International Journal of Research in Medical Sciences
Naik SV et al. Int J Res Med Sci. 2024 Sep;12(9):3213-3218
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20242297

Original Research Article

Clinical study of effect of low dose atropine drops on progression of myopia in children

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Received: 29 July 2024
Revised: 12 August 2024
Accepted: 13 August 2024

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ABSTRACT

Background: As an eye condition, myopia is prevalent and often confusing. In modern times, a higher risk of many eye illnesses is linked to myopia, even at modest levels. Improving eye health and quality of life may be possible by halting the development of myopia.
Methods: It was a prospective, experimental study, designed to look at the effect of 0.01% atropine eye drop on myopia progression, conducted in outpatient tertiary medical centre, total 66 patients were enrolled. Inclusion criteria include having age of ≥6 years and ≤15 years with myopia or myopic astigmatism and whose parents have given consent to participate in the study. Exclusion criteria include children with congenital/developmental delay or systemic diseases, ocular pathology like amblyopia, strabismus, cataract, allergy to atropine were not included.
Results: The result showed that the comparison of spherical equivalent between the baseline measurements and the follow-up measurements after the use of low dose atropine drops indicates that a significant correlation is found between the baseline and follow-up of 12 months (p=0.043) and 18 months (p=0.038). The 6-month follow-up comparison does not show statistically significant association.
Conclusions: We concluded that the low dose atropine should be considered as one the myopia progression control remedy. Recommendation of carry out further research in the similar population of a longer duration of three years and above to better understand the effect of low dose atropine in myopia progression should be considered.

Keywords: Myopia, Atropine, Axial length, Macular thickness, Spherical equivalent

INTRODUCTION

In terms of refractive disorders affecting the human eye, myopia is by far the most prevalent. had an impact on kids and young adults. Having myopia increases the likelihood of eye pathological consequences and also puts a socio-economic strain on others. According to the literature, the probabilities of developing myopic maculopathy, retinal detachment, cataracts, or glaucoma are significantly greater for mild to moderate myopia, and they continue to rise with more severe myopia.[1]

As an eye condition, myopia is prevalent and often confusing. At one point thought of as a harmless refractive disorder. In modern times, a higher risk of many eye illnesses is linked to myopia, even at modest levels.[2] Myopia is on the rise, just as scientists had expected. The specific cause of myopia is yet unknown, although it seems to contain environmental and hereditary components, which makes prevention and therapy complicated and personalized. Improving eye health and quality of life may be possible by halting the development of myopia.[3]A major public health problem, myopia and its development impact people all over the

globe. It is one of the most frequent eye ailments. Extreme myopia is quite common in Asian countries. According to the world health organization, by the year 2050, myopia might affect half of the global population.[4] A key risk factor for myopia development and progression has been identified in recent years as inadequate time spent outside.[5] Another risk factor for myopia is engaging in repetitive, close-up tasks for long periods of time.[6] Current prevalence of myopia is 22.9% (2.7% high myopes) and by 2050 it is expected to affect 50%, (4758 million) of world population with 10% (938 million) being high myope.[4] In developed East Asian and South East Asian countries, myopia is most common among young people; estimates range from 80 to 90% in Japan, Hong Kong, Taiwan, South Korea, and Singapore.[7]

A new meta-analysis paper reveals growing trend of myopia in the previous 4 decades in India, with a prevalence of roughly 7.5%.[8] The myopia distribution in India is 8.5% in urban areas and 6.1% in rural areas. (4.6% in 1980-2008 to 6.8 % in 2009-2019). Though the real figure may seem astonishing, the incidence of myopia is relatively low in India due to the country's large population. The predicted incidence of myopia in urban India is 48% by the year 2050.[9] It ranks high among the world's most pressing public health issues, including in India. According to Brennan, if we could slow progressions by 38%, we could stop myopia from progressing beyond 5D by 73%. Myopia over 5D might be reduced by 90% if the reduction rate was increased to 50%. Since recent environmental changes have led to a dramatic rise in the prevalence of myopia globally, an increase in the age of progression, and an increase in the degree of refractive error, myopia management becomes an increasingly essential problem.[10]Due to its association with the development of many pathological disorders, including macular degeneration, retinal detachments, glaucoma, and cataracts, there has been a recent upsurge in attempts to curtail the advancement of myopia. In our assessment of the literature, we found that additional effective treatments for myopia are: Low dose atropine (LDA 0.01%), high dose atropine (0.05%, 0.1% and 1%), progressive addition lenses (PAL spectacles), specially designed spectacle lenses for controlling myopia progression-defocus incorporated multiple segments (DIMS), highly aspheric lenslets (HALT), hultifocal contact lenses and orthokeratology.

