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Therapeutic Effect of Topical Pilocarpine in Presbyopia Treatment

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ABSTRACT

Purpose: To evaluate the safety, efficacy, and patient satisfaction during the application of low-dose Pilocarpine 1.25% as a treatment option in presbyopia.

Study Type: A Prospective Interventional Clinical Trial.

Materials and Methods: 120 patients with presbyopia were enrolled in this study, patients ages were between 40 and 55 years. A full history was taken and a detailed ocular examination was done. Measurements of refractive errors, uncorrected distant visual acuity (UCDVA), uncorrected near visual acuity (UCNVA), intraocular pressure, and pupil diameter and iris color assessment were performed before the enrollment and after half an hour, an hour, and three hours from the installation of topical pilocarpine 1.25%. Pilocarpine 1.25% drops were given for a month at a rate of one drop in the morning. Finally, a questionnaire was taken about the extent of satisfaction and reported side effects of the treatment.

Results: Our study shows that the application of pilocarpine improved the average UCNVA from J3-J7 to J1-J2 with statistically significant differences (p=0.0001). A slight decrease in the mean UCDVA from 0.7-1.0 to 0.6-0.9 was noticed without statistically significant differences (p=0.09), and a decrease in intraocular pressure with statistically significant differences (p=0.01) was recorded. The self-assessment showed safety and patients were relatively satisfied when using the treatment.

Conclusion: The application of low-dose pilocarpine 1.25% drops in a daily dose for the treatment of presbyopia is safe and improves near visual acuity, without a statistically significant effect on uncorrected distant visual acuity, while maintaining its efficacy during the month of the study.

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Introduction

Presbyopia is a common age-related visual disorder characterized by a gradual decline in visual acuity, especially near vision. It assumed that the cause of presbyopia is either weakness of the ciliary muscles or loss of flexibility of the lens, which prevents the change of the near point [1, 2].

The prevalence and severity of presbyopia increase with age, with about 85% of people aged 40 years or older developing presbyopia [3]. In a 2015 study, it estimated that 1.8 billion people globally suffer from presbyopia and the prevalence is expected to peak at approximately 2.1 billion in 2030 [3].

In the same previous study, 826 million estimated to have functional presbyopia were found to be living with uncorrected near vision impairment because they had no access to vision correction or were utilizing inadequate correction. Without optical correction, presbyopia can have multiple effects on quality of life, such as problems reading (inability to read fine print, need for increased lighting, diplopia, epiphora, headache fatigue or asthenopia), and other tasks, such as threading a needle or seeing fine details on proximal objects [3].

It is estimated that 94% of those with significant near vision impairment due to uncorrected presbyopia live in developing countries [4]. Studies have revealed that presbyopia is under-corrected in many countries, with reading glasses available for only 6–45% of patients living in developing countries [4].

Uncorrected or under-corrected presbyopia affects quality of life, regardless of the nature of daily activities performed. At the same time, in developed countries, widespread access to corrective devices such as reading glasses may mean that potential alternative treatment options for presbyopia are often overlooked [5].

Presbyopia is usually diagnosed around the age of 50, and some studies indicate that individuals residing in developed countries who have not had an eye examination before the age of 50 are more likely to be normal or myopic [6].

Methods to correct presbyopia include both fixed- and variable-focus lens systems, as well as surgical interventions that modify the optics of the cornea, replace the crystalline lens, or attempt to at least partially restore active accommodation, with ongoing efforts to improve the presbyopic visual experience [7].

Recently, the need to use glasses for near vision has increased with the increasing prevalence of smartphones, mobile devices, and digital devices in our daily lives. It has requirements for near vision, especially for patients who use glasses for distant vision as well. These patients are forced to constantly change between glasses if they use two different glasses for far and near, or are unable to purchase high-cost bifocal, trifocal, and progressive glasses. In addition, dependence on glasses is one of the main reasons for changing the quality of life in people over 45 years [4].

