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The Effect Of 0.01% Atropine On Myopia Progression

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Abstract

Objective: Our study aims to assess the efficacy of a low dose of atropine (0.01%) in slowing the progression of myopia.
Method: This prospective randomized controlled trial was conducted in the Ophthalmology department of Ziauddin University Hospital, Karachi. The study spanned a duration of four years, from July 1 2019 to June 30, 2023. A group of individuals presented at the eye outpatient department (OPD) with complaints of blurred vision underwent clinical examination and were diagnosed with myopia based on inclusion criteria. Data was collected and analyzed using SPSS 23, with the paired t-test employed for variable comparisons.
Results: Our study analyzed and compared the results of the interventional group, where atropine eye drops (0.01%) were administered daily at bedtime, with the control group, which received Tear Natural II eye drops as a placebo. Patients were followed for three years, with two years dedicated to observing treatment responses and a one-year washout period for the drug. A comparison of baseline and 24-month means revealed an increase in myopia of 0.84 in the interventional group and 1.55 in the control group.
Conclusion: Myopia is one of the leading causes of the development of sight-threatening conditions. Its progression can be slowed down by proper treatment with Atropine. The 0.01% dosage of atropine exhibited a favourable risk-benefit profile with minimal impact on visual function.

Keywords: Myopia, Atropine 0.01%, Refractive error.

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1. Introduction

Myopia is a common preventable cause of visual impairment in younger population worldwide. It is estimated that 36% of the global population experiences visual impairment due to refractive errors, and a 50% increase is predicted by 2050.[1] Myopia is a type of refractive error in which parallel rays of light focus in front of the retina when the eye is in an un-accommodative state. The prevalence of myopia varies depending on ethnicity, geographical location, and socio-economic status.[2,3] The progression of myopia is observed in the young population due to increased indoor activities and the extensive use of electronic devices and gadgets.[4,5] The progression of myopia can be slowed down through lifestyle modifications and the proper use of spectacles. Additionally, low doses of topical atropine have been found to be effective in slowing down the progression of myopia. Atropine is a muscarinic receptor antagonist used topically to slow down the progression of myopia in children.[6,7] The mechanism of action of topical atropine in slowing down myopia is still unclear, although it regulates the retinal and scleral muscarinic receptors, increases choroid thickness, and reduces the rate of axial length progression.[8,9] A low dose of topical atropine may cause mild adverse effects on pupil diameter and accommodation, which does not significantly impact the patient's the daily life.[10] The purpose of this study is to assess the effectiveness of low-dose atropine in controlling the progression of myopia.

2. Materials & Methods

We divided the participants equally into intervention and control groups. The allocation of participants to the intervention group, which received atropine 0.01%, and the placebo is a control group, was determined through computer-randomized double-masking. Initially, a total of 226 participants were equally divided into the experimental and control groups. However, approximately 40 patients were lost to follow-up, resulting in a total of 186 participants included in this study. Since the low dose of atropine 0.01% is not commercially available in Pakistan, we prepared topical 0.01% atropine in the pharmacy under the supervision of a single pharmacist. Drugs, 0.01% atropine and the placebo (artificial tear), were administered to the patients off-label. To prepare the 0.01% atropine solution, we used atropine 1% and Tear Natural II eye drops. Tear Natural II eye drops are available in 15 ml bottles. After removing 5 ml of natural tear, we added 0.1 ml of atropine into 10 ml of Tear Natural II. This drug remained stable at room temperature after

preparation for up to 28 days. We use Tear Natural II eye drops off label as placebo drug. The treatment regimen require to instill one drop of 0.01% atropine or tear natural II eye drops daily at bed according to assigned group. Before starting treatment parents were educated regarding the possible side effects of treatment including blurred vision, photophobia, increased glare and redness of the eye.

A questionnaire form regarding patient demography and presenting complaint and clinical assessment on every 6th month follow up was filled by resident. The patient was then examined thoroughly by single ophthalmologist for visual acuity test, cycloplegic refraction, axial length, slit lamp examination and fundus examination on 6th, 12th, 18th and 24th month. Interventional and control group were prescribed full correction for constant use. At each follow up, possible side effects of the drug in group 1 were also accessed. The two groups were kept for a further 1 year follow up to assess the washout time period after stopping the drug. There were two follow ups at 6month and 12 month to check the progression of myopia.

The data were analyzed and entered into SPSS version 23. Quantitative variables, such as age, will be presented as mean ± standard deviation. Qualitative variables, like gender, will be presented as frequency and percentage. Comparative data will be analyzed using a paired t-test, with significance indicated by a p-value < 0.05.

3. Results

This study included 226 myopic participants which were equally divided into interventional group (1) and control group (2). Out of 226 patients 40 were lost follow-up and finally 93 participants remained in group 1 and 93 in group 2. The mean age of participants in both groups was 8.5±2.3. The gender distribution for group 1 was 51 boys (54.8%) and 42 girls (45.2%), while group 2 had 47 boys (50.5%) and 46 girls (49.5%). The baseline means for refractive errors of both groups were compared, group 1 came out to 3.14 ±0.16 while group 2 was 3.31±0.17. At the 6 months follow up, the mean refractive error for group 1 showed 3.31±0.17 and group 2 was 3.73±0.18, showing a greater increase in group 2. Similarly the means were also compared at the 12th month and 18th month follow ups where group 1 was 3.45±0.17 and 3.78±0.17 respectively, while group 2 was 4.09± 0.18 and 4.44±0.18 respectively. The final follow up at 24th months showed mean refractive errors of group 1 as 3.98±0.16 and group 2 as 4.85±0.18. A comparison of the baseline and 24 month means showed an increase of 0.84 in group 1 and 1.55 in group 2. This shows a 0.71 difference in increase between the two groups.

