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Pseudophakic Vision with residual ametropia after pilocarpine 2% instillation

A visão em pseudofácicos com ametropia residual após instilação de pilocarpina a 2%

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Abstract

Objective: *Evaluate the visual acuity, refraction, visual field changes and pupillary diameter in pseudophakic patients after instillation of 2% pilocarpine eye drops.* ***Methods:*** *Controlled, masked and randomized clinical trial carried out between May, 2015 and September, 2016 at the Gaffrée and Guinle University Hospital, RJ, Brazil. Forty patients, divided into 2 groups, were followed up in the postoperative period of a facectomy with intraocular lens implant. The patients in the group of cases were submitted to a drop of 2% pilocarpine and those of the control group to a drop of lubricant in the operated eye. Before eye drop instillation nd one hour after it, the authors evaluated: visual acuity for distance and near; refraction; pupillary diameter and visual field.* ***Results:*** *In case group visual acuity increased from 0.33 to 0.57 for far (p = 0.0001)and also increased for near, 13 patients (59.09%) had visual acuity of J1 or J2 before instillation and 18 or 81.81% after it (p = 0.0054). The median pupillary diameters raised from 2.00 mms to 1.85 mm(p <0.0001). Central visual fields did not have significant alteration. In the control group, there were no statistically or clinically significant changes in any of the measured parameters.* ***Conclusion:*** *Topical administration of a 2% pilocarpine eye drop was effective to improve pseudophakic patients vision with residual ametropia for far and near. Additional dose-effectiveness studies may indicate better concentrations and dosages to achieve greater improvements in visual acuity.*

Keywords: *Pilocarpine; Pseudophakia; Refractive errors; Visual acuity*

Resumo

Objetivo: Avaliar modificações de acuidade visual, refração, campo visual e diâmetro pupilar, em pacientes pseudofácicos, após a instilação de pilocarpina a 2%. **Métodos:** Ensaio clínico, controlado, mascarado e randomizado realizado entre maio de 2015 e setembro de 2016 no Hospital Universitário Gaffrée e Guinle, RJ, Brasil. Quarenta pacientes divididos em 2 grupos foram acompanhados em pós-operatório de facectomia com implante de LIO. No grupo de casos houve aplicação de uma gota de pilocarpina a 2%, no grupo controle, uma gota de lubrificante no olho operado. Foram avaliadas antes e 1 hora após a instilação do colirio: a acuidade visual para longe e perto com e sem correção; a refração; o diâmetro pupilar e o campo visual. **Resultados:** No grupo de casos, a acuidade visual s/c para longe aumentou de 0,33 para 0,57 (p = 0,0001) e para perto melhorou também, 13 pacientes (59,09%) possuíam acuidade visual de J1 ou J2 antes da instilação e depois o número aumentou para 18 ou 81,81% (p = 0,0054). O diâmetro pupilar reduziu de 2,00mm para 1,85mm (p < 0,0001). Não houve alteração do campo visual central. No grupo controle, não houve variação estatisticamente ou clinicamente significativa de qualquer um dos parâmetros medidos. **Conclusão:** A administração tópica de uma gota de pilocarpina a 2% melhorou a visão de pacientes pseudofácicos com ametropia residual para longe e para perto. Estudos de dose-efetividade adicionais podem indicar melhores concentrações e posologias para alcançar maiores melhoras de acuidade visual.

Descritores: Pilocarpina; Pseudofacia; Erros de refração; Acuidade visual

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Introduction

Nowadays, the increasing requirement of the patients in relation to the visual result obtained after a cataract surgery is evident. This fact is justified both by the improvement of the surgical technique and the development of modern instrumentation by the pharmaceutical industries.[1]

In this sense, the cataract surgeon nowadays deals with a highly demanding public regarding achieving an excellent visual acuity in a short period of time, either by medical marketing or reports of the patients themselves.[2]

Recently, intraocular devices have been developed in order to achieve these results. After the creation of the toric and multifocal intraocular lenses, the intraocular implant of "Pinhole" was created in 2014.[3]

The latter is based on the principle of the pinhole in which an opening of approximately 2 mm for the entrance of light rays into the eye is capable of isolating the peripheral rays suffering more aberrations and restricting the vision to the central rays focusing on the macula. Thus, there is improvement of visual acuity and depth of focus of patients.[4-6]

Despite the good results reported in the medical literature of the "Pinhole" intraocular implant, it has some limitations such as the high cost, the need for more surgical experience, and additional pre- and postoperative care.[3]

Therefore, an option of lower cost and greater ease of use is the topical ocular pilocarpine. This drug is used in ophthalmology since 1876, mainly to reduce the intraocular pressure in patients with glaucoma,[7]with direct cholinergic action on the muscarinic receptors of the smooth musculature of the iris and ciliary body. Thus, pilocarpine increases the drainage of aqueous humor via trabecular, and contracts the sphincter muscle of the iris producing miose capable of inducing the formation of a natural pinhole.[8]

Pilocarpine had its proven efficacy to improve presbyopia in emetopic patients[9] and reduce hyperopia after radial keratotomy,[10] and now can have a new use to improve visual acuity in pseudophakic patients who remained with residual refractive error.