Pharmacological treatment is an alternative that should be considered as an option among the treatment options for presbyopia, and among the available pharmacological options is the application of pilocarpine [8]. Pilocarpine is a cholinergic muscarinic receptor agonist that acts through M3 muscarinic receptors located on smooth muscles, such as the iris sphincter and ciliary muscle. Activation of these receptors leads to contraction of the iris sphincter, constricting the pupil (miosis) and creating a pinhole effect. Reduction of the pupil diameter increases the depth of focus and allows for greater ranges in uninterrupted near and intermediate vision that cannot be achieved using spectacle lens correction [9,10]. Meanwhile, contraction of the ciliary muscle changes the lens thickness, stimulating accommodation to improve near vision [9,10-12]. Pilocarpine HCl has long been used to decrease intraocular pressure in patients with glaucoma, but its use in this indication has declined steadily due to side effects such as brow ache, headaches, and vision blur, along with the emergence of other (more effective) glaucoma medications [13]. More recently, however, pilocarpine HCl has been investigated as a treatment for presbyopia, due to its ability to enhance both depth of focus and accommodation [9,10].

Since accommodation is the ability of the eye to increase its strength and refractive power when looking at close objects, it depends largely on pupil constriction and increasing the convexity of the lens. Considering that patients with presbyopia lack this accommodation ability, one of the objectives of our study was to evaluate the safety, effectiveness, and satisfaction of people with presbyopia after treatment with low-dose pilocarpine 1.25% [14].

Place and Time of Study

Ophthalmology Department at Tishreen University Hospital - Lattakia between 2023-2024.

Methods and Materials

120-presbyopic patients were enrolled in the study. Inclusion criteria were individuals aged between 40-55 years, experiencing decreased near visual acuity impacting daily activities and distant visual acuity equal to or exceeding 0.7 (20/25) in both eyes. Exclusion criteria included any refractive error values less than -0.50 or more than +2.00 or astigmatism more than 1.50, pregnancy, history of severe dry eyes, history of intraocular surgery (excluding Lasik or PRK), history of glaucoma or high eye pressure, severe posterior subcapsular and cortical cataract, anisocoria more than 1 mm and pupil diameter is less than 3 mm. We conducted a thorough assessment, including a review of relevant medical history and a comprehensive ophthalmological examination. Refraction was evaluated using an automated refractometer. Uncorrected distant visual acuity (UCDVA), and uncorrected near visual acuity (UCNVA), measuring intraocular pressure, iris color, and pupil diameter were assessed. After that, topical pilocarpine 1.25% was applied, and the patient was examined after half an hour, one hour, and three hours by assessing UCDVA, UCNVA, and intraocular pressure, evaluating the pupil diameter before and after applying pilocarpine. Patients were then given a drop of Pilocarpine 1.25% to be used once daily for a month. Finally, a satisfaction and side effects questionnaire were administrated to gauge the overall treatment experience.

The pilocarpine 1.25% drops used in the study were prepared as follows: 3 ml of a 0.5% Carboxymethyl cellulose artificial teardrop added to 5 ml of a 2% pilocarpine hydrochloride drop to obtain 1.25% pilocarpine concentration.

Statistical Study

The study design was a clinical trial (prospective) interventional. Program accreditation IBM SPSS statistics (version 20) to calculate statistical coefficients and analyze results and the results are considered statistically significant with a p-value < 5 %.

Results

The age range of participants was between 40 to 55 years with an average of 47.75±3.8 years. 59.2% were males and 40.8% were females with Sex Ratio (M: F) =1.4:1. Notably, 49.2 % of the sample had a light brown iris, followed by dark brown at a rate of 25.8 %.

The parameters measured included UCDVA (range: 1.0 - 0.7), UCNVA between (range: J7-J3), Intraocular pressure (range: 11-20 mmHg), the spherical equivalent of the refractive error measured in diopter (D) (range: -0.50 → +2.00) and the pupil diameter measured in millimeters (range: 3- 5.20) (Table 1).

Table 1: The Minimum and Maximum Variables and their Average Values

Mean ± SD	Max	Min	Variables
Uncorrected distant visual acuity	0.7	1.0	0.89±0.08
Uncorrected near visual acuity (J)	7	2	4.74±1.4
Intraocular pressure (mmHg)	11	20	15.84±2.01
Refraction (D)	- 0.50	+2.00	0.47±0.7
Pupil diameter (mm)	3	5.20	4.29±0.5

The refractive error range among the study sample was observed to be varied; with 46.7 % having refractive error within the range of +0.50 - +1 (Table 2).

