

## Influence of Different Concentrations of Carbachol Drops on the Outcome of Presbyopia Treatment – A Randomized Study

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### ABSTRACT

**AIM:** To evaluate and compare in a masked fashion the influence of using two different concentrations of carbachol drops on the outcome of presbyopia treatment.

**METHODS:** This was a prospective, double-masked, randomized study in which 57 emmetropic and presbyopic subjects participated. Subjects were divided into 2 groups. Group 1 ( $n = 32$  eyes) received single dose of 2.25% carbachol plus 0.2% brimonidine eye drops. Group 2 ( $n=25$ ) received single dose of 3% carbachol plus 0.2% brimonidine eye drops. The subjects' pupil size and both near and distance visual acuities were measured before and after treatment at 1, 2, 4, 8 and 12 hr, by an independent examiner at the same room

illumination.

**RESULTS:** There was a statistically significant improvement in mean near visual acuity (NVA) in all subjects who received both concentrations of carbachol plus brimonidine drops ( $p < 0.0001$ ). Significant and sustained improvement in mean NVA was reported in higher concentrations of carbachol drops than in lower concentrations ( $p < 0.0001$ ). No serious adverse ocular effects were observed in any of the subjects of both groups.

**CONCLUSION:** Based on the data, higher concentration of carbachol was found to be safe and provided greater efficacy in improving near visual acuity than lower concentration with extended duration of action.

**Key words:** Presbyopia, Carbachol; Brimonidine; Depth of focus

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### BACKGROUND

Presbyopia is defined as an age-related visual disorder that results in a blurry vision when targeting near objects<sup>[1-3]</sup>. In presbyopia, the ability of the ciliary muscle to accommodate, is often reduced<sup>[4,5]</sup>. Near vision can be improved by increasing the depth of focus. Increased depth of focus can be created from making the pupil smaller. Wearing pinhole spectacles was a traditional way to improve near vision in presbyopes. The KAMRA (AcuFocus, Irvine, California, USA) corneal inlay is designed to create a pinhole-type effect that increases the depth of focus and improves near visual acuity in presbyopes with preserved distance vision<sup>[6-11]</sup>. I attempted to use drops to approach this effect but in a noninvasive way. In this study, I used two different concentrations of carbachol to evaluate and compare in a masked fashion the influence of each concentration on the outcome of presbyopia treatment.

## METHODS

Each participant gave written informed consent and the study was performed according to the tenets of the Declaration of Helsinki. Participants were randomly selected volunteers. Presbyopia was considered present if an uncorrected endpoint print size  $\geq$  Jaeger (J) 5 improved by  $\geq 1$  optotype with the use of a lens  $\geq +1.00$  D. Inclusion criteria were as follows: age between 44 and 60 years, emmetropia [cycloplegic spherical equivalent (SE),  $\pm 0.25$  D; astigmatism,  $\leq 0.25$  D] and binocular uncorrected distance visual acuity  $\geq 20/20$ . Exclusion criteria included patients with myopia, hyperopia and astigmatism higher than 0.25 D as well as those with corneal, lens and vitreous opacities, pupil irregularities, and retinal disorders. Group 1 and 2 received a single dose of 2.25% and 3% carbachol, respectively combined with 0.2% brimonidine in their non-dominant eyes. Pupil size and both near and distance visual acuities were documented before treatment and at 1, 2, 4, 8 and 12 hour after treatment by the same independent examiner. Near visual acuity (NVA) was assessed at 40 cm using a hand-held Rosenbaum chart with Jaeger notation. Pupil size (PS) was measured using Colvard handheld Infrared pupillometer (Oasis Medical, Glendora, CA, USA). Drug side effects and subject satisfaction with near and distance vision were also monitored.

### Statistical Analysis

Statistical analysis was performed using the Student's t test and a p value of less than 0.05 was considered statistically significant. Data were expressed as mean  $\pm$  standard deviation (SD). Calculations were performed using the Statistical Package for the Social Sciences (SPSS) version 18.0 system for personal computers (SPSS Inc., Chicago, IL).

## RESULTS

57 emmetropic and presbyopic subjects aged between 44 and 60 years were enrolled in the study. The uncorrected distance visual acuity was at least 20/20 in both eyes. The mean age of group 1 (2.25% carbachol) was  $51.1 \pm 4.5$  years (range, 44-55 years); 18 men and 14 women. The mean age of group 2 (3% carbachol) was  $52.8 \pm 3.9$  years (range, 47-60 years); 14 men and 11 women. No statistically significant difference in mean age or sex was found among the two groups. In group 1, the mean (NVA) improved significantly from J  $7.37 \pm 1.6$  before treatment to J  $2.96 \pm 0.8$  at 1 h,

**Table 1** Mean change in near visual acuity (NVA) (Jaeger) and pupil size (PS) (mm) over time for group 1 receiving 2.25% carbachol plus brimonidine versus group 2 receiving 3% carbachol plus brimonidine.