Objectives

To evaluate changes in visual acuity, refraction and visual field as a function of pupillary diameter variation in pseudophakic patients with 2% pilocarpine eyedrops.

Methods

The research was carried out from May 2015 to September 2016 at the ophthalmology ambulatory of Hospital Universitário Gaffrée e Guinle (HUGG) - RJ. A randomized, double-masked, controlled clinical trial was carried out in a series of 40 patients who underwent phacoectomy with intraocular lens implant by the phacoemulsification method.

The inclusion criteria in the study were:

1) Patients in the period from one to six months postoperatively without complications and operated only by the author.
2) Show a refractive error greater than or equal to 1 spherical or cylindrical diopter in the operated eye.

The exclusion criteria were:

1) Anisocoriasis and/or any iris alteration.
2) Presence of any systemic disease affecting the autonomic nervous system.
3) Presence of posterior synechiae.
4) Presence of inflammatory ocular diseases.
5) Presence of eye disease preventing the pupillary diameter measurement
6) Refusal to sign the Free and Informed Consent Term.

All patients who agreed to participate in the study signed an informed consent form. Patients were divided into two groups randomly. In one group pilocarpine 2% was applied to the operated eye, and in the other group a placebo (Lacrifilm®) was instilled. Both the patients and the doctor who instilled the eyedrops and performed the visual measurements did not know which eyedrop were instilled. Prior to instillation of the eyedrops and after one hour afterwards, the operated eye was measured for: visual acuity, refraction, visual field, and pupillary diameter.

Visual acuity was measured by the Snellen optotype projector at a distance of 6 meters; the objective refraction was measured with the manual and subjective refractors with the Greens refractor; the pupillary diameter was measured with a pupilometer, and the visual field with Humphrey Central strategy apparatus, "full threshold", 24.2.

Patients were randomly inserted into the study groups using an Excel table of pseudorandom numbers.

One vial of pilocarpine 2% ocular solution eyedrops (Pilosol®) and one vial of ocular lubricant (Lacrifilm®) were used.

The descriptive statistics were made from the database created in the program Epi info 7.2®, and a table was generated by the program Microsoft Excel®. The Wilcoxon Signed Rank test from the website "vassarstats.net" was used to analyze the groups before and after administration of pilocarpine, showing the differences between visual acuity for near and far sight, pupillary diameter, and the refraction spherical equivalent. The McNemar test was used to analyze the presence or absence of visual field alterations.

Results

We examined 40 eyes of 40 patients. Of the eyes examined, 22 belonged to the case group in which a drop of Pilocarpine 2% was administrated, and 18 belonged to the control group which received a drop of Lacrifilm®.

The most frequent gender in the study groups was female, with 14 patients (63.64%) in the case group and 10 patients (55.56%) in the control group.

The predominant race was the white race: 13 patients (59.09%) in the case group, and 12 patients (66.67%) in the control group.

The average age of the patients in the case group was 67.86 years with a standard deviation of 8.11 years, whereas in the control group it was 67.0 years with a standard deviation of 10.39 years.

The most frequent iris color in both groups was brown: 18 patients in the case group (81.82%), and 17 in the control group (94,44).

The average postoperative day in the case group was 73.18 days with standard deviation of 41.97 days, and in the control group it was 66.05 days with standard deviation of 38.91 days.

Regarding visual acuity without correction for far sight in the case group, we noticed an increase in the average of 0.33 to 0.57 after 1 hour of instillation of pilocarpine 2% eyedrops ($p = 0.0001$). In the same group, we also observed improvement in the frequency of visual acuity without correction for near sight ($p = 0.005$) corresponding to J1 vision from 9 patients (40.91%) to 12 (54.55%), see table 1.

Table 1
Comparison between corrected and uncorrected visual acuity for far and near sight in cataract-operated eyes with and without instillation of Pilocarpine 2%

	Visual acuity Control Group			Visual acuity Case group		
	Before	After	P-value	Before	After	P-value
Far without correction	0.295	0.275	NS	0.3	0.67	0.0001
Near without correction	2.5	0.5	NS	1.0	0	0.0054
Far with correction	1.0	0.9	NS	0.9	1.0	NS
Near with correction	0	0	NS	0	0	NS

*NS- not statistically significant value

It was possible to analyze that the average pupillary diameter in the case group had a statistically significant variation after the use of eyedrops, presenting a median of 2.00mm before and 1.85mm after with p <0.0001. On the other hand, the control group had a median of 3.0 mm before and after the intervention (Table 2).

Table 2
Comparison between the spherical equivalent and pupillary diameter in cataract-operated eyes with and without instillation of Pilocarpine 2%

	Before	After	P-value
Spherical Equivalent Case group	-1.37	-1.06	0.091
Spherical Equivalent Control Group	-1.44	-1.52	0.8103
Pupillary Diameter Case group	2.0	1.85	<0.0001
Pupillay diameter Control Group	3.0	3.0	NS

The spherical equivalent of the refraction did not show clinically or statistically significant differences between the groups.

