Original Article

Atropine 0.01% Eye Drops for Myopia Control in a tertiary care center of Pakistan: An interventional case series

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ABSTRACT

Purpose: To evaluate the real time results of once-daily Atropine 0.01% eye drops in controlling myopia.

Study Design: Interventional case series.

Place and Duration of Study: The Eye Centre, South City Hospital, Karachi from September 2020 to August 2021.

Methods: One hundred (both) eyes of 50 children were included in the study using non-probability consecutive sampling technique. Baseline spherical equivalent refraction (SER) was recorded at the initiation of treatment. The endpoint was measuring the rate of progression in SER at one year after treatment. Responders were defined as the ones with either no progression of myopia or worsening of myopia of ≤ -0.50 SER and non-responders were defined as ones with a progression rate of myopia of greater than0.50 SER.

Results: The baseline means SER for 100 eyes was 3.25±1.37 D. On follow-up after 12 months of treatment with Atropine 0.01% eye drops, the mean SER was -3.74 ± 1.34 D. The rate of SER progression was significantly lower at one year follow-up (p-value<0.001). The percentage of responders was 84%.

Conclusion: Significant reduction in myopia progression occurred after treatment with Atropine 0.01% eye drops in a greater percentage of children. This has led us to be confident in providing Atropine 0.01% eye drops along with simple spectacles as an effective treatment strategy to control myopia progression.

Key words: Myopia, Spherical equivalent refraction

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INTRODUCTION

Myopia, characterized by increasing incidence and severity, is becoming a significant public health concern worldwide. In the USA, the prevalence of myopia has risen from 25% to 42% of the population since the 1970s.[1] The typical age for presentation of myopia is between 6 and 12 years and one out of every three children will become myopic by adulthood and this proportion is progressively increasing.[2]The globally accepted measure for quantifying myopia is the rate of progression of primary myopia, where a yearly increase of 0.5 diopters in the Spherical Equivalent Refraction (SER) is defined as myopia progression.[2] However, it is important to note that this inference is primarily based on studies involving Caucasian children.[3] Increasing proportion of children with higher myopia (-6.0 D or higher) is also increasing the percentage of accompanied risk of severe and irreversible visual impairment as well as the risk of complications including retinal detachment, sub-retinal neovascularization, early cataracts, and glaucoma.[4] In the recent past, industrialized nations have shown a great urge in finding methods to curb myopia progression and have succeeded up to a great

extent in finding different solutions. Atropine concentrations ranging from 1% to 0.01% were evaluated and Atropine 0.01% stands out for showing the durable effect on stabilizing the SER, the lowest risk of regression following cessation of treatment as well as the lowest incidence of treatment-related side effects.[5,6] Refractive change in SER/year is considered as a relevant clinical marker to assess myopia progression. In the Atropine for treatment of childhood myopia (ATOM 1) study, Chua WH and colleagues included children between 6–12 years of age with (-1.0 to -6.0 D) myopia in the Atropine1% treatment group and after the two years, the mean change in SER of -1.20(0.69 D)for children in the placebo group was greater than that of the Atropine group, which was only -0.28(0.92).[5] Similarly, in the ATOM2 study, after 24 months of Atropine therapy, the mean myopic progression was -0.30 ± 0.60, -0.38 ± 0.60, and -0.49 ± 0.63 D in the Atropine 0.5%, 0.1%, and 0.01% treatment groups respectively.[6] It indicated that the high-concentration of Atropine i.e. 0.5% and 0.1%was more potent and more effective than the low-concentration of Atropine (0.01%). However, on discontinuation of treatment after 2 years period, higher concentration groups underwent greater rebound myopia whereas, Atropine 0.01% treated group had a minor (-0.28 D) change, while in 74% of cases decrease in myopia progression was achieved.[7]

In USA, Clark TY and Clark RA conducted a small, case–control study and reached the conclusion that Atropine 0.01% significantly reduced the rate of myopia progression over 1 year with the advantage of negligible treatment-related side effects.[8] In Germany, a study detected 1mm pupillary dilation in comparison to the untreated eye and a minimal reduction in the accommodation after initiating treatment, and a significant decrease in myopia progression of 0.40D/ year as compared to 1.05D/year prior to treatment in school children.[9] A larger study to assess the validity of the prior data and results in a larger population and to assess the pattern and proportion of myopia progression in a much larger, multiethnic pediatric population in America administered low dose topical Atropine at night.[10] The current study is also based on prior studies' outcomes, with the aim to assess the real-time efficacy of low-concentration Atropine 0.01% on the rate of myopia progression in the local pediatric group. This study is conducted on the hypothesis that over the period of one year, the mean increase in Spherical Equivalent Refraction from baseline would be less for myopic children, undergoing treatment with Atropine 0.01% eye drops nightly for one year.

