CLINICAL STUDY OF EFFECT OF LOW DOSE ATROPINE DROPS ON PROGRESSION OF MYOPIA IN CHILDREN

Dr. Shubhay V. Naik[1] , *Dr. B. S. Joshi[2]

[1]*DEPARTMENT OF OPHTHALMOLOGY, KRISHNA INSTITUTE OF MEDICAL SCIENCES, KRISHNA VISHWA VIDYAPEETH (DEEMED TO BE UNIVERSITY), KARAD 415110 MAHARASHTRA*
[2]*Associate Professor*

KEYWORDS

ATROPINE, Myopia, keratometric value

ABSTRACT:

Introduction: Myopia, a prevalent refractive disorder, affects 22.9% of the global population, potentially affecting half by 2050. Risk factors include insufficient outdoor time and repetitive tasks. Early interventions are crucial. **Aims:** The study examines the impact of daily atropine drop doses on the progression of myopia in children, their effects on axial length and macular thickness, and the reverse effect of local atropine drops. **Methodology:** The study examined the impact of 0.01% atropine eye drops on myopia progression in 66 children aged 6-15 at the Krishna Institute of Medical Sciences Deemed University, Karad, India. Participants were assessed for symptoms like glare, photophobia, and reading difficulties, and adverse effects documented. **Results:** The study analyzed 132 eligible children aged 7-15, revealing non-normal distribution and needing further statistical correlations. Results showed a significant correlation between low dose atropine drops and keratometric values at 12 and 18 months, but no significant changes in axial length or macular thickness. **Discussion:** A study in India found that low-dose atropine significantly impacts myopia progression in 66 children aged 6-15. The study found no significant changes in axial length or macular thickness over three follow-ups, suggesting 0.01% atropine effectively prevents myopia advancement. Over a three-year period, it is more effective in slowing myopia progression with minimal adverse effects. **Conclusion:** Myopia, caused by genes and environment, can be treated with orthokeratology, atropine, or soft multifocal contact lenses, with low-dose atropine slowing development but requiring further research.

Introduction

Myopia is the most prevalent refractive disorder affecting the human eye, impacting children and young adults, increasing the likelihood of pathological consequences and socio-economic strain, with severity increasing the risk. [1]

Over half of developed nations' population suffers from myopia, a major cause of blindness. Studying origin, epidemiology, and treatment effects is crucial to reduce morbidity. [1]

Research indicates that myopia is influenced by heredity and close work, with increased exposure to optical blur potentially contributing to the condition. [1]

Myopia, once considered harmless, is now linked to higher eye illnesses and is on the rise. Its cause is unknown, but it contains environmental and hereditary components, making prevention and therapy complex. Improving eye health and quality of life may be possible. [2,3]

Myopia, a major public health issue, is prevalent globally, particularly in Asian countries, and by 2050, it could affect half of the global population. [4]

Insufficient outdoor time and repetitive, close-up tasks for extended periods are identified as key risk factors for myopia development and progression. [5]