For myopic patients, the goal of all strategies save atropine is to lessen peripheral hyperopic haze. Multiple animal investigations have shown that peripheral hyperopic blur causes axial length elongation.

Pharmacological intervention

The most studied and widely used medication in clinical practice is low-dose atropine. Research conducted in India has shown that atropine treatment is still the gold standard for controlling myopia. For patients with progressive simple myopia, the Mumbai group of paediatric ophthalmologists and strabismologists (GPOS) has suggested using atropine 0.01%.[11]

By reducing the rate of axial length elongation, it slows down the evolution of myopia. There are four possible concentrations:0.01%,0.025%,0.05%, and 0.1%. It has been authorized by the central drug standard control organization (CDSCO) to sell atropine eye drops in India at a concentration of 0.01%.[12]

Chia et al study was to examine the efficacy and visual side effects of three lower dosages of atropine: 0.5%, 0.1%, and 0.01%.[13] A randomized study with a single center and double masking. There were a total of 400 children ages 6 to 12. Myopia progression at two years 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% groups, respectively ($p=0.02$ between the 0.01% and 0.5% groups; $p>0.05$). The axial length increased by 0.27±0.25, 0.28±0.28, and 0.41±0.32 mm in the 0.5%, 0.1%, and 0.01% groups, respectively ($p<0.01$ between the 0.01% and 0.1% groups and the 0.01% and 0.5% groups). Atropine 0.01% has less adverse effects than atropine 0.1% or 0.5%.

Clark et al conducted retrospective case-control study was conducted on 60 children (6-15 years old) whose initial myopic spherical equivalents ranged from -0.25 to -8.00 diopters (D).[14] The average beginning age (10.2 years) and refraction (-2.0 D) were identical in both groups. After 1.1±0.3 years of follow-up, atropine individuals exhibited considerably lower rates of myopic progression (-0.1±0.6 D/year) than controls (-0.6±0.4 D/year) ($p=0.001$). This included 24 of 32 (75%) with slow progression ≤-0.25 D/year, compared to only 5 of 28 (18%) controls. Three atropine and four control patients experienced fast progression (≥-1.00 D/year). Atropine 0.01% effectively reduced myopia development over a year with only a few adverse reactions.

The aim of the study is seeing the effect of low dose atropine drops on progression of myopia in children and their primary objectives is to analyse the effect of low dose atropine drops once daily on progress of myopia, secondary objective is to analyse the effect of low dose atropine drops once daily on axial length, tertiary objective is to analyse the effect of low dose atropine drops once daily on macular thickness, quaterenary objective to study the adverse effect of local atropine drops.

METHODS

Study type

It was a prospective, descriptive, experimental study designed to look at the effect of 0.01% atropine eye drop on myopia progression which was conducted in tertiary medical centre.

Study location and duration

The study was conducted in department of ophthalmology, Krishna institute of medical sciences deemed university, Karad, Maharashtra, India, from May 2022 to December 2023.

Sample size and sampling technique

A purposive convenient sampling method was used through which a total of 66 patients were enrolled in the study."

Sample size={4 x (SD)2}/ (mean ×precision)

SD=0.6, mean=0.49 from the previous study, precision=0.3

Study population

The 66 children presenting to ophthalmology OPD of Krishna institute of medical sciences deemed university, Karad, Maharashtra, India.

Inclusion criteria

Children having age of ≥6 years and ≤15 years with myopia or myopic astigmatism and whose parents have given consent to participate in the study were included.

Exclusion criteria

Children with congenital/developmental delay or systemic diseases, who are unable to communicate or take a complete ophthalmic examination, children with ocular pathology like Amblyopia, strabismus, cataract, allergy to atropine, systemic ill health, cardiac and respiratory illness, H/o eye surgery, children with prematurity, parental history of high/pathological myopia were not included.

Ethical consideration

The institutional ethical committee approval was taken from the institute. The study followed all guidelines laid forth by the declaration of Helsinki, which are standards for any study involving human beings. Parents or guardians gave their written informed permission, and youngsters gave their verbal agreement. In order to maintain the confidentiality of the participants, each one was assigned a unique research number. At any moment throughout the research, participants were free to opt out.

