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ORIGINAL PAPER

The effects of tropicamide and cyclopentolate hydrochloride on laser flare meter measurements in uveitis patients: a comparative study

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Abstract

Purpose To investigate the effects of 1% cyclopentolate hydrochloride and 1% tropicamide eye drops on aqueous flare measurements by using the laser flare meter.

Methods One hundred forty eight eyes of 83 patients with inactive uveitis were enrolled. The patients were randomly assigned to receive either 1% tropicamide (Group 1) or 1% cyclopentolate hydrochloride (Group 2) as the mydriatic agent. Best corrected visual acuity (BCVA), intraocular pressure (IOP), aqueous flare reaction levels measured by laser flare meter device (FM 600, Kowa, Kowa Company Ltd, Nagoya, Japan) before and post dilatation agents were evaluated.

Results Group 1 consisted of 75 eyes and Group 2 consisted of 77 eyes. The mean age of Group 1 patients was 34.85 ± 12.60 (range, 12–64) years; the mean age of Group 2 was 36.92 ± 13.30 (range, 12–70) years ($p > 0.05$). The mean BCVAs of two groups were 0.16 ± 0.43 (range, 0.00–3.10) logMAR and 0.17 ± 0.42 (range, 0.00–3.10) logMAR, respectively. There were no statistically significant differences between Groups 1 and 2 regarding gender or clinical characteristics ($p > 0.05$). No significant differences were detected in pre- or post-dilatation values between two groups ($p = 0.470$, $p = 0.998$).

Conclusions As a result, anterior chamber flare values in uveitis patients do not differ significantly between 1% tropicamide and 1% cyclopentolate hydrochloride, and both agents can be safely used for dilatation during examination of patients with uveitis.

Keywords Cyclopentolate hydrochloride · Laser flare meter · Tropicamide · Uveitis

Introduction

The anterior chamber is an optically empty space under normal conditions. The optical transparency of the aqueous humor enables the preservation of optimal visual function. In pathological conditions, disruption of the blood-aqueous barrier results in the infiltration of inflammatory cells as well as serum proteins from inflamed uveal tissues into the anterior chamber. This infiltration changes the optical properties of the aqueous humor [1]. Clinicians estimate the concentration of cells in the aqueous humor by counting the number of cells in a certain volume [2]. In addition, reduced aqueous flow or disrupted blood-aqueous barrier lead to protein leakage from the blood vessels of the ciliary body or inflamed iris, resulting in increased protein concentration in the aqueous humor.

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This condition is clinically characterized by flare (anterior chamber turbidity) and in severe cases gives a hazy or milky appearance to the aqueous humor [3].

Laser flare meter is a non-invasive, non-contact, quantitative method of measuring cells and protein in the aqueous humor [4]. Flare measurement is useful for evaluating intraocular inflammation in both anterior and posterior uveitis [5]. Consisting of a diode laser with a wave length of 650 nm, the device determines the amount of flare by measuring the intensity of scattered light detected by its photomultipliers. This method requires minimal patient cooperation and is quick, sensitive, and reproducible [5]. However, previous studies have shown that laser flare photometry values are variable and may be affected by non-disease factors that influence levels of aqueous protein and the amount of light back-scattered by the anterior chamber. These factors include use of mydriatic agents and pupil diameter [3, 4, 6–9]. Studies have shown that laser flare values are reduced by 10–20% following dilatation in normal eyes [9]. A similar decrease in laser flare meter values has been shown in pseudophakic eyes, as well [8]. However, there was no significant alteration in flare values of patients with chronic anterior uveitis after pupillary dilation [3].

As these contradictory findings point out, the mechanisms underlying the change in laser flare meter measurements after pupillary dilation are still unclear. Furthermore, the consequence of mydriatic agents in eyes with uveitis, in terms of flare levels, has not yet been established in detail. Cyclopentolate hydrochloride and tropicamide are midriatic agents which are commonly used for fundoscopic evaluation and treatment of uveitis patients. The possible effect of both agents on flare values may interprete the decision of management of these patients. Therefore, in this study we aimed to investigate the effects of 1% cyclopentolate hydrochloride and 1% tropicamide eye drops on the measurements performed in eyes with inactive uveitis.

Materials and methods

This study was approved by Institutional Ethics Committee of Ege University and data were collected in accordance with the Declaration of Helsinki. A written informed consent was obtained from all cases or their parents for subjects under 18 years of age. The analysis included 148 eyes of 83 patients with uveitis who attended the Uvea Unit of the Ege University School of Medicine, Department of Ophthalmology and consecutively presented for follow-up examination between January and June 2018.