A forceful strategy to reduce axial elongation is crucial due to the fast development of myopia in youngsters, and preventing its progression through slow eye developmen t paradigms like removing diffusers or fitting positive power lenses. [6]
Research suggests a link between peripheral hyperopia and axial myopia in preschoolers, highlighting the importance of the peripheral retina in refractive error development. However, minimal evidence exists for Chinese children. [7]
Myopia affects 22.9% of the world population, with an expected 50% prevalence by 2050. It is most common among young people in developed East Asian and South East Asian countries. India has a growing trend of 7.5% myopia prevalence in the past four decades, with a predicted 48% incidence in urban areas by 2050. [8,9]
Early onset and progression of myopia can lead to various visual complications, negatively impacting academic performance, psychological well-being, and personal quality of life.
Myopia negatively impacts the global economy by reducing productivity and healthcare costs. Uncorrected myopia causes an annual loss of 244 billion USD in productivity, with $16 billion spent on correcting myopia alone. This condition increases the likelihood of developing eye diseases like cataracts, glaucoma, retinal detachments, and maculopathy. Early interventions are crucial to control and prevent myopia. [10]
Myopia, once thought to be a hereditary condition with minimal environmental impact, is now recognized as a symptom of 261 genetic diseases. It is more common in middle-years of infancy and is influenced by a complex interplay of environmental variables and genes. The link between myopia and schooling is mediated by the increasing intensity of education and the need for adjustment in close-up tasks like reading and writing. Research shows that myopia is more common in Singaporean children who read more than two novels weekly, and near-work hours are just a modest influence. The exact biological relationship between schooling and myopia remains unclear.
Myopia is a condition that can be predicted by various risk factors, including genetics, age, gender, family history, ethnicity, visual environment, outdoor activity, nearwork, educational curriculum, higher academic degree, accommodation anomalies, and physical factors such as height, weight, body mass index, history of lowbirth weight, prematurity, increased digital screentime, socioeconomic states, improved diet, reduced physical activity, and irregular sleep patterns. The risk of acquiring myopia increases with higher levels of genetic load and educational attainment. Secondary myopia is a monogenic condition with a strong hereditary component, and high myopia is associated with an even greater sibling risk ratio than the average high myopia.

Myopia treatment focuses on preventing myopia in youngsters who do not yet need corrective lenses. It is possible for myopia to worsen throughout childhood and even into adulthood, especially in cases with extreme myopia. Any measure taken to slow or stop the disease's advancement is welcome. Maintaining a myopia correction of -1.00D instead of -3.00D lowers the risk of macular degeneration and retinal detachment by a factor of four and a factor of three. If we could slow progressions by 38%, we could stop myopia from progressing beyond 5D by 73%, and myopia over 5D might be reduced by 90% if the reduction rate was increased to 50%. [11]
Myopia, linked to various disorders, has seen an increase in treatments. These include lowdose atropine, highdose atropine, progressive additional lenses, specially designed spectacles, defocus integrated multiplesegments, highly aspheric lenses, multifocal contact lenses, and orthokeratology.
Low-dose atropine is the gold standard for controlling myopia in India, with the Mumbai Group of Paediatric Ophthalmologists and Strabismologists suggesting 0.01% for progressive simple

myopia. It reduces axial length elongation and is an irreversible antimuscarinic agent. Authorized by CDSCO in India. [12,13]
Atropine, a medication used to treat myopia, does not specifically inhibit muscarinic receptors, but it is believed to affect the sclera's thinning or stretching, potentially reducing the development of the eye. [14]
Atropine causes pupil widening due to blocking neurotransmitter acetylcholine, relaxing the eye's ciliary muscles. Exposure to UV radiation may slow collagen cross-linking. Progressive addition lenses (PALs) may reduce these effects. Long-term atropine patients do not show ERG abnormalities, slowing myopia development. Atropine may act directly on scleral fibroblasts, affecting retinal MI/M4 receptors at lower doses. [15,16]
Atropine is a medication used to treat myopia in children, causing a thickening of the choroidal layer and influencing the release of dopamine, which has been linked to a decrease in the pace of axial development. It acts on both dopamine and retinal amacrine cells and may act directly on the sclera. Parasympathetic inhibition is brought about by atropine, which prevents the acetylcholine fixation. Its main cardiovascular adverse effects include palpitations, rapid heartbeats, atrial arrhythmias, and premature atrial beats.

Atropine is easily available, easy to administer, affordable, and has minimal side effects. However, it has disadvantages such as temporary transient burning, stinging, blurred vision, sensitivity to light, allergic conjunctivitis, rebound phenomenon after stopping the drug, and should be prescribed with caution in patients with accommodation lag.

The World Health Organization recommends limiting the duration of atropine treatment to 2 years. Non-responders or poor responders show progression of myopia despite the best of treatment. Treatment strategies include determining the rate of progression, ethnicity, baseline refractive error, age, binocular vision status, safety, environmental and lifestyle modifications, and discussion with parents/guardians/patients.