METHOD

In this case series study, we included children visiting the outpatient clinic of The Eye Centre, South City Hospital, Karachi from September 2020 to August 2021. A total of 100 eyes (both eyes) of 50 children, age between 6 and 12 years were included in the study using non-probability consecutive sampling technique. Keeping a confidence interval of 90%, desired precision of 8.25% and considering the population proportion to be 50%, the sample size was determined by using the WHO sample size calculator for one-sample situations. They were treated with a nightly Atropine 0.01% eye drop for at least one year. All patients were followed up at 6 weeks, 6 months, and 12 months after their baseline visit.

The proposal for the study was approved by the Institutional Review Board of the institute. The aim of the study was to determine the magnitude of myopic progression in children after treating them with topical Atropine 0.01% for 12 months. Spherical Equivalent Refraction was performed and recorded at baseline and follow-up visit at one year. Demographic data included gender, age, duration of myopia, number of follow-up visits, medical and ocular treatment history. Treatment charts documenting the administration of Atropine 0.01% once nightly in both eyes were provided to patients.

The inclusion criteria for the patients was age 6 to 12 years at the commencement of the treatment, baseline SER of -0.25 to -6.0D in one or both eyes, astigmatism up to -2.0D, and complete follow-up visits during the treatment period. At first visit, cycloplegic refraction was performed and recorded. On every follow-up, refraction was performed with or without cycloplegia, variation was case and investigator dependent. Distance best-corrected visual acuity (BCVA) values were measured using Snellen chart. Anterior and posterior segment assessment was performed on slit lamp. Intra-ocular pressure was measured by a non-contact tonometer.

Treatment of myopia included prescribing corrective spectacles. Atropine 0.01% eye drops were prepared and dispensed by the Aga Khan University Hospital, Karachi. Patients with associated pathologies (Marfan syndrome, Stickler's syndrome, Retinopathy

of Prematurity) and abnormal ocular refractive anatomy (keratoconus, spherophakia, lenticonus), concurrent ocular disease/condition (e.g., amblyopia, strabismus, glaucoma, cataract, corneal scar, retinal disease) or history of intraocular or ocular laser surgery were excluded.

The primary outcome of the study was to see the rate of progression of myopia, which was calculated as, the difference between the mean SER at the baseline line and the mean SER at 12 months after treatment for all 100 eyes. Treated patients were considered either responders (If SER progression was ≤ 0.50D after 1 year of treatment with topical Atropine 0.01%) or non-responders (if SER progression was ≥0.75D after 1 year of treatment with topical Atropine 0.01%).

Descriptive statistics were calculated using SPSS 23. Paired t-test was used to determine significance of results before and after the treatment. Categorical data was analyzed by applying Chi-square test, to observe the effect of modifiers on the outcome of the study. P-value of ≤ 0.05 was considered significant.

RESULTS

Out of total participants, 54% (27/50) were male and 46% (23/50) were females. The mean age was 8.8 ± 1.8 years (range 6–12 years). The association of categorical variables was analyzed using Chi-square test. No association was seen between gender and SE of right and left eyes after treatment with 0.01% Atropine eye drops (p-value 0.177 and 0.45 respectively). Similarly, no association was seen between age and SE of right and left eyes after treatment with 0.01% Atropine eye drops, with a p-value of 0.24 and 0.31 respectively (p≤0.05).

Table 1: *Summary of variables of patients in the Atropine0.01% treatment group.*

Variable	Statistics	Values No. of Patients(n)
Age	6 to <8 years	14
	8 to < 10 years	17
	10 to < 12 years	14
	12 to < 15 years	5
	Mean(SD)	8.8 ±1.8 years
Progression in myopia at one year after treatment	No progression	02
	None to 0.25D	07
	0.25D to 0.5D	33
	> 0.5D	08
Baseline SER for 100 eyes (D)	Mean (SD) (α)	-3.25(1.37)
SER for 100 eyes after one year of treatment (D)	Mean (SD)(β)	-3.74(1.34)
Change in SER from baseline in 1 year (D)	β-α	-0.49(0.17)

The baseline mean (SD) SER for 100eyes (both eyes of 50 cases) was -3.25 ± 1.37D,compared with the mean(SD) SER at 1 year after treatment -3.74 ± 1.34 D. The difference between the two is 0.49D (CI 90%, p-value <0.001). On follow-up at 1 year after treatment, the average change in SER of the cases was -0.49 ± 0.17 D(p-value<0.001).

There were 42/50 (84%) responders. Out of these, 4% (2/50) showed no progression in myopia in the one year period of treatment, 14% (7/50) showed up to -0.25 D progression and 66% (33/50) showed up to -0.50 D progression. Non-responders were 16% (8/50), who showed worsening of myopia>-0.50 D in the Atropine group.

