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Effect of Pilocarpine 0.2% for the Treatment of Presbyopia

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ABSTRACT

Objective: To determine the effect of Pilocarpine 0.2% for the treatment of presbyopia.
Study Design: Quasi-experimental Study.
Place and Duration of Study: Ophthalmology Department, POF Hospital, Wah Cantt, Pakistan from Jul to Sep 2024.
Methodology: One hundred and five patients (40–55 years) with presbyopia impacting daily activities were selected. Near vision was recorded before and after 1 hour of instillation of 0.2 % Pilocarpine drops and improvement in the number of lines in near vision was recorded. Patients were further divided into three Groups based on their age, i.e., 35 patients in each Group. Group 1 (40 to 45 years); Group 2 (46 to 50 years); and Group 3 (51 to 55 years). Improvement in near vision in each Group was also recorded.
Results: Among 105 participants, 48(46.0%) were females and 57(54.0%) were males. Topical Pilocarpine 0.2% was instilled in 105 individuals; 93 of them had an improvement in their near vision, whereas 12(11.4%) patients showed no improvement. Out of 93 patients who showed improvement, 56(53.3%) patients showed improvement of 1 line, 32(30.5%) patients showed improvement of 2 lines, and 5(4.8%) patients showed improvement of 3 lines in near vision. Improvement in near vision in each Group was also analyzed and it was statistically significant (*p*-value 0.024). Younger age Group showed more improvement as compared to older patients with Pilocarpine 0.2%.
Conclusion: Topical Pilocarpine 0.2% for the treatment of presbyopia is effective and has encouraging excellent results, especially in early presbyopia.

Keywords: Near vision, Presbyopia, Pilocarpine.

How to Cite This Article: *Shafi M, Lodhi Y, Aftab A, Sarfraz H, Khan MA, Khan AA. Effect of Pilocarpine 0.2% for the Treatment of Presbyopia. Pak Armed Forces Med J 2026; 76(Suppl-1): S97-S101. DOI: https://doi.org/10.51253/pafmj.v76iSUPPL-1.12900*

INTRODUCTION

Presbyopia is a normal age-related condition characterized by progressive loss of accommodation with decreased near vision.[1] It impairs the quality of life over the age of 40 years.[2] It is going to be one of the main persistent visual concerns due to its high prevalence globally. In 2015, an estimated 1.8 billion people had presbyopia worldwide, and in 2030, the prevalence is anticipated to rise to approximately 2.1 billion.[3] The prevalence of presbyopia in Pakistan was 57.5% (60.45% in males and 55.23% in females).[4]

Glasses, contact lenses, and new surgical interventions are available for the treatment of presbyopia.[5] Over-the-counter glasses are used to correct near vision. Because they are simple to use and non-invasive but many patients consider wearing glasses to be uncomfortable. Contact lenses are another popular option because of the characteristics like cosmetic effect, lack of fogging, and stability of their optics on the visual axis with eye movement.[6] However, contact lenses can be problematic for patients with dry eyes and other ocular surface diseases. Surgical interventions include modification of the optics of the cornea and replacement of the crystalline lens, but these are invasive and irreversible.[7,8]

However, during last decade, pharmacological treatment for treating presbyopia has emerged.[9] Pharmacological treatment is a non-invasive option for those who do not want to wear glasses for near task and is no doubt an encouraging research field in ophthalmology, as it helps to meet the dynamic visual requirements of the patient throughout the day. Pilocarpine 1.25% has been approved by U.S. Food and Drug Administration (FDA) as a treatment for presbyopia to improve near vision by enhancing depth of perception and accommodation.[10] The current study is conducted to determine the effect of Pilocarpine 0.2%, a minimum concentration for the treatment of presbyopia which is tested for the first time in Pakistan.

METHODOLOGY

The Quasi-experimental study was conducted at the Ophthalmology Department, Pakistan ordnance factories (POF) hospital, Wah Cantt, for 3 months (July

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Received: 25 Nov 2024; revision received: 19 Aug 2025; accepted: 05 Sep 2025

2024 to September 2024). Patients were selected through non-probability consecutive sampling. Institutional review board permission was obtained before the conduct of this study. (ERB No. ETC/POFH/20-06-2024/OPTH/07). A sample size of 105 patients was calculated by using the World Health Organization's (WHO) sample size calculator, taking 85% power of test, 7% level of significance, and 57.5% population proportion of patients with presbyopia.[4] A total of 105 patients were divided into three Groups based on their age, i.e., 35 patients in each Group. Group 1 (40 to 45 years); Group 2 (46 to 50 years); and Group 3 (51 to 55 years). Participating patients signed written consent before conducting this study.