The analysis of the computerized campimetry exam showed that the group subject to the use of pilocarpine eyedrops had 5 patients (22.73%) with mild limitation in the peripheral field, whereas the control group did not show alteration in the exam (p=0.1093)

Discussion

Topical pilocarpine 2% is a parasympathomimetic drug with direct cholinergic action on the muscarinic receptors and smooth muscles of the iris and ciliary body. This drug causes the contraction of the pupil by increasing the tension in the scleral spur and providing the opening of the spaces of the trabecular meshwork. It is traditionally used to reduce the intraocular pressure in the treatment of glaucoma,[1] and for increased salivation in patients with Sjogren's Syndrome.[2] Recent articles show the use of topical pilocarpine for pupillary manipulation in order to reduce the positive and negative dysphotopies in pseudophakic patients in the postoperative cataract surgery.[3,4] The effect of pilocarpine for this purpose comes from the miosis and creation of a pupillary pinhole excluding the peripheral rays in the formation of the image and improving the depth of focus. As the central light rays suffer less aberrations, they provide greater sharpness of the images formed. In cases of irregular astigmatism, the pinhole can provide better visual acuity than the isolated refraction.[5]

Several devices based on pinhole have been recently studied in order to improve visual acuity and associated symptoms in pseudophakic patients.[5-8] After extensive bibliographic research in digital databases (Medline, Scielo, LILacs, etc.), we found no articles on the miotic effect of pilocarpine ("pupillary pinhole") on the improvement of visual acuity in pseudophakic patients. Unlike the implanted optic devices, the miotic effect of pilocarpine has the advantage of being reversible, and can also be applied to temporary tasks like work with computer (improvement of the near sight), daytime automotive direction, participation in social events.

Trindade et al.,[5] created an intraocular pinhole implant aimed at improving vision and photosensitivity in pseudophakic patients with irregular astigmatism. In the case report published the implant allowed improvement of four lines in visual acuity for far sight without correction, and 5 lines with correction after the surgical procedure. In our study, 22 eyes of pseudophakic patients with residual ametropia greater than 1.0D were studied. There was an average improvement of 2 lines of visual acuity not corrected for far sight, being the greater equivalent to 4 lines. The major improvement in the case reported by Trindade probably occurred because the patient had a corneal irregularity which impaired vision along with the high ametropi. In the present study, all corneas showed regular astigmatism and minor ametropias.

Colored contact lenses and corneal tattoos can also make use of the pinhole principle. According to Pitz et al., the corneal tattoo has good results with the introduction of pigment in the corneal stroma when used to camouflage anti-aesthetic corneal scars.[9] However, the procedure does not tend to be long-lasting, because with corneal punctures there is activation of macrophages that phagocyte the pigments. In addition, there are risks such as recurrent erosion of the epithelium, inflammation and toxicity.[9-11] The use of pilocarpine may also have ocular side effects such as miosis, myopia, ciliary spasm, and cataract, but it is not usually associated with aesthetic alterations or adverse corneal reactions.

Colored contact lenses are an option to form a pinhole, and are used to treat presbyopia.[7] Garcia-Lazaro et al. studied the sight of patients with 4 different diameters of pinhole in contact lenses. They realized that due to the ocular globe is an asymmetrical optical system, in most patients the center of the cornea, the visual axis, and the center of the pinhole in the contact lens took different positions and became misaligned.[6] The study also revealed that the pinhole in the lens moves with the blink of the eye or accommodation movement, which decreases its effectiveness. The use of pilocarpine causes myoses regardless of alignment of the visual axis or palpebral

and ocular movement. In addition, the use of contact lenses requires manual ability for lens placement and extensive hygiene measures, with the risk of long-term corneal alterations, and even infectious ulcers with inadequate use of these lenses.[12] In addition, there was no relevant visual improvement for near visual acuity. Regarding pilocarpine, there is no need for very strict hygienic care, and the majority of patients had visual acuity better than J2 for near sight without correction.

Another recent advent based on the pinhole principle is the "Acufocus Inlay", which consists of an opaque disc with a 1.6mm aperture capable of simulating a pinhole. By means of a surgical procedure, the disc is positioned in the intracorneal space through a LASIK flap in the non-dominant eye. A study carried out by Seyeddain et al. showed that of the 37 patients who underwent Acufocus Inlay, 91% showed J3 near sight without correction, but many reported problems with night sight.[8, 13] Pilocarpine is clinically applied without the need for exposure to the risks inherent to surgery such as ocular infection, difficulty in healing, and need for rest.

Further studies are needed to evaluate the time and effective level of miosis to improve the visual acuity of pseudophakic patients with residual ametropia. The current study shows benefits mainly for SUS patients (pilocarpine has low cost), and for far sight, but it was done during an intense pilocarpine effect, i.e., 1 hour after instillation.[14] If this medication is used for the purpose of improving visual acuity, we can expect that the existence of adverse effects will be lower than to control glaucoma, since its use need not be continuous.

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