A Novel Pharmacological Treatment of Pseudophakic Presbyopia

Almamoun Abdelkader

Almamoun Abdelkader, MD. Department of Ophthalmology, Faculty of medicine, Al-Azhar University, Cairo, Egypt

Conflict-of-interest statement: The author has no funding or conflict of interest regarding the publication of this paper.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

INTRODUCTION

Presbyopia is a physiologic inevitability that causes gradual loss of accommodation resulting in loss of the visual ability to focus on objects located at different distances. Near visual acuity can be improved by increasing the depth of focus as well as by increasing the accommodation. Increased depth of focus can come from making the pupil small like a smaller aperture in a camera. The common traditional ways for improving vision in presbyopes was through wearing corrective lenses including pinhole spectacles or invasive procedures. Different approaches on the cornea (inlays), the crystalline lens and the sclera are being pursued to achieve surgical correction of this disability. There are however, a number of 3% carbachol plus 0.2% brimonidine eye drops. Control group (n = 15 eyes) received placebo drops. Drops were given to all subjects in a masked fashion, in their non-dominant eye. The subjects’ pupil size and both near and distance visual acuities were evaluated pre- and posttreatment at 1, 2, 4, and 8 hours, by a masked examiner at the same room illumination.

RESULTS: Statistically significant improvement in near visual acuity was achieved in all pseudophakic subjects who received carbachol plus brimonidine drops (p < 0.0001). In this masked study, they all liked and would use this therapy if it was available. None would use the placebo.

CONCLUSIONS: Improving the depth of focus by making the pupil small caused statistically significant improvement in near visual acuity in pseudophakic subjects. Carbachol plus brimonidine seem to be an acceptable and safe alternative to corrective lenses and surgical procedures.

Key words: Presbyopia; Pseudophakia; Carbachol; Brimonidine; Depth of focus; Miosis

© 2018 The Author(s). Published by ACT Publishing Group Ltd. All rights reserved.
of limitations and considerations that have prevented widespread acceptance of surgical correction for presbyopia. There remains a need for new non-invasive ways of ameliorating or reducing presbyopia for patients that do not wish to undergo surgery or use corrective lenses.

Presbyopia symptoms are present in patients after cataract lens extraction. The treatment of such patients is a main challenge of modern ophthalmology. Pseudophakic presbyopia corrections primarily include: (1) implantation of multifocal intraocular lens (IOLs); (2) implantation of accommodative IOLs; (3) pseudophakic monovision induced by monofocal IOLs[11] and (4) corneal inlays. The KAMRA (AcuFocus, Irvine, California, USA) corneal inlay is an annular aperture inlaid in the cornea of one eye where a small entrance pupil is exploited to create a pinhole-type effect that increases the depth of focus and enables improvement in near visual acuity[12-17]. Regarding monovision, one eye is corrected for distance vision and the fellow for near vision. In the majority of the cases, the dominant eye is corrected for distance vision and the recessive one for near vision. We attempt her with drops to approach this effect without surgery.

We present here a non-invasive alternative which is a medical treatment to improve near vision in pseudophakic pseudophakes by means of ophthalmic drops, which contain two drugs: a parasympathomimetic (3% Carbachol) and an alpha agonist agent (0.2% brimonidine) (treatment group). Placebo eye drops were used in some subjects as a control. The pharmacological treatment of the treatment group has two purposes namely a stimulation of the parasympathetic innervation primarily and mainly by increasing depth of focus and perhaps the accommodation and its potentiation and prolongation by an alpha agonist. The aim of this pilot study is to evaluate in a masked fashion the efficacy of using a parasympathomimetic drug together with an alpha agonist to create optically beneficial miosis to temporarily improve vision in pseudophakic subjects by improving the depth of focus.

**PATIENTS AND METHODS**

This study was begun after approval was obtained from The RCRC Independent Review Board, LLC 2111 West Baker Lane, Suite 400 Austin, Texas 78758. Each participant gave written informed consent, and the study followed the tenets of the Declaration of Helsinki. The pharmacological stimulation protocol was developed in accordance with that used previously in the invention of Dr. Herbert Kaufman[18].

Study participants were randomly selected volunteers. Pseudophakia was considered present if an uncorrected end-point print size ≥ Jaeger (J) 5 improved by ≥ 1 optotype with the use of a lens ≥ +1.00 D. All pseudophakic subjects were screened to be in good physical and ocular health and they completed a questionnaire to ascertain any contraindications for participation or predisposition to complications (eg, heart or respiratory conditions, migraines, high myopia, ocular or systemic medications, or ocular surgeries). All subjects had a fully dilated eye examination before they are considered eligible for the study. The examination screened for contraindications to the drugs, susceptibility to retinal detachment, ocular pathology, or peripheral retinal degeneration. Inclusion criteria were as follows: age between 30 and 80 years, emmetropic pseudophakes [cycloplegic spherical equivalent (SE), ≤ 0.25 D; astigmatism, ≤ 0.25 D], round pupil, good position of the implant and binocular uncorrected distance visual acuity ≥ 20/20. Exclusion criteria concerned patients with myopia, hyperopia and astigmatism higher than 0.25 diopter as well as those with corneal and vitreous opacities, pupil irregularities, anisocoria, amblyopia, chronic general pathologies and medications that would interact unfavorably with carbachol and brimonidine. None of the subjects included in the study had received any topical medication that could cause pupil mydriasis or miosis. During the study, the subjects were closely monitored and regularly asked to report on any ocular, systemic, or physiological reactions they experienced. Atropine was available in the event of adverse effects, although none was reported. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation.