Table 2: Distribution of the Study Sample According to the Values of the Spherical Equivalent of the Worst Refraction Measured in Diopter (D)

Auto Refraction SE(D)	Number	Ratio
- 0.50 → 0	21	17.5%
0 → +0.50	39	32.5%
+ 0.50 → +1	56	46.7%
+1 → +2	4	3.3%
Total	120	100%

The Average values of the studied variables and their assessment at different points in time, it was noted that there are statistically significant differences regarding all variables studied except for UCDVA (Table 3).

Table 3: The Average Values of the Studied Variables Mean values of uncorrected distant visual acuity (UCDVA) in the study sample

Time	Mean ± SD (UCDVA)	Mean ± SD (UCNVA)	Mean ± SD (IOP)	Mean ± SD (Pupil diameter)
Before Treatment	0.89±0.08	4.74±1.4	15.84±2.01	4.29±0.5
Half An Hour	0.77±0.09	3.26±1.2	15.60±2.06	2.59±0.2
Hour	0.80±0.1	2.73±1.09	15.56±2.1	2.13±0.1
Three Hours	0.83±0.09	1.96±0.7	14.92±2.02	2.30±0.1
P-Value	0.09	0.0001	0.01	0.00001
Decline	0.06	2.78	0.92	1.99

A reduction in the average values of UCDVA was observed after half an hour of treatment. The pre-treatment value was 0.89 and decreased to 0.77, subsequently returning to the value proximate to the pre-treatment measurement (0.83 after three hours). No statistically significant differences (p-value = 0.09).

Mean values of uncorrected near visual acuity (UCNVA) in the study sample

A progressive decrease in the average values of UCNVA was noted, demonstrating statistically significant differences (p-value = 0.0001), the initial value was 4.74 before treatment and decreased to 3.26 after half an hour, reaching 1.96 after three hours. The decline reached 2.78 at that time compared to the value before treatment (Chart 1).

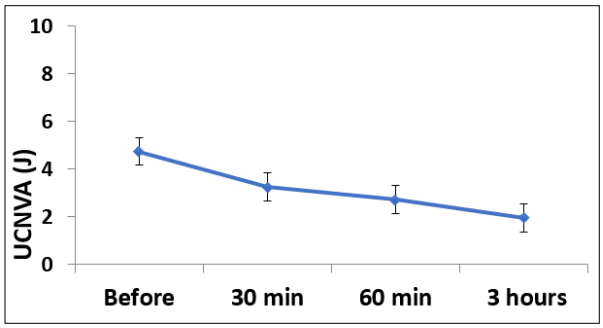

Chart 1: Mean Values of Uncorrected Near Visual Acuity (UCNVA) in the study sample

Average Values of Intraocular Pressure (IOP) in the study sample

A gradual decrease in the average values of IOP was noted, with statistically significant differences (p-value=0.01). It was 15.84 mmHg before treatment and decreased after half an hour to 15.60 mmHg, reaching 14.92 mmHg after three hours. The decrease reached 0.92 mmHg at that time compared to the value before treatment (Chart 2).

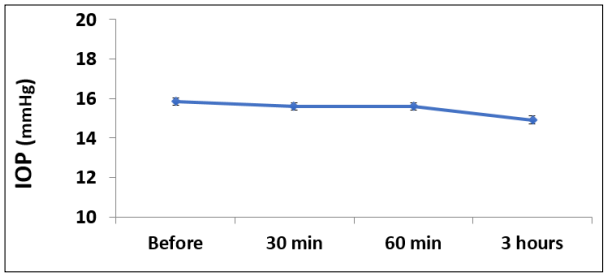

Chart 2: Average values for IOP in the study sample

Average values of Pupil Diameter in the Study Sample During Follow-Up Periods

It was noted that there is a gradual decrease in the average values of pupil diameter, with statistically significant differences (p-value=0.0001). It was 4.29 mm before treatment and decreased after half an hour to 2.59 mm, reaching 2.30 mm after three hours, where the decrease reached 1.99 mm at that time compared to the value before treatment (Chart 3).