Inclusion Criteria: Patients of both genders aged 40 to 55 years at the time of the OPD visit, with good general health, had complaints of decreased near vision that affected daily life activities (Jaeger's near vision chart < N6), emmetropes for distant vision (6/6 by Snellen's chart) in each eye at the time of screening.

Exclusion Criteria: At the screening visit, we also excluded patients with any pre-existing ocular pathology, uncontrolled systemic disease, cataract surgery, refractive surgery, corneal inlay surgery, or any other intraocular surgical intervention.

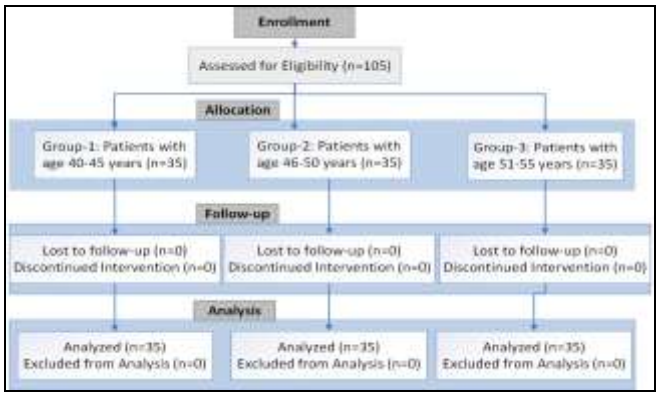

Figure-1: Patient Flow Diagram (n=105)

All patients with presbyopia who met the inclusion criteria and agreed to participate in the study were selected. A senior ophthalmologist performed the anterior segment and dilated fundus examination on a slit lamp biomicroscope. Intraocular pressure was also measured with an air puff tonometer before instillation of Pilocarpine drops. Near vision was recorded using Jaeger's near vision chart. Then one drop of 0.2% Pilocarpine was instilled in both eyes of patients. After 1 hour of instillation of drops, near vision was again noted using Jaeger's near vision chart, and improvement in the number of near vision lines was recorded in each Group. Patients who showed no improvement in number of near vision lines were also recorded.

Statistical Package for Social Sciences (SPSS) version 25 was used for data analysis. Frequency and percentages were calculated for categorical variables like gender and near vision improvement.A Chi-square test was applied to determine the statistically significant association between age Group and near vision line improvement after instillation of Pilocarpine 0.2% drops.The p value ≤ 0.05 was considered as significant.

RESULTS

One hundred and five participants were enrolled in the study; among them 48(46%) were females and 57(54%) were males. Age of the participants ranged from 40–55 years. Figure-2 displays the age-wise distribution of patients with near vision.

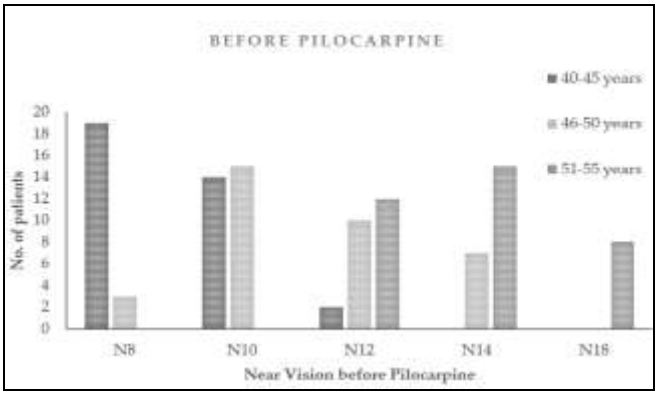

Figure-2: Age wise distribution of near vision before Pilocarpine (n=105)

Following the application of 0.2% Pilocarpine drops, 93 out of 105 patients demonstrated an improvement in their near vision, whereas 12(11.4%) patients did not. Out of 93 patients, 56(53.3%) patients showed improvement of 1 line in near vision, 32(30.5%) patients showed improvement of 2 lines in near vision, and (4.8%) patients showed improvement of 3 lines (Table-I).

Improvement in near vision was demonstrated by the majority of the patients after instillation of 0.2% Pilocarpine. The younger age Group showed more improvement in near vision as compared to older patients (Figure-3). In the 40–45 year age Group, 22(62.9%) patients improved near vision by 1 line, compared to 20(57.1%) patients in the 46–50 year age Group and 14(40.0%) patients in the 51–55 years age

Group. The most common response was a 1-line improvement, predominantly in the younger age Group. Two- and three-line improvements were also observed among all age Groups but were less common. 9(25.7%) patients showed no improvement in near vision in the 51-55 years age Group compared to 1 (2.9%) in the 40-45 years age Group and 2 (5.7%) in the 46-50 years age Group.

