

A Novel Pharmacological Treatment of Pseudophakic Presbyopia

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ABSTRACT

AIM: To evaluate the efficacy of using a parasympathomimetic drops (carbachol) together with an alpha agonist (brimonidine) to create beneficial miosis aiming to ameliorate the effect of presbyopia in pseudophakic subjects.

METHODS: A prospective, double-masked, randomized, placebo-controlled clinical trial. 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 without additional ocular pathology were eligible for inclusion. Subjects were divided into 2 groups. Treatment group ($n = 25$ eyes) received single dose of

3% carbachol combined with 0.2% brimonidine eye drops in their non-dominant eyes. Control group ($n = 15$ eyes) received placebo drops. Initial pupil size and both near and distance visual acuities were measured before treatment and at 1, 2, 4, and 8 hours after treatment by the same independent 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 ($p < 0.0001$). All subjects were satisfied with the drops and none liked the placebo.

CONCLUSIONS: Making the pupil small creates a pinhole camera like effect which safely improves near visual acuity in pseudophakic candidates through increased depth of focus.

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

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INTRODUCTION

Near vision 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 smaller like a smaller aperture in a camera. Corrective lenses and invasive procedures are common traditional ways for correcting presbyopia. Invasive procedures involve different approaches on the cornea (inlays), the crystalline lens and the sclera. There still remains a need for new non-invasive ways of reducing presbyopia for patients that do not like to undergo invasive procedures or use corrective lenses.

Presbyopia symptoms are present in patients after cataract lens extraction. Methods of corrections of pseudophakic presbyopia primarily include: (1) implantation of multifocal and accommodative intraocular lens (IOLs); (2) pseudophakic monovision induced by monofocal IOLs^[1] and (3) corneal inlays. The KAMRA (AcuFocus,

Irvine, California, USA) corneal inlay creates a pinhole-type effect that increases the depth of focus and improves near visual acuity¹²⁻⁷¹. I attempt here with drops to approach this goal without surgery.

I present here a non-invasive alternative which is a pharmacological treatment to improve near vision in presbyopic 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 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 temporarily improve near vision in pseudophakic subjects by increasing 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. Written informed consent was obtained from each participant, 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 Kaufman⁸¹.

Study participants were randomly selected volunteers. Presbyopia was considered present if an uncorrected end-point print size \geq Jaeger (J) 5 improved by ≥ 1 optotype with the use of a lens $\geq +1.00$ D. All pseudophakic subjects were screened to be in good physical and ocular health. Dilated fundus examination was performed for all subjects before they are considered eligible for the study. The examination screened for contraindications to the drops and susceptibility to retinal detachment. 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 $\geq 20/20$. Exclusion criteria included patients with refractive errors higher than 0.25 diopter as well as those with ocular media opacities, pupil irregularities, and drugs that would potentially interact with carbachol and brimonidine.

Procedures

A single dose of 3% carbachol combined with 0.2% brimonidine, or placebo was instilled in a masked fashion in the non-dominant eye of the subjects. 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 at the same room illumination. Distance visual acuity was measured using the standard Snellen projector chart at 4 meter. Near visual acuity (NVA) was measured at 40 cm using a hand-held Rosenbaum chart with Jaeger notation, always employing the same luminosity of 160 cd/m². Pupil 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 pupil 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, 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 following treatment.

Groups' satisfaction

Carbachol plus brimonidine group (treatment group)

All subjects who received carbachol plus brimonidine would use this drops if it were 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, dimness, browache or burning sensation.

Placebo group

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 pilot study aimed at pharmacologically improving near vision in pseudophakic subjects. Rather than improving presbyopia using corrective lenses; pharmacologic treatment relies on the pinhole effect - increasing depth of focus. The principle is being successfully applied in corneal inlays implanted in the non-dominant eye to enhance near vision through increased depth of focus. Although there are some concerns with centering the implant and Pulfrich effect, it is clear that the principle of a small pupil that follows eye movement can improve near vision and preserve distance vision as well^{7,9,101}. I attempted with drops to target this effect without invasive 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 by making the pupil smaller. Both drugs are FDA approved and have been used for years as safe and effective treatment for glaucoma. Brimonidine has been effectively used to

decrease pupil dilatation under scotopic conditions, and thereby reduces scotopic symptom after laser refractive surgeries.

In monocular treatment, the vision in the fellow eye with the normal untreated 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 vision at both near and distance without having dimness. Carbachol and brimonidine can be used once daily to achieve an 8-hour effect.

CONCLUSION

The topical treatment of pseudophakic presbyopia using one drop a day of carbachol combined with brimonidine, offers acceptable reading vision for many pseudophakic candidates. Additional studies are planned in the future to use this topical therapy in presbyopia with different refractive errors.

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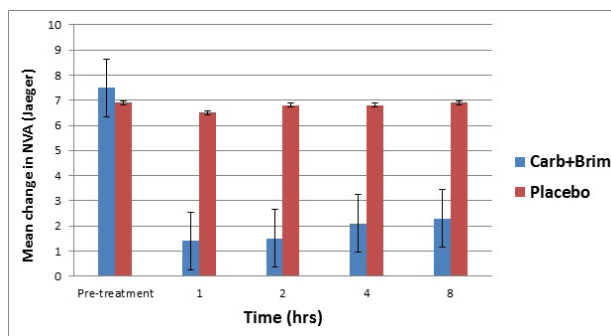


Figure 1 Distribution of mean change in near visual acuity (Jaeger) over time for treatment and control groups.

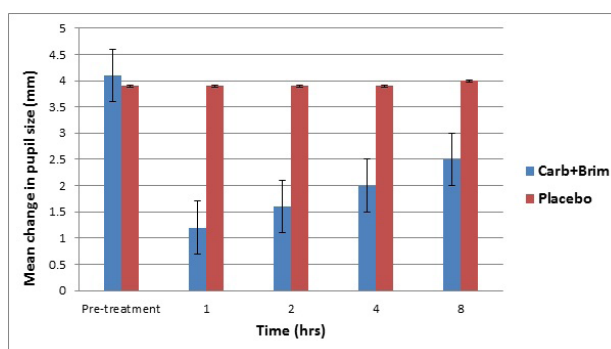


Figure 2 Distribution of mean change in pupil size (mm) over time for treatment and control groups.

Table 1 Mean change in near visual acuity (NVA) (J) and pupil size (PS) (mm) overtime using 3% Carbachol plus 0.2% brimonidine drops vs placebo.

Time (Hrs)		Carb+Brim drops	Placebo	P value
Pre-treatment	NVA	7.5	6.9	0.1
	PS	4.1	3.9	0.4
1- hour	NVA	1.4	6.5	< 0.0001
	PS	1.2	3.9	< 0.0001
2- hour	NVA	1.5	6.8	< 0.0001
	PS	1.6	3.9	< 0.0001
4- hour	NVA	2.1	6.8	< 0.0001
	PS	1.9	3.9	< 0.0001
8- hour	NVA	2.3	6.8	< 0.0001
	PS	2.5	4	< 0.0001

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