Optical intervention, such as Deco-Incorporated Multiple Segment (DIMS) eyewear, has been used to reduce the rate of myopic refractive error development by 52% and axial length by 62% when compared to single vision glasses. Peripheral defocus contact lenses are also available for myopic youngsters aged 6 to 12 and can help mitigate myopia and slow eye development.

Aims and Objective

The study aims to analyze the daily flow dose of atropine drops on the progression of myopia in children, their effects on axial length, macular thickness, and the reverse effect of local atropine drops.

Materials and 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.

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.
The study involved 66 children presenting to ophthalmology at KIMS Karad, using a purposive convenient sampling method.

Inclusion criteria: The study is open to children aged 6-15 years old, with their parents' consent being required for participation.

Exclusion criteria: Children with congenital/developmental delays, systemic diseases, communication difficulties, eye conditions affecting visual acuity, ocular pathology, and those undergoing surgical or intravitreal eye treatment are excluded.
The Krishna Institute of Medical Sciences Deemed University, Karad, approved a research protocol following the Declaration of Helsinki guidelines. Participants were assigned unique research numbers to maintain confidentiality, and they had the freedom to opt out at any time.

Methodology:
The study involved enrolling children who met inclusion criteria and underwent a comprehensive eye examination. The children were prescribed Atropine 0.01% eye drops, and follow-ups were scheduled at 6, 12, and 18 months. The study assessed susceptibility to symptoms like glare of light, photophobia, and difficulty in reading. Adverse effects of the medication were documented. Data was analyzed using SPSS Version 20 and visualized using PicChart and Barchart. No financial conflicts of interest were disclosed.

Observation and Results
The study included 132 eligible children, analyzing age, gender distribution, and other measurements for each eye, resulting in a total of 66 eligible children for further analysis.

Table1: 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 study included children aged 7-15, with a mean age of 11.28 years.
The study included 23 males (35%), and 43 females (65%), as per the gender distribution.

Table 2: Descriptive analysis of the Baseline Measurement of Parameters Measured at the First Visit of Subjects (N = 132 Eyes).

Base line Measurement of Parameters Measured at 1st Visit(N=132Eyes)						
		Mean	**Median**	**Standard Deviation**	**Kurtosis**	**Skewness**
SE(Spherical Equivalent)		**-2.78**	**-1.88**	**2.45**	**2.38**	**-1.57**
K(Keratometric Reading)	**K1**	**43.48**	**43.50**	**1.54**	**0.41**	**0.13**
	K2	**44.45**	**44.50**	**1.51**	**0.42**	**0.11**
AL(Axial Length)		**24.27**	**24.02**	**1.34**	**1.01**	**0.89**
MT(Macular Thickness)		**244.63**	**244.00**	**6.93**	**-0.94**	**0.04**

The table presents a descriptive data analysis of 132 eyes of 66 subjects, examining refractive error, corneal power, axial length, and macular thickness, revealing non-normal distribution and needing further statistical correlations.

Table 3: Comparison of Spherical Equivalent between baseline with at 6 months, 12 Months and 18 Months using Wilcoxon test.

	N	Mean	Median	Std. Deviation	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		

The Wilcoxon signed rank test showed a significant correlation between baseline and follow-up measurements of low dose atropine drops at 12 and 18 months, but no statistically significant association at 6-month follow-up.

Table 4:Comparison of axial length between baseline with at 6 months ,12 Months and 18 Months using Wilcoxon test.

	N	Mean	Median	Std. Deviation	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		

The Wilcoxon signed rank test showed no significant changes in axial length between baseline and follow-ups of 6, 12, and 18 months.

Table 5: Comparison of K1 between baseline with at 6 months, 12 Months and 18 Months using Wilcoxon test.

	N	Mean	Median	Std. Deviation	Z Value	P-Value
BASELINE-6 Months	132	43.48	43.50	1.54	-4.24	<0.001
		43.51	43.50	1.52		
BASELINE-12 Months	132	43.48	43.50	1.54	-4.37	<0.001
		43.52	43.50	1.52		
BASELINE-18 Months	132	43.48	43.50	1.50	-4.84	<0.001
		43.53	43.50	1.52		

The Wilcoxon signed rank test K1 was used to assess keratometric values, revealing a statistically significant correlation between baseline measurements and all three follow-ups.