Patients with inactive non-infectious uveitis, no other ocular disease that may cause inflammation, flare meter measurement below 15 photon/ms before drop instillation, and dilated pupil diameter of at least 6 mm were included in the study. Patients with a history of intraocular surgery and with severe posterior synechia that hindered pupil dilatation were excluded.

After Best Corrected Visual Acuity (BCVA) assessment, anterior chamber turbidity was measured prior to dilatation using the laser flare meter (KowaFM-600, Tokyo, Japan). A sample window of 0.3 mm by 0.5 mm is scanned at intervals of 0.5 to measure the amount of light, and the background is measured using laser beams above and below. The measurements from the sample window are averaged and the background signal is subtracted to yield laser flare photometry values. The flare value is expressed in photons per millisecond (photon/ms). The patients were randomly assigned to receive either 1% tropicamide (Tropamid, Bilim Ilaç, Turkey) (Group 1) or 1% cyclopentolate hydrochloride (Cycloplegine, Abdi Ibrahim, Turkey) (Group 2) as mydriatic agent. Forty-five minutes after instilling the eye drop, anterior chamber flare was reassessed using the same flare meter. The patients underwent a full ophthalmologic examination including BCVA, slit-lamp anterior segment examination, fundus inspection with 90 *D* lens, intraocular pressure (IOP) measurement.

The data were coded and transferred to computer software. Statistical analysis was done using SPSS (Statistical Package for the Social Sciences, SPSS Inc., USA) version 17.0 for Windows. Numerical variables' conformance to normal distribution were checked using the Shapiro–Wilk test. Categorical variables were expressed as frequency and percent, while numerical variables were expressed as mean and standard deviation or median and minimum–maximum values. Correlations between pairs of categorical variables were tested using the Chi-square test. Student's t test was used in comparisons with independent means and the Mann–Whitney U test was used in comparing independent medians. Differences between dependent medians were analyzed

using Wilcoxon signed-rank test. P values < 0.05 were considered statistically significant.

Results

The uveitis type was anterior in 62 eyes (including idiopathic, Fuchs heterochromic, juvenile idiopathic arthritis and HLA B27 uveitis), posterior in 15 eyes (due to White Dot Syndromes and polyarteritis nodosa), and panuveitis in 75 eyes (associated with Sarcoidosis, Vogt-Koyanagi- Harada Syndrome, Behçet's disease). All cases were in inactive stage with flare measurements below 15 photon/ms and the patients who had underlying systemic diseases received immunsupresive treatments (methotrexate, azothiopurine, cyclosporine A,interferon-alpha 2a, infliliximab or adalimumab) for disease control.

The patients were randomly divided into two groups according to the used mydriatic agent. Group 1 received 1% tropicamide and Group 2 received 1% cyclopentolate hydrochloride.

Group 1 included 75 eyes of 40 patients (20 females, 20 males) with a mean age of 34.85 (range, 12–64) years; Group 2 included 77 eyes of 43 cases (20 females, 23 males) with a mean age of 36.92 (range, 12–70) years. There were no statistically significant differences between Groups 1 and 2 regarding age, gender, or clinical characteristics ($p > 0.05$) (Table 1).

In Group 1, the median laser flare value decreased insignificantly from 5.60 (range, 1.10–14.80) photon/ms pre-dilatation to 5.40 (range, 1.20–23.70) photon/ms post-dilatation ($p = 0.470$; dependent t test). In Group 2, the median laser flare value also decreased insignificantly from 5.70 (range, 1.80–14.80) photon/ms pre-dilatation to 5.40 (range, 1.60–25.00) photon/ms post-dilatation ($p = 0.998$; dependent t test) (Table 2).

Discussion

Uveitis is characterized by intraocular inflammation that affects the uveal tract**.** Aqueous flare and anterior chamber cells are useful parameters to evaluate the inflammation [10]. Previous studies have shown that the quantification of aqueous flare by laser flaremeter has a strong correlation with the clinical grading of anterior chamber cells, and enables objective measurement of intraocular inflammation [1]. Grading of inflammatory findings are of the greatest significance in management of uveitis patients [11]**.** Herbort et al. [11] proposed that flare measurements are helpful to monitor and also to adjust therapy in both anterior and posterior uveitis. Even it has been shown that higher flare values were associated with a higher risk of recurrent uveitis attacks [5].