Examination procedure

Visual acuity testing (Using LCD display LogMAR chart), objective refraction (By autorefractometer), subjective refraction (Following standard protocol): BCVA (best corrected visual acuity was obtained), keratometry (Using auto keratometer), Axial length (Biometry using contact A-scan), macular thickness measured with OCT, baseline data was recorded following comprehensive eye examination, refractive error was documented as spherical equivalent. All selected children were prescribed atropine 0.01% eye drops to be instilled one drop each eye at night. Successive follow-ups were scheduled at 6, 12 and 18 months, all the above tests were repeated during each review visit. Susceptive symptoms of glare of light, photophobia, difficulty in bear work, were asked in particular. Children and parents were evaluated and asked about acceptance of medication and whether it interfered with daily tasks and discontinuation for any reason. If/any systemic side effects were elicited and documented. Any child having adverse effect of lower concentration atropine eye drops was advised to stop the drops and was removed from the study. Children who were advised to start lower concentration atropine eye drops but did not start were also removed from study. Findings were collected for analysis purpose.

RESULTS

A total of 66 eligible children were included in the study. A part from age and gender distribution, the analysis of other measurements was done considering each eye hence a total of 132 eyes are included for further analysis of results. The age of the total study population ranged between 7 years being the youngest and 15 years. The mean age was 11.28 years.

Table 1: Age distribution of the study participants.

Age in years at the time of first enrolment, (n=66)		
Minimum	**Maximum**	**Mean**
7	15	11.28

The age of the total study population ranged between 7 years being the youngest and 15 years becoming the eldest child took part in the study with mean age remained 11.28 years.

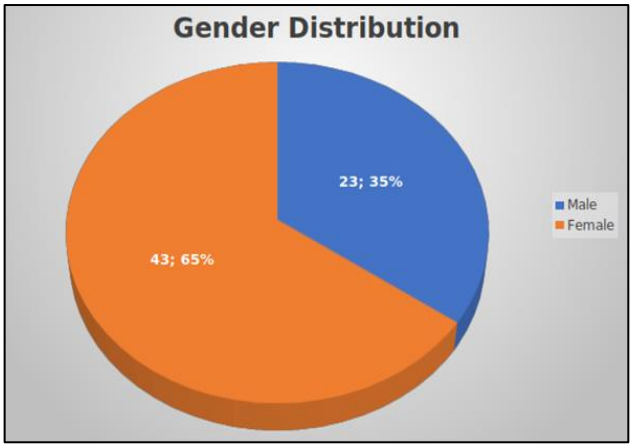

Figure 1: Gender distribution of the study participants, (n=66).

The gender distribution indicates that a total of 23 male which accounts for 35% and 43 female accounts for 65% were part of the study (Figure 1).

Since the data is not normally distributed, Wilcoxon signed rank test was performed to do assessment of the correlation of spherical equivalent between the baseline measurements and the follow-up measurements after the use of low dose atropine drops. The analysis indicates that a significant correlation is found between the baseline and follow-up of 12 months (p=0.043) and 18 months (p=0.038). The 6-month follow-up comparison does not show statistically significant association.

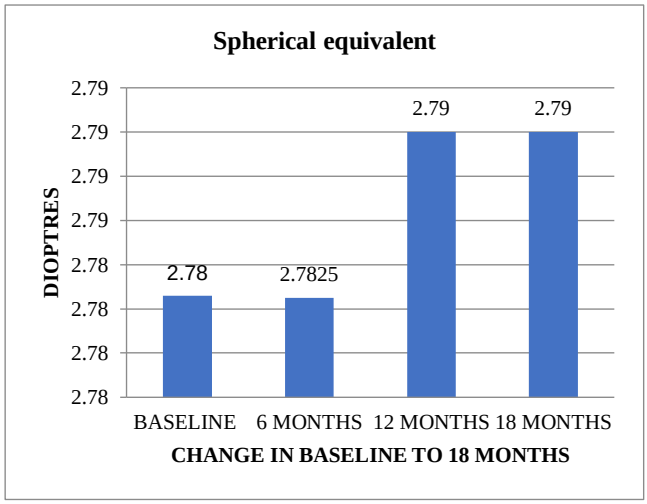

Figure 2: Changes in spherical equivalent baseline to 18 months with at 6 months, 12 months and 18 months using Wilcoxon test.

Comparison of axial length using Wilcoxon signed rank test was performed. The analysis indicates not much significant changes in axial length between the baseline and follow-up of 6, 12 and 18 months.

Comparison of macular thickness using Wilcoxon signed rank test was performed. The analysis indicates not much significant changes in macular thickness between the baseline and follow-up of 6 and 12 months. The comparison of macular thickness between baseline and follow-up at 18 months shown a significant correlation (p=0.02).