Time		Group 1 (2.25% Carbachol plus Brimonidine)	Group 2 (3% Carbachol plus Brimonidine)	p-value
Pre-treatment	NVA	7.37	7.72	0.4
	PS	4.74	4.55	0.1
1- h	NVA	2.96	1.36	$p < 0.0001$
	PS	2.68	1.2	$p < 0.0001$
2- h	NVA	3.34	1.4	$p < 0.0001$
	PS	3	1.34	$p < 0.0001$
4- h	NVA	3.93	1.8	$p < 0.0001$
	PS	3.35	1.64	$p < 0.0001$
8- h	NVA	4.68	2.32	$p < 0.0001$
	PS	3.58	2.04	$p < 0.0001$
12-h	NVA	6.75	2.64	$p < 0.0001$
	PS	4.51	2.27	$p < 0.0001$

J  $3.34 \pm 1.1$  at 2 h, J  $3.93 \pm 0.98$  at 4 h, and J  $4.98 \pm 0.85$  at 8 h post-treatment ( $p < 0.0001$ ). At 12 h post-treatment, mean NVA was  $6.75 \pm 1.58$  J ( $p = 0.11$ ). The mean pupil size (PS) decreased significantly from  $4.74 \pm 0.47$  mm before treatment to  $2.68 \pm 0.41$  mm at 1 h,  $3 \pm 0.37$  mm at 2 h,  $3.35 \pm 0.4$  mm at 4 h and  $3.58 \pm 0.43$  mm at 8 h post-treatment ( $p < 0.0001$ ). At 12 h post-treatment, mean pupil size was  $4.51 \pm 0.69$  mm ( $p = 0.12$ ). In group 2, the mean (NVA) improved significantly from J  $7.72 \pm 1.48$  before treatment to J  $1.36 \pm 0.56$  at 1 h, J  $1.4 \pm 0.57$  at 2 h, J  $1.8 \pm 0.58$  at 4 h, J  $2.32 \pm 0.47$  at 8 h and  $2.64 \pm 0.7$  at 12 h post-treatment ( $p < 0.0001$ ). The mean pupil size (PS) decreased significantly from  $4.55 \pm 0.55$  mm before treatment to  $1.2 \pm 0.25$  mm at 1 h,  $1.34 \pm 0.31$  mm at 2 h,  $1.64 \pm 0.3$  mm at 4 h,  $2 \pm 0.28$  mm at 8 h and  $2.27 \pm 0.34$  mm at 12 h post-treatment ( $p < 0.0001$ ). In group 2 when 3% carbachol was instilled, the improvement in NVA was statistically significant up to 12 h post-treatment whereas in group 1, the improvement in NVA was only significant up to 8 h post-treatment. The improvement in mean NVA was more significant in subjects who received higher concentration of carbachol and brimonidine drops compared to those who received lower concentration of the compound ( $p < 0.0001$ ).

Data are summarized in Table 1. Figures 1 and 2 show the mean change in near visual acuity (Jaeger) and pupil size (mm) over time for both groups.

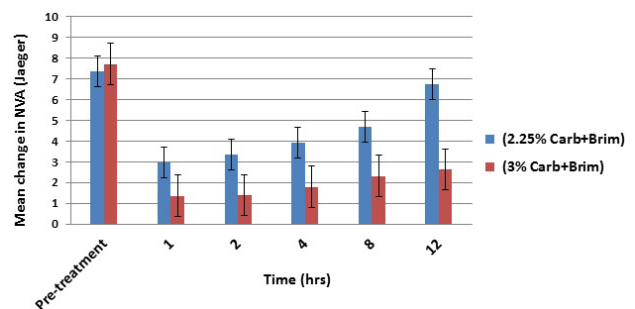
Burning sensation, browache, dimness or any other serious adverse ocular effects were not observed in any of the patients of both groups.

### Distance Visual Acuity

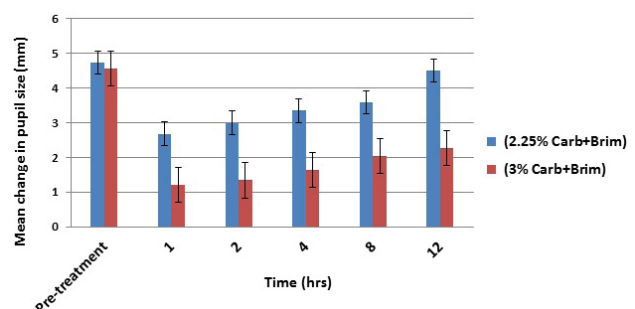
The uncorrected distance visual acuity was 20/20 of both eyes in all subjects before treatment and remained at 20/20 at all periods after treatment.

## DISCUSSION

Several researches have been performed to figure out how much each factor involved in the accommodative process shares to it<sup>12-</sup>



**Figure 1** Distribution of mean change in near visual acuity (Jaeger) over time for group 1 receiving 2.25% carbachol plus brimonidine versus group 2 receiving 3% carbachol plus brimonidine.



**Figure 2** Distribution of mean change in pupil size (mm) over time for group 1 receiving 2.25% carbachol plus brimonidine versus group 2 receiving 3% carbachol plus brimonidine.

<sup>16]</sup>. This study aimed at investigating and evaluating the optimal concentration of carbachol to effectively and safely improve near vision in presbyopic subjects for a prolonged time. The depth of focus was improved by the pinhole effect of drops. No patient in this study experienced dimness of vision as the other untreated eye fills in brightness. Statistically significant improvement in NVA and mean pupil size (PS) was achieved in all subjects who received both concentrations of carbachol plus brimonidine drops ( $p < 0.0001$ ), however, the improvement in mean NVA and PS was more significant in all subjects who received 3% carbachol drops up to 12 hours posttreatment ( $p < 0.0001$ ). No serious adverse ocular effects were observed in higher concentrations of carbachol. Further studies with larger cohorts of patients and longer follow up period are necessary to confirm our outcomes.

In conclusion, based on the data, higher concentration of carbachol was found to be safe and provided greater efficacy in improving near visual acuity than lower concentration with sustained and prolonged duration of action.

#### Authors' contributions

AA collected the clinical data, conducted the statistical analyses and interpretation of the data, prepared the manuscript and conceived the study design. The author read and approved the final manuscript.

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