Table-I: Improvement in number of Lines in Near Vision with Pilocarpine 0.2% (n=105)

Result	Frequency (%)
No Improvement	12 (11.4%)
Improvement of 1 Line	56 (53.3%)
Improvement of 2 Lines	32 (30.5%)
Improvement of 3 Lines	5 (4.8%)

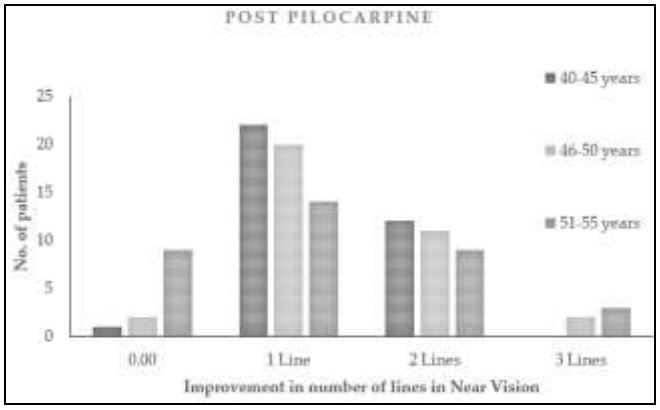

Figure-3: Improvement in number of lines in near vision in different age Groups with Pilocarpine 0.2 % (n=105)

A statistically significant association was observed between different age Groups and near vision line improvement (*p*-value <0.05) after 0.2% Pilocarpine instillation. (Table-II) Pilocarpine 0.2% effectively improved near vision in patients with presbyopia, with younger patients benefitting the most.

Table-II: Improvement in number of lines after Pilocarpine among different age Groups (n=105)

Improvement in no. of Lines after Pilocarpnie	40–45 years (n=35)	46–50 years (n=35)	51–55 years (n=35)	*p*-value
No improvement	1(2.9%)	2(5.7%)	9(25.7%)	0.024
Improvement of 1 line	22(62.9%)	20(57.1%)	14(40.0%)	
Improvement of 2 lines	12(34.3%)	11(31.4%)	9(25.7%)	
Improvement of 3 lines	0(0.0%)	2 (5.7%)	3(8.6%)	

DISCUSSION

Presbyopia impacts a person's everyday activities, life satisfaction, and psychological health. It is very challenging to manage or correct presbyopia, as it is practically impossible to provide flawless vision at all distances. Although there are many amelioration options available, they are frequently inaccessible in developing nations, and, even in wealthy nations, prescribing is typically not the best course of action. Pilocarpine 1.25 % has been approved by the FDA for the treatment of presbyopia.[11] Researchers have used and investigated Pilocarpine in a variety of forms, concentrations, and combinations with other medications.[12] The possibility of ocular and systemic side effects, such as headache, conjunctival hyperemia, blurred vision, and impaired night vision, are side effects of this drug. It is important to note that the concentration of Pilocarpine for treating presbyopia is 1.25%. But in this study, we have used a minimal concentration of Pilocarpine, i.e., 0.2% Pilocarpine to minimize the side effects. Pilocarpine 0.2% is assessed for the first time, which showed promising results in patients with early presbyopia. Pilocarpine binds to and activates muscarinic M3 receptors to contract the ciliary and iris sphincter muscles. Compared to surgical methods, topical pharmacological treatment for presbyopia is reversible, non-invasive, and has no significant adverse effects. Pharmacological treatment is a very fascinating option for emmetropic patients, especially for early presbyopes. It permits total liberation from glasses and their restrictions.

In this study, younger patients showed more gain in near vision as compared to older patients, though all patients showed a significant improvement in near vision after topical instillation of 0.2% Pilocarpine. One likely justification for the difference between age Groups can be that the young patients have more accommodative reserve than the old patients. Vargas *et al.*, also reported that young individuals with presbyopia improved near vision by more lines than the old patients. His study presented that topical pharmacological combination therapy improved near vision by one or more lines in 92.3% of the patients.[13]

Edward and co-workers evaluated the efficacy and safety of topical 0.4% Pilocarpine for presbyopia and demonstrated improvement in near visual acuity in patients with presbyopia without affecting distant vision with a favorable safety profile. The treatment related adverse events (TRAE) were mild and transient.[14] But we employed a minimal concentration

of Pilocarpine, i.e., 0.2% and observed improvement in near vision in patients with presbyopia. Positive feedback indicates that treating early presbyopia with 0.2% Pilocarpine is acceptable. Price *at el*., studied various concentrations of Pilocarpine and reported that the ideal concentration of Pilocarpine is 1.2% for the treatment of presbyopia.[15] The peak effect of the drug was achieved after 1 hour of instillation of drops. The most common side effect was mild headache; most started 1 hour after dose and relieved by hour 3 without any treatment. He also stated that distant vision was not compromised. We employed the lowest possible Pilocarpine concentration in our investigation, and improvement in near vision was noted, as Price *et al*. also observed in their phase 2 studies.