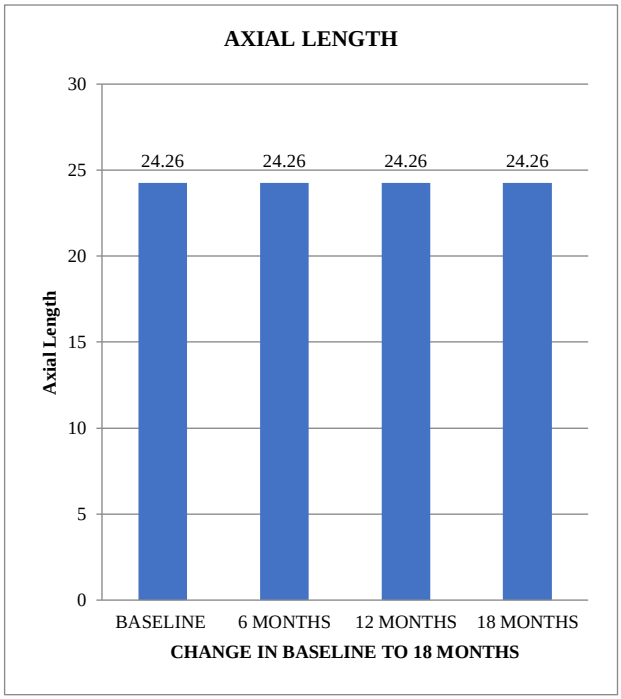

Figure 3: Changes in axial length baseline to 18 months.

Table 2: Comparison of spherical equivalent between baseline with at 6 months, 12 months and 18 months using Wilcoxon test.

Variables	N	Mean	Median	SD	Z value	P value
Baseline-6 months	132	-2.78	-1.87	2.45	-1.08	0.279
		-2.78	-1.82	2.45		
Baseline-12 months	132	-2.78	-1.87	2.45	-2.02	0.043
		-2.79	-1.87	2.46		
Baseline-18 months	132	-2.78	-1.87	2.45	-2.07	0.038
		-2.79	-1.87	2.45		

Table 3: Comparison of axial length between baseline with at 6 months, 12 months and 18 months using Wilcoxon test.

Variables	N	Mean	Median	SD	Z value	P value
Baseline-6 months	132	24.26	24.02	1.34052	-1.41	0.15
		24.26	24.02	1.34054		
Baseline-12 months	132	24.26	24.02	1.34052	-1.00	0.31
		24.26	24.02	1.34012		
Baseline-18 months	132	24.26	24.02	1.34052	-1.00	0.31
		24.26	24.02	1.34462		

Table 4: Comparison of macular thickness between baseline with at 6 months, 12 months and 18 months using Wilcoxon test.

Variables	N	Mean	Median	SD	Z value	P value
Baseline-6 months	132	244.6	244.00	6.93	-1.31	0.190
		244.5	244.00	6.83		
Baseline-12 months	132	244.6	244.00	6.93	-1.77	0.075
		244.5	244.00	6.81		
Baseline-18 months	132	244.6	244.00	6.93	-2.32	0.02
		244.5	244.00	6.80		

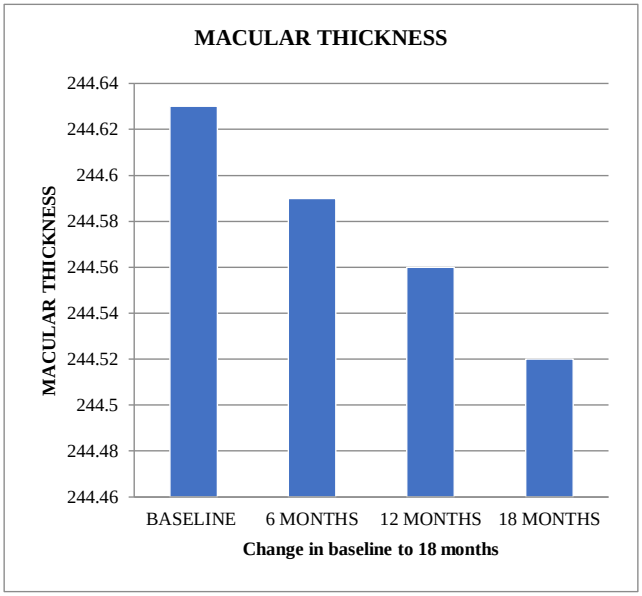

Figure 4: Changes in central macular thickness baseline to 18 months.

Assessment of adverse effect of low dose atropine

A qualitative assessment was done through history taking at each follow-up with all the study participants to assess if they have experienced any adverse effect of low dose atropine. All of them have reported of not experiencing any severe adverse effect, however very few have experienced occasional symptoms like mild irritation, difficulty in focusing near object, color halos.

