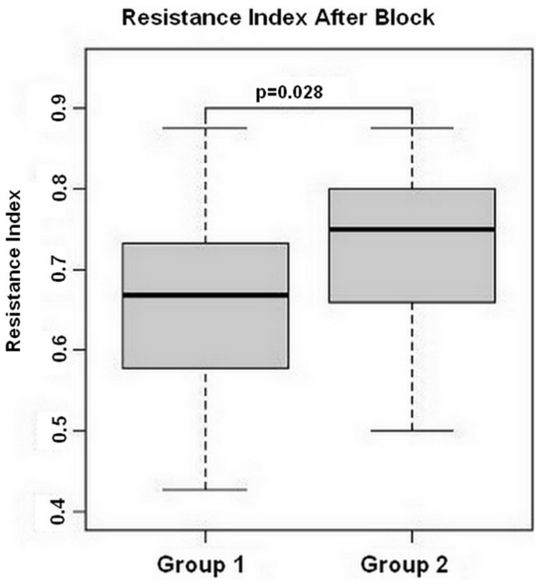

Fig. 2 Comparison of the resistance index after the block

variations in blood pressure (BP), suggesting different regulatory mechanisms. In a previous study, a variation in BP was obtained by inflating bilateral BP cuffs around the wrists and thighs for approximately 3 min and then quickly deflating them. MCA flow rates return to baseline before systemic BP, indicating peripheral vasodilation due to a self-regulating response [25, 26]. However, in the OA, the flow velocities return to baseline later than the systemic BP, suggesting peripheral vasoconstriction due to an unknown mechanism [25, 27]. Another mechanism that decreases the RI is the respiration with CO_2. A study with a CO_2 level 15% above what is normally inhaled in the environment induced vasodilation in the ocular vasculature, with a consequent increase in flow velocity in the retrobulbar vessels and an increase in PSV and EDV [10, 28]. It was observed that patients with severe obstructive sleep apnea syndrome, which causes a persistent increase in partial CO_2 during sleep, show an increase in the RI in the posterior ciliary artery (PCA) and no alteration was observed in OA [29]. However, this factor does not appear to have affected the results of the present study, as none of the patients were sedated, a state that could increase the CO_2 concentration in the blood.

The observed reduction in the RI with the use of an anesthetic with vasoconstrictor is in accordance with the theory of drug-induced vasoconstriction; adrenaline-induced vasoconstriction could trigger self-regulation mechanisms that act to maintain flow. Bradykinin contributes to regulation of ocular blood flow [26], and in fact, a previous study showed that pig ciliary arteries were found to not exhibit vasodilation under the presence of bradykinin when its receptors were blocked with amide-type anesthetics [30]. We could extrapolate that after inhibition of those receptors with amide-type anesthetics, the observed effects on the RI were only induced by the action of

Table 3 Generalized estimating equation linear regression for peak systolic velocity

	β	E.P. (β)	CI 95%	p value	Cohen's d
Category					
Group 1 before–after	− 1.620	2.574	[− 6.66; 3.42]	0.529	0.111
Group 2 before–after	0.164	3.398	[− 6.50; 6.82]	0.961	0.008
Control variables					
Gender (male or female)	− 1.194	2.106	[− 5.32; 2.93]	0.571	
Hypertension (presence)	3.339	2.061	[− 0.64; 7.44]	0.099	
Age	− 0.081	0.089	[− 0.25; 0.09]	0.358	

Table 4 Generalized estimating equation linear regression for end diastolic velocity peak systolic

	β	E.P. (β)	CI 95%	p value	Cohen's d
Category					
Group 1 before–after	0.190	0.913	[− 1.60; 1.98]	0.835	0.030
Group 2 before–after	0.125	0.960	[− 1.76; 2.01]	0.896	0.021
Control variables					
Gender (male or female)	− 0.047	0.028	[− 0.10; 0.01]	0.091	
Hypertension (presence)	− 0.057	0.605	[− 1.24; 1.13]	0.924	
Age	1.097	0.681	[− 0.24; 2.43]	0.107	

epinephrine; at low doses, epinephrine acts on ß-2 receptors, causing vasodilation. However, the relationship between the RI and vascular resistance is not entirely clear. The value depends largely on vascular compliance, which is defined as the ability of a vessel to distend and increase intravascular volume with increasing transmural pressure [20].

The study has some limitations associated with a number of factors. The method of examination used was dependent on the observer, but because the same person performed all the exams that limitation was somewhat minimized. Another limitation was the time available for observation after the block. The mechanisms involved in ocular blood flow are dynamic and interact with each other; thus, a single measurement cannot possibly reflect the extent of the consequences of those regulatory mechanisms. However, due to ethical reasons, we were unable to take another set of measurements because that would cause discomfort to the patients and delay the surgical procedure. Another limitation was the impossibility of having a control group (no block administered and/or a block performed without any anesthetic). The opposite eye could be thought of as the control, but dispersion of anesthetic from one eye to the other can occur, and thus, we cannot make that assumption. Moreover, for medical and ethical reasons, we cannot perform a block without drugs. Finally, the sample calculation for a significance level of 5%, effect size of 0.80 and test power of 80% indicated that 26 subjects would be needed in each of the evaluated groups. However, 24 individuals were evaluated in group 2, and 32 were evaluated in group 1. Nevertheless, this fact does not seem to have affected the analysis because the test power after patient randomization was 83%.

In conclusion, a decrease in the RI was observed in the OA after peribulbar anesthesia with a vasoconstrictor. Other studies are necessary to confirm these results and demonstrate the benefits of using adrenaline in peribulbar anesthesia.

Authors' contributions IPM, GCV and RSG contributed to the study conception and design. Data collection was performed by IPM and RSL. Material preparation and analysis were performed by IPM, GCV and RSG. The first draft of the manuscript was written by IPM. All authors commented on early versions of the manuscript, and all authors read and approved the final manuscript.

Compliance with ethical standards

Conflict of interest All authors declare that they have no conflicts of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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