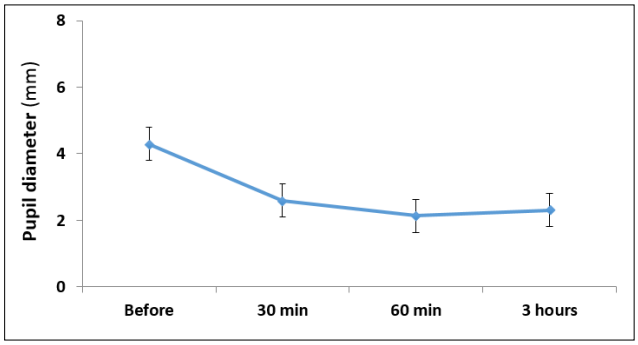

Chart 3: The average Values of Pupil Diameter in the Study Sample During the Follow-Up Period

Evaluating the Relationship Between the average Values of Pupil Diameter and iris Color in the Study Sample

No statistically significant differences between the averages of pupil diameter at each time point, based on iris color. The calculated p-value exceeded 0.005, as detailed in (Table 4). This suggests that variation in pupil diameter was not significantly associated with the color of the iris.

Table 4: Average Values of Pupil Diameter Concerning Iris Color in the Study Sample

Iris color	Before treat-ment	half an hour	hour	three hours
Blue	4.5±0.3	2.6±0.2	2.1±0.1	2.2±0.1
Green	4.1±0.8	2.6±0.4	2.07±0.1	2.1±0.1
light brown	4.06±0.3	2.7±0.2	2.2±0.09	2.2±0.1
Dark brown	4.3±0.5	2.8±0.2	2.3±0.06	2.3±0.1
P-value	0.08	0.1	0.7	0.5

Evaluation of the Side Effects of Using Pilocarpine 1.25% and their incidence, during a full month of use

The self-reported data collected through the questionnaire indicate that 40% of the sample studied had irritation and redness, 25.8% dimness of vision, 15% lacrimation, 14.2% headache, and 5% drowsiness (Chart 4).

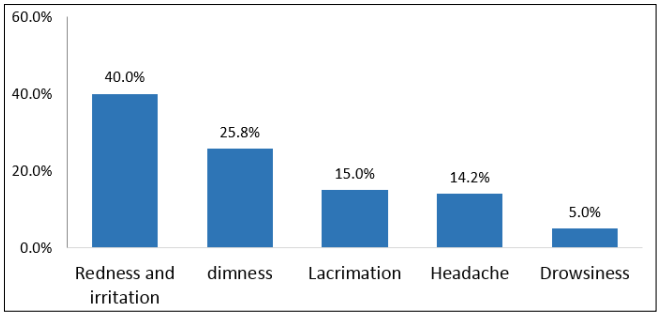

Chart 4: Side Effects of Using Pilocarpine 1.25% And Their Incidence, During A Full Month of Use

Evaluation of the Satisfaction Rate with the Use of Pilocarpine 1.25% Among the study sample after a full month of use

It noted that 43.3 % of the study sample had excellent and 22.5 % had good results after a full month of use (Table 5; Chart 5).

Table 5: The satisfaction rate for using pilocarpine is 1.25% among the study sample after a full month of use

Degree of satisfaction	the number	The ratio
Not Satisfied	6	5 %
Fair	17	14.2 %
Average	18	15 %
Good	27	22.5 %
Excellent	52	43.3 %

(Excellent = 100% of the time, Good = 75% of the time, Average = 50% of the time, Fair = 25% of the time, Not satisfied = did not improve)

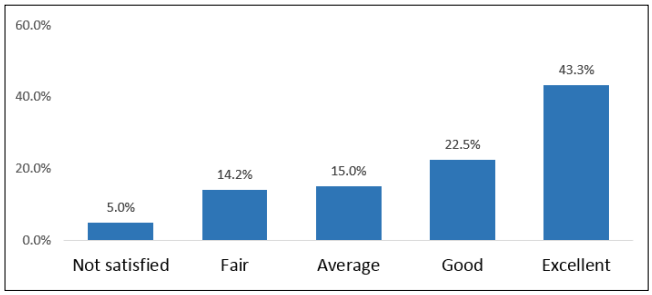

Chart 5: Degree of Satisfaction of the Study Sample After a Month of Using Pilocarpine 1.25% drops, by assessing the percentage of improvement in near vision