**Procedures**

A single dose of 3% carbachol plus 0.2% brimonidine, or placebo was instilled in a masked fashion in the non-dominant eye of the subjects. All of the drugs administered in this study are approved by the US Food and Drug Administration and have been used for years as safe and effective agents for treating ocular pathologies. Initial pupil size and both near and distance visual acuities were documented before treatment and at 1, 2, 4, and 8 hours after treatment by the same independent examiner in the same room with the same instruments. Distance visual acuity was measured using the standard Snellen projector chart at 4 meter. Near visual acuity (NVA) was assessed at 40 cm using a hand-held Rosenbaum chart with Jaeger notation, always employing the same luminosity of 160 cd/m². Pupillary size (PS) was measured using Colvard handheld Infrared pupillometer (Oasis Medical, Glendora, CA, USA). Any adverse symptoms and subject satisfaction with near and distance vision were also monitored.

**Statistical analysis**

Data analysis was carried out with the Mann-Whitney U test, using MedCalc version 16.8 statistical software. P value of less than 0.05 was considered statistically significant. Data were expressed as mean, range, and standard deviation (SD).

**RESULTS**

Forty emmetropic and presbyopic pseudophakes between 30 years and 80 years old with an uncorrected distance visual acuity of at least 20/20 in both eyes were included in the study. The mean age of the treatment group (n = 25 eyes) was 54.21 ± 14.49 years (range, 30-80 years); 16 males and 9 females. The mean age of the control group (n = 15 eyes) was 54.42 ± 3.1 years (range, 40-75 years); 10 males and 5 females. No statistically significant difference in mean age or sex was found among the 2 groups.

In the treatment group, the mean near visual acuity (NVA) improved significantly from J-7.5 ± 1 before treatment to J- 1.42 ± 0.5 at 1 hour, J- 1.57 ± 0.5 at 2 hours, J- 2.14 ± 0.5 at 4 hours and J-2.35 ± 0.49 at 8 hours posttreatment (p < 0.0001). The mean pupillary size (PS) decreased significantly from 4.1 ± 0.5 mm before treatment to 1.2 ± 0.3 mm at 1 hour, 1.6 ± 0.3 mm at 2 hours, and 2 ± 0.2 mm at 4 hours and 2.5 ± 0.4 mm at 8 hours posttreatment (p < 0.0001).

**Placebo (control) group**

No statistically significant difference in mean (NVA) or mean pupil size was found in this group before treatment and at any time point after treatment. Data are summarized in table 1. Figures 1 and 2 show the mean changes in near visual acuity (Jaeger) and pupil size (mm) respectively over time for treatment and control groups.

**Distance visual acuity**

The uncorrected distance visual acuity was 20/20 of both eyes in all subjects before treatment and remained at 20/20 at all time periods...
after treatment.

**Groups' satisfaction**

*Carbachol plus brimonidine group (treatment group)*

All presbyopes in these masked studies who received carbachol plus brimonidine liked and would use this therapy if it was available. They showed satisfaction with both near and distance vision. 8 subjects out of 25 (32%) reported that the effect was excellent for the first 8 hours then gradually faded.

No subject in the treatment group reported headache, temporary difficulty in low luminosity (dimness), browache or burning sensation. Systemic side effects such as bradychardia, bronchospasm, and digestive problems were not found.

*Placebo group*

None would use the placebo. All subjects who received placebo reported that the drops did not improve their near vision, so that, they would discontinue using the drops.

**DISCUSSION**

This study piloted a simple maneuver aimed at improving near vision in pseudophakic subjects. Rather than tackling presbyopia with multifocal or accommodating lenses; pharmacologic treatment relies on the pinhole effect – increasing depth of focus by reducing aperture. The principle is being successfully applied in corneal inlays implanted in the non-dominant eye to enhance near vision. AcuFocus implant[2] is a corneal implant with a small central artificial pupil. It restores reading vision through increased depth of focus. Although there are some problems with centering the implant, Pulfrich effect and some surgical complications, it is clear that the principle of a small pupil that moves with the eye can give a good near vision and preserve distance acuity as well[7,9,10]. We attempted with drops to approach this effect without surgical interference.

Significant improvement in near visual acuity was found in all subjects who received 3% Carbachol and brimonidine compared to placebo (*p* < 0.0001).

The present study used 3% carbachol and an alpha agonist (0.2% brimonidine) to improve vision in pseudophakic presbyopes through increased depth of focus. Increase depth of focus allowed many presbyopes even older ones to benefit from using the drops. Brimonidine has little effect on the photopic pupil, but has been effectively used for many years to prevent excessive pupil dilatation in the dark, and thereby reduces scotopic symptoms, usually from the peripheral cornea after refractive surgery. It has not been used to ameliorate presbyopia.

In monocular treatment, the vision in the fellow eye with the normal pupil will have some blurry near vision, but distant objects are clear and there is no diminished light perception. When the images are merged, all subjects of treatment group had clear focus at near and distance with no perception of dimness. Carbachol and brimonidine can be used once daily to achieve an 8-hour effect.

**CONCLUSION**

The monocular pharmacologic treatment of presbyopia in pseudophakes with one drop a day of carbachol and brimonidine in the non-dominant eye, permits acceptable reading vision for many presbyopes even in older subjects. This topical agent is noninvasive and, we believe, it meets all of the criteria for an ideal treatment of presbyopia. Additional studies are planned in the future to use each drug separately and to try using the drops in presbyopia with different refractive errors as in hyperopic and myopic presbyopes.

**ACKNOWLEDGEMENT**

Herbert E. Kaufman was the primary researcher in the development of the study, contributed to data interpretation and took part in the manuscript preparation.

**REFERENCES**


Abdelkader A. Pharmacological treatment of pseudophakic presbyopia


Peer Reviewer: Muawyah Al Bdour