Gonzales et al. [12] reported a strong relationship between high laser flare photometry values and

Table 1 Demographic data and clinical characteristics of the patients

	Group 1 (75 eyes)	Group 2 (77 eyes)	P value
Mean age ± SD (range) year	34.85 ± 12.60 (12–64)	36.92 ± 13.30 (12–70)	0.253*
Sex (female/male) (n, %)	20/20 (50/50)	20/23 (53.50) (46.50/53.50)	0.750**
Type of uveitis			
Anterior uveitis	28 (37%)	34 (44%)	0.690**
Posterior uveitis	8 (11%)	7 (9%)	
Panuveitis	39 (52%)	36 (47%)	
IOP (mmHg)	13.65 ± 2.66	13.99 ± 2.50	0.406***
BCVA (logMAR)	0.16 ± 0.43 (0.00–3.10)	0.17 ± 0.42 (0.00–3.10)	0.861*
Pre-dilatation flare value (photon/ms)(Mean ± SD, range)	6.70 ± 3.10 (1.1–14.80)	6.80 ± 3.40 (1.8–14.80)	0.919***

*Student's t test; **Chi-square test; ***Mann Whitney U test; n: number of subjects; *SD* standard deviation; *IOP* intraocular pressure; *BCVA* best corrected visual acuity; *logMAR* logarithm of the Minimum Angle of Resolution

Table 2 Pre- and post-dilatation flare values in Group 1 and 2

	Pre-dilatation flare values (photon/ms) mean, mean ± SD (min–max)	Post-dilatation flare values (photon/ms) Mean, Mean ± SD (min–max)	%95 Confidence interval of the difference (lower–upper)	*P* value
Group 1 (75 eyes of 40 patients)	5.60, 6.70 ± 3.10 (1.10–14.80)	5.40, 6.70 ± 4.20 (1.20–23.70)	(− 0.977, 0.872)	0.470*
Group 2 (77 eyes of 43 patients)	5.70, 6.80 ± 3.40 (1.80–14.80)	5.40, 6.90 ± 4.50 (1.60–25.00)	(− 1.043, 0.766)	0.998*

*Wilcoxon signed-rank test

complications of various uveitis types especially with flare higher than 20 photons/ms. Schalnus et al. [13]. demonstrated that flare values increased in both anterior and posterior uveitis compared to normal eyes, but did not significantly differ between them. Laser flare meter studies have also shown an increase in various non-uveitic disorders, such as epidemic keratoconjunctivitis, diabetic retinopathy, retinal vein occlusion, and retinitis pigmentosa [14–17].

Laser flare meter measurements are affected by several factors including mydriatic agents and pupillary dilation [18]. In healthy population, as well as in pseudophakic eyes, there is a significant decrement obtained with laser flare meter following pupillary dilation [6, 19]. El-Haraziet al. [19] reported that flare value was reduced after pupillary dilatation and associated aqueous protein concentration with aqueous flow rate. Shah et al. [9] showed in their study that a slight reduction in flare meter measurements performed after pupil dilatation may be an artifact. They attributed the lower flare meter measurements to reduced light scattering as the iris moves away from the scanning window. Other evidence put forward to account for this reduction focused on the pharmacological effects of mydriatic agents [9]. Oshika et al. [6] reported a reduction in photometric measurements following maximum pupil dilatation and associated their findings with decreased permeability of the blood-aqueous barrier. However, they did not evaluate the influence of pupil diameter size on the measurements [6].

On the other hand, Ikejiet al. [3] detected no significant difference between flare measurements of patients with chronic anterior uveitis obtained before and after pupil dilatation with 1% tropicamide and 2.5% phenylephrine. Post-dilatation flare was increased in some patients and was decreased in others. The pharmacology of tropicamide might manifest differently in patients with chronic anterior uveitis with blood-aqueous barrier disruption in comparison to healthy individuals [3]. In another study, Chin et al. [20] instilled 1% tropicamide to one eye and 2.5% phenylephrine and 1% tropicamide to the other and observed no statistical difference in flare measurements of these groups. Similar results were reported with 1% tropicamide in patients with pseudoexfoliation [21]. However, effect of cyclopentolate hydrochloride has not been previously investigated on flare measurements. Tropicamide and cyclopentolate hydrochloride are mydriatic agents and are used commonly during biomicroscopic examination of uveitic eyes. They are also frequently prescribed for treatment of anterior uveitis.

We undertook this project to investigate whether these mydriatic agents effect flare values after their usage in inactive uveitic eyes. For this purpose, in the present study, the comparison of flare measurements obtained pre- and post-dilatation with 1% tropicamide and 1% cyclopentolate hydrochloride revealed no statistically significant differences. For this reason, it can be concluded that these agents, which are commonly used in uveitis patients, do not influence flare measurements and do not cause errors in routine examination and follow-up. On the other hand, this topic in active uveitis patients should also be investigated in order to make sure that the use of these agents also do not interfere with anterior chamber flare measurements in active periods of uveitis.

Conclusion

In conclusion, this study has shown that there is no significant change in anterior chamber flare values in uveitis patients following pupillary dilation with 1% tropicamide and 1% cyclopentolate hydrochloride. Therefore, both agents can safely be used for pupillary dilation during ophthalmic examination and treatment of uveitic eyes.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict 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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