(Excellent = 100% of the time, Good = 75% of the time, Average = 50% of the time, Fair = 25% of the time, not satisfied = did not improve)

Discussion

In our study, we evaluated the effects of applying low-dose pilocarpine 1.25% on presbyopia patients aged between 40-55 years. We assessed the improvement in uncorrected near visual acuity (UCNVA), the impact on uncorrected distant visual acuity (UCDVA), the degree of miosis during follow-up periods, and the correlation between miosis degree and iris color. Additionally, we examined the influence of pilocarpine 1.25% on intraocular pressure and conducted a questionnaire on side effects and satisfaction over a month of use. We observed a gradual improvement in mean UCNVA values, with statistically significant differences (p-value=0.0001). Before treatment, it was J 4.74, improving to J 3.26 after half an hour and reaching J 1.96 after three hours. This improvement attributed to pupil constriction and ciliary muscle contraction, thus enhancing accommodation effectiveness. Our findings align with a study by Francis et al, concluding a significant improvement in mean UCNVA values ($p<0.001$), and with Kannarr et al, supporting improvement by 3 or more lines [15,16].

We observed a decrease in mean UCDVA values half an hour after treatment, from 0.89 before treatment to 0.77. After three hours, it returned to 0.83, with no statistically significant differences (p-value=0.09). This decrease may be due to diminution of vision because of pupil constriction and returns to normal because of physiological adaptation to dim light and Subsequent return to normal. These findings align with studies by Francis et al [15], George et al [18], and Benozzi et al [17]; they found a decrease in mean UCDVA values without statistically significant differences [15,17,18].

We observed a gradual decrease in average pupil diameter values (p-value=0.0001), from 4.29 mm before treatment to 2.59 mm after half an hour, reaching 2.30 mm after three hours. No statistically significant differences were found in pupil diameter in relation to iris color (p-value>0.05). In addition, we observed a gradual decrease in average intraocular pressure (IOP) values (p-value=0.01), from 15.84 mmHg before treatment to 15.60 mmHg after half an hour, reaching 18.92 mmHg after three hours.

After one-month questionnaire result revealed 40% of the sample suffered from irritation and redness, 25.8% experienced dimness, 15% had lacrimation, 14.2% reported headaches, and 5% experienced dizziness. Our findings align with Benozzi et al, where 65% reported side effects, including blurred vision (24%), headaches (11%), and redness and irritation (6%) [17]. The satisfaction rate after a month of use, 43.3% reported excellent results, and 22.5% reported good results. in other hand 5% of study sample reported that they not get satisfy at all and 14.2% of study sample reported that the satisfaction was fair.

Conclusion

The application of low-dose pilocarpine 1.25% drops in a daily dose for the treatment of presbyopia is safe and improves near visual acuity, without a statistically significant effect on uncorrected distant visual acuity, while maintaining its efficacy during the month of the study.

Abbreviations

J: Jaeger near visual acuity measure; UCDVA: Uncorrected distant visual acuity; UCNVA: Uncorrected near visual acuity; mmHg: Millimeter Mercury; LASIK: Laser assisted in situ keratomileusis; PRK: Photorefractive keratectomy; IOP: Intraocular pressure.

Ethical Issue

Written informed consent was obtained from all patients participating in the study (the approved form at the Faculty of Human Medicine at Tishreen University). The study was also approved by the Scientific Research Ethics Committee at the Faculty of Medicine at Tishreen University and by the Council of Tishreen University (Resolution No. 2292 dated / 8/2/2023)

Patient Consent

Written informed consent was obtained from the patients for participation publication of this paper and any accompanying images.

Funding and Competing Interests

The authors declare that there is no conflict of interest regarding the publication of this paper. This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data Availability

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Contributor

AQ performs examinations, follows up, prepares the drops, and writes the manuscript. TD direct supervision and revive. MR co-supervisor and review. All authors read and approved the final manuscript.

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