Table 6: Comparison of K2 between baseline with at 6 months, 12 Months and 18 Months using Wilcoxon test.

	N	Mean	Median	Std. Deviation	Z Value	P-Value
BASELINE-6 Months	**132**	**44.44**	**44.50**	**1.51**	**-3.00**	**0.003**
		44.46	**44.50**	**1.49**		
BASELINE-12 Months	**132**	**44.44**	**44.50**	**1.51**	**-3.87**	**<0.001**
		44.47	**44.50**	**1.48**		
BASELINE-18 Months	**132**	**44.44**	**44.50**	**1.51**	**-4.37**	**<0.001**
		44.48	**44.50**	**1.48**		

The Wilcoxon signed rank test revealed a statistically significant correlation between baseline measurements and all three follow-ups of the keratometric values.

Table7:Comparison of Macular thickness between baseline with at 6 months, 12 Months and 18 Months using Wilcoxon test.

	N	Mean	Median	Std. Deviation	Z Value	P-Value
BASELINE-6 Months	**132**	**244.63**	**244.00**	**6.93**	**-1.31**	**0.190**
		244.59	**244.00**	**6.83**		
BASELINE-12 Months	**132**	**244.63**	**244.00**	**6.93**	**-1.77**	**0.075**
		244.56	**244.00**	**6.81**		
BASELINE-18 Months	**132**	**244.63**	**244.00**	**6.93**	**-2.32**	**0.02**
		244.52	**244.00**	**6.80**		

The study found no significant changes in macular thickness between baseline and follow-ups of 6 and 12 months, but a significant correlation was observed at 18 months.
A qualitative assessment of low dose atropine adverse effects was conducted, revealing that all participants reported no severe effects, with occasional symptoms like mild irritation and difficulty focusing.

Discussion

The study in India examined the impact of low-dose atropine on myopia in 66 children aged 6-15. After starting atropine, the children were monitored every six months for three periods. The study evaluated 132 eyes to determine the impact of low-dose atropine on spherical equivalent, axial length, keratometric readings, and central macular thickness.
The study found that the mean spherical equivalent of a child's macular tissue is -2.78D, with a median of -1.88D, similar to a 2015 study on non-Asian children. [17]
Low dose atropine significantly impacts myopia progression in terms of spherical equivalent, with median spherical equivalent remaining constant throughout three follow-ups, indicating statistical significance over longer use periods.
The study found no significant changes in axial length over three follow-ups, possibly due to the shorter duration (18 months) of the study, which suggests a significant effect of 0.01% atropine.

The study found no significant changes in macular thickness during the first and second follow-ups of myopia, but statistically significant changes in the third follow-up, likely due to higher spherical equivalent refractive error.
Low dose atropine may not affect corneal curvature, but small changes in K1 and K2 have been observed in some patients, indicating statistical significance and should not be considered LCA effect.
The study found that while only three patients experienced occasional blurred vision or light sensitivity, these symptoms were not severe enough to warrant stopping therapy. [18]
Research shows atropine 0.01% effectively prevents myopia advancement, with lesser doses reducing myopic development. Over a three-year period, it is more effective in preventing myopia from worsening. [18]
The experiment shows that 0.01% atropine eye drops, used for at least 18 months, slow the progression of myopia, especially in progressive myopia, with minimal adverse effects.

Conclusions

Myopia is caused by a complex interplay between genes and environment, and various interventions can mitigate its progression. Parents should know which treatments work and their potential side effects. Treatment preferences vary between countries and occupations, with orthokeratology in China, atropine in Singapore and Taiwan, and soft multifocal contact lenses in America. Low-dose atropine is useful in slowing myopia development, but therapy should last longer than 18 months. Further research is needed to better understand its effect on myopia progression.

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