Similarly the axial length was also compared at baseline, 6th, 12th, 18th and 24th month follow up, as shown in Table 2. At baseline group 1 and group 2 had means of 23.2±0.07 and 23.3±0.07 respectively. The 6th month follow up showed a slight increase with group 1 being 23.4±0.06 and group 2 being 23.5±0.07. The 12th and 18th month follow up means were 23.4±0.06 and 23.5±0.06 for group 1 and 23.7±0.07 and 23.9±0.08 for group 2 respectively. The final 24th follow up showed group 1axial length mean as 23.5±0.07 and group 2 as 24.2±0.10. A comparison of axial length means of baseline and 24 month showed an increase of 0.3 in group 1 and 0.9 in group 2. This shows a 0.6 difference in increase of axial length between the two groups.

There were no such significant side effects of 0.01% atropine seen in this study which would require immediate cessation of the drug. However, 7% percent of the patients experienced mild symptoms such as photophobia and conjunctival hyperemia.

The two groups were then followed up for another year to see the myopia progression during washout period. Group 2 had a similar increase in mean as the follow ups before with 0.38±0.39. However, Group 1, which was given atropine, experienced the rebound effect due to the sudden cessation of medicine and a slightly greater increase in the mean was seen as 0.28±0.33.

Table 1: Comparison of control and atropine groups axial length at each follow up

Follow up	Mean	Std. deviation	Std. Error Mean	95% Confidence Interval of the Difference		t	df	Sig 2 tailed
Baseline	-.09032	.56819	.05892	-.20734	.02669	-1.533	92	.012
6th month	-.12796	.61633	.06391	-.25489	-.00103	-2.002	92	.048
12th month	-.25376	.60855	.06310	-.37909	-.12843	-4.021	92	.000
18th month	-.42688	.65044	.06745	-.56084	-.29292	-6.329	92	.000
24th month	-.65914	.74414	.07716	-.81239	-.50589	-8.542	92	.000

Table 2: Comparison of control and atropine groups refractive errors at each follow up

Group	Mean	Number	Stander deviation	Stander error mean
Baseline group 1	3.1425	93	1.59073	.16495
Baseline group 2	3.3091	93	1.68610	.17484
6th month group 1	3.3091	93	1.62538	.16854
6th month group 2	3.7312	93	1.70447	.17675
12th month group 1	3.4543	93	1.63892	.16995
12th month group 2	4.0914	93	1.75960	.18246
18th month group 1	3.7849	93	1.59593	.16549
18th month group 2	4.4435	93	1.73524	.17994
24th month group 1	3.9839	93	1.57761	.16359
24th month group 2	4.8522	93	1.73778	.18020

4. Discussion

Myopia has become a significant cause for concern in recent years due to its increasing prevalence worldwide.[11,12] Recent studies have shown that Asian children are more prone to myopia progression compared to Europeans.[13-15] Myopia ranks as the 6th most prevalent cause of blindness. Currently, multiple methods are employed to reduce the progression of myopia, but the most effective approach is the use of topical atropine drops.[16-18]

A similar study conducted by Akdemir SC et al included 46 myopic children, who used 0.01% and 0.05% atropine eye drops every other day. After 1 year of follow-up, 0.01%atropine showed significant improvement as compared to 0.05% atropine.

Ashraf A et al conducted a study and divided patients into high and low myopic groups. After one year of atropine treatment, the induced change in spherical equivalent was 0.81±0.26D for the high myopia group and 0.76±0.21D for the low myopia group.

Perez-Flores et al. conducted a multicenter study that examined the efficacy and safety of 0.01% atropine eye drops in a Spanish cohort. Before treatment, the mean spherical equivalent progression was -1.01 (SD 0.38) D per year, which significantly decreased to -0.44 (SD 0.41) D per year when using 0.01% atropine eye drops ($p < 0.001$).

Our study shows that 0.01% atropine is effective in slowing the progression of myopia in children. It was noted that not only does it slow down the progression but also has a very small rebound effect during the washout period. A comparison of the baseline and 24 month means showed an increase of 0.84 in group 1 and 1.55 in group 2. This shows a 0.71 difference in increase between the two groups. A comparison of axial length means of baseline and 24 month showed an increase of 0.3 in group 1 and 0.9 in group 2. This shows a 0.6 difference in increase of axial length between the two groups. The washout time showed a rebound effect at the cessation of the drug with an increase in the 6th-month mean difference to 0.28±0.33.

5. Conclusion

This study demonstrates that atropine 0.01%, effectively reduces myopia progression in children over two years. The drug with its once-a-day dosage ensures patient compliance and its affordability relieves the financial burden. Its minimal side effects make it a great option for improving myopia in children.

INSTITUTIONAL REVIEW BOARD

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Contributions:

A.K - Conception of study
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A.K - Analysis/Interpretation/Discussion
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