DISCUSSION

This case series was designed to evaluate the efficacy of low-concentration Atropine eye drops for the treatment of progressive childhood myopia. Atropine 0.01% drops for one year of treatment has shown promising outcome. This suggests that Atropine 0.01% can be an effective medication to slow childhood myopia and supports previous prospective, controlled clinical trials conducted in different populations of East Asia, Spain, and America.

The mean progression of myopia of -0.49 D after a 12 months' period of treatment in this study was similar to -0.42D after the 12 months' period of treatment in the ATOM 1 study.[5]In this study, the proportion of non-responders was 16%.

Alberto Chierigo and colleagues concluded that lower concentrations of Atropine provided optimal clinical efficacy, lesser ocular side effects and rebound phenomenon as compared to the higher concentrations i.e. 1% and 0.5%.[11] The outcome of this study is comparable to that conducted by Matteo Sacchi et al, in the European population. This study demonstrated that in the Atropine-treated group, the mean myopic progression was -0.54(0.61) D after 12 months.[12] The responders in the European population were 41/52 (79%), whereas, the non-responders were 11/52 patients (21%).

Our data is also comparable to that of the previous study on the multiethnic American population which

showed an average increase in SER from baseline to be significantly less for the Atropine group (-0.2 ± 0.8 D) as compared to the control group (-0.6 ± 0.4 D) at 1 year. Non-responders with a worsening myopia of at least -0.75 D were 37% of the Atropine group.[13] Outcomes in the Asian studies are also consistent with the outcome of this study. In a randomized clinical trial in Chinese children by Wei S et al., the mean progression in myopia at 1-year follow-up was −0.49 (0.42 D) D in the Atropine 0.01% group.[14]

Our study demonstrated promising results with 16% of the patients showing progression of -0.75D despite being compliant with therapy. However, the patients showing a progression of myopia greater than 0.5D needed correction of their refractive error with spectacles. Atropine 0.05% and 0.1% have been shown to slow myopic progression, but clinically it is limited by side effects such as glare, blurring of near vision and photophobia. Serious side effects of the drug were not reported by patients. However, photophobia and poor near acuity in 6.3% and 2.3% of subjects in the low-dose atropine group has been reported.[13] Whereas, a treatment regimen comprising of 0.1% Atropine loading dose for six months and then 0.01% Atropine for 18 months has no significant adverse effects.[15]

While the drug is proving to be beneficial, precise mechanism of action of Atropine in reducing myopic progression is yet to be determined. Research shows that by modulating the dopamine release it can increase choroidal thickness in children, which in turn plays role in reducing the rate of axial growth of the eye.[16] In another study, a significant increase in SER and axial length of the right and left eyes of the placebo group was observed as compared to the Atropine 0.01% group in whom, the rate of change in SER and axial length were not significant over a period of one year.[17] Scleral remodeling is also said to be associated with progressive myopia, which might be the function of scleral fibroblasts modulated by the scleral muscarinic receptors. Role of low dose Atropine has been considered significant for bringing changes in scleral fibroblasts at molecular level. The exact mechanism may include a combination of these effects.[18]

The LAMP study reported a concentration-dependent increase in subfoveal choroidal thickness over 4 months with lower concentrations i.e. 0.05%, 0.025% and 0.01% Atropine, i.e. higher the concentration, the thicker the choroid becomes.[19,20]

Further randomized control trials are needed to evaluate the efficacy of Atropine eye drops in stabilizing the SER and axial length of the eye, so that accurate Atropine concentrations are administered to children in whom Atropine 0.01% drops do not help reduce the progression of myopia or alternative therapies must be devised in such cases.

CONCLUSION

The study indicates that Atropine 0.01% eye drops is an effective and well-tolerated medical intervention for slowing down the progression of childhood myopia and thereby decreasing the likelihood of possible complication associated with the high myopia. Once nightly dose of topical Atropine 0.01% is highly compatible without serious adverse events. Further studies spanning longer duration are warranted to determine the effects of the treatment in controlling the pathologic changes in myopic eyes in future.

Conflict of Interest: Authors declared no conflict of interest.

Ethical Approval: The study was approved by the Institutional review board/Ethical review board **(SCH-IRB-2022-04).**

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Authors Designation and Contribution

Tiabbah Saleem; Senior Registrar: *Concepts, Design, Literature search, Data analysis, Statistical analysis, Manuscript preparation.*

Syeda Aisha Bokhari; Consultant Ophthalmologist: *Concepts, Design, Literature search, Data acquisition, Data analysis, Manuscript preparation, Manuscript editing, Manuscript review.*