Some studies assessed a combination of drugs for presbyopia and justified that Pilocarpine enhances the depth of focus and produces miosis by contracting the ciliary muscle. Other drugs in this combination, like naphazoline, nepafenac and pheniramine, augment the action of Pilocarpine by other mechanisms. Numerous pharmacological combinations are being tested to lessen adverse effects and boost the effectiveness of medications that are already on the market.[16] Renna *et al*., published a study in which a combination of drugs improved near vision by 2–3 lines without affecting far vision, but in this proposed study, a single drug is used.[17] We employed the lowest possible Pilocarpine concentration in our investigation. The use of 0.2% Pilocarpine validated a notable improvement in near vision, indicating Pilocarpine 's beneficial therapeutic efficacy.

Benozzi *et al*., evaluated the efficacy and safety of a combination of Pilocarpine 1% with diclofenac 0.1% eye drops for the treatment of presbyopia and reported that presbyopia can be treated well and safely without glasses and surgeries. All the patients improved near vision, and there was no effect of the drug on distant vision. The reported side effects were headache, dry eye, dizziness and decreased perception of light, but these adverse effects were resolved with time without any treatment.[18] Some clinical trials reported that near vision is improved by pharmacological drug therapy, but all these studies compared the pharmacological drug therapy with placebo, not with the other options for the treatment of presbyopia. The key benefit of pharmacological drug therapy is that the effect is reversible and transient, so if any side effect like headache does arise, it vanishes as the drug stops. Topical drug therapy representsa novel approach to the non- invasive management of presbyopia.[19, 20]

The FDA approved the administration of topical Pilocarpine hydrochloride 1.25% once-daily or twice-daily as the first pharmacological therapy for presbyopia. The results of the randomized, vehicle controlled, phase 3 GEMINI 1 and GEMINI 2 recommended the administration of Pilocarpine 1.25% once daily.[21] The randomized, vehicle- controlled, phase 3 VIRGO study's results reported administering Pilocarpine 1.25 % twice daily.[22] Pilocarpine 1.25% was well tolerated, but minor side effects were observed, and slight systemic accumulation was also noted after the use of Pilocarpine 1.25%. The most severe side effect associated with Pilocarpine 1.25% is the rare risk of retinal detachment, which is more expected to occur in patients who already have retinal disease. Therefore, retinal examination is mandatory or recommended prior to the start of this drug.[23] This makes it more important for the ophthalmologist to thoroughly examine the retinal periphery before writing a prescription for the medication. As Pilocarpine induces a decrease in anterior chamber depth, it can potentially trigger an acute angle closure attack. This is especially concerning for patients whose angles are narrow. According to some reports, long-term treatment with Pilocarpine could cause persistent ultrastructural alterations in the ciliary muscle and trabecular meshwork. Therefore, the treating ophthalmologist should perform gonioscopy both before starting treatment and occasionally during follow-up, as an additional responsibility. As this is a direct-acting cholinergic agent, it can modify the permeability of lens and may accelerate the lenticular changes due to the accumulation of water in lens. As it causes pupillary constriction by reducing the tone of dilator pupillae and by producing fibrosis of sphincter pupillae, it may lead to the formation of posterior synachae, which results in poor dilation of the pupil for retinal examination and for cataract surgery if required in the future. While using Pilocarpine 1.25% continuously and consistently to treat presbyopia, several concerns about side effects may need to be addressed. For this reason, patients should be counseled to use caution and undergo routine monitoring.

LIMITATION OF STUDY

By keeping all the adverse effects in mind, studies with long-term follow ups are required to determine the lifelong efficacy of this drug. To find new avenues for patients with

presbyopia to improve their near vision, patient-driven factors must be taken into account. Longer follow-up studies are also required in the future to evaluate patient tolerance and satisfaction.

CONCLUSION

Topical Pilocarpine 0.2% is an effective treatment for presbyopia with promising outcomes particularly in cases of early presbyopia. Though, many of the studies are on-going and are in registered clinical trials, so in the near-term, we will have more updates about the safety and efficacy of this drug. To meet the situational and dynamic requirements of the patients with presbyopia, it may be considered a viable option.

Conflict of Interest: None.

Funding Source: None.

Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

MS & YL: Data acquisition, critical review, approval of the final version to be published.

AA & HS: Conception, study design, drafting the manuscript, approval of the final version to be published.

MAK & AAK: Data analysis, data interpretation, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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