DISCUSSION

In a clinical environment in India, this research set out to examine how few drops of atropine affected the course of myopia in youngsters. The 66 youngsters, ranging in age from 6 to 15, who suffered from myopia and myopic astigmatism were given 0.01% Atropine eye drops before going to sleep. After starting low-dose atropine, all children were monitored every six months for three separate periods: six months, twelve months, and eighteen months. There are 66 children in all, with an average age of 11.28 years old and 23 males and 43 females (or 65% and 35% respectively). A total of 132 eyes were evaluated to determine the impact of low dosage atropine on spherical equivalent, axial length, keratometric readings, and central macular thickness. The clinical measurements were analysed based on the number of eyes. These parameters were assessed at each follow-up. To determine the impact of therapy, we computed the median of all these parameters and used the Wilcoxon signed rank test for statistical analysis.

Base line measurement at first visit before initiation of treatment indicates mean spherical equivalent of -2.78D and median spherical equivalent was -1.88D, mean and median axial length 24.27 mm and 24.02 mm respectively, mean macular thickness remains 244.63 micron and median macular thickness remains 244.00 micron. These findings are similar with a study done by Clark and Clark to see the effect of 0.01% atropine in non-Asian children.[14]

The effects of low dose atropine on the progression of myopia in terms of spherical equivalent was seen more in the 2nd and 3rd follow-up p=0.043 and 0.038 respectively, the median spherical equivalent remain same -1.87D in all 3 follow-up but the Wilcoxon signed rank test indicates statistical significance of the effect of low dose atropine over longer period of use.

The changes in axial length over all three follow-ups were not significant where the Wilcoxon test suggests a p value of 0.15,0.31 and 0.31 respectively. Most of the studies including atom II[13] suggests that the effect of 0.01% atropine can be seen significantly over longer use of the drug at least 3 years and above. Possibly due to a shorter duration (18 months) of our study the greater effect on axial length has not been seen.

Macular thickness is one of the ocular parameters which changes as the myopia progresses, in our findings no significant changes have been observed during the measurement of macular thickness in 1st and 2nd follow-up (p=0.190 and 0.075), however analysis of the 3rd follow-up measurements shows statistically significant changes (p=0.02), which is probably due to changes in the macular thickness of those subjects whose spherical equivalent refractive error was higher (>-6.00D).

Although literature does not suggest effects of low dose atropine on corneal curvature, we measured the corneal curvature at each follow-up and very small changes in K1 and K2 has been observed in some patients, the changes

in K-readings were not >0.25D in a given meridian. Due to these changes, computerised statistical analysis is showing a statistical significance with p=0.003, 0.001 and 0.001 over 1st, 2nd and 3rd follow-up which should not be considered as the effect of lower concentration atropine.

In our qualitative assessment of side effects of low-dose atropine, we observed that, like in studies conducted by Clark and Clark, only 3 patients reported occasional blurred vision/light sensitivity; nevertheless, these symptoms not severe enough to warrant stopping therapy. Pupil dilation, accommodation, and near-sightedness are all severely impaired at 0.01% atropine level.[13,14]

The effectiveness of atropine 0.01% in preventing myopia advancement is comparable to that of higher concentrations; moreover, children given lesser doses of atropine had reduced myopic development after its discontinuation, Chia suggesting that 0.01% is the more effective dosage. Over a three-year period, it is more effective in preventing myopia from worsening, according to the research.[13]

Based on our experiment and its finding we can conclude that low dose atropine eye drop (0.01% atropine sulfate) slows progression of myopia if used for longer duration, at-least more than 18 months. It slows the progression of axial length specially in progressive myopia. Adverse effects seen with 0.01% atropine eye drops are minimal and of negligible significance, hence it is also safer drug to be used for myopia progression control.

Limitations

The long term efficacy and safety are uncertain, as our studies have short follow up periods and may not capture the rebound effect of potential side effects like photophobia and near vision issues. Smaller sample size or may be limited to a specific population is also the limitation of the study.

ACKNOWLEDGEMENTS

Authors would like to thank Dr. Vijay Kumar Karambelkar, professor (HOD) and all of the ophthalmology staff at Krishna institute of medical sciences for their support.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee no. KIMSDU/IEC/ 07/2022.

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Cite this article as: Naik SV, Joshi BS. Clinical study of effect of low dose atropine drops on progression of myopia in children. Int J Res Med Sci 2024;12:3213-8.