

Efficacy and Safety of Low Dose Atropine 0.01% in Slowing of Progression of Myopia

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Abstract

Background: We conducted this study to evaluate the efficacy & safety of topical 0.01% atropine eye drops in slowing down the progression of myopia and axial length elongation.

Methods: In this study had 50 patients (100 eyes) divided in two groups , 25 patients (50 eyes) in interventional groups and 25 patients (50 eyes) in control group.

Results: Autorefractometer (AR) readings change from base line $2.11\pm 0.11D$ to after 12 month $2.09\pm 0.12D$ so increases in AR reading was $-0.02D$ in interventional group at one year follow up. AR reading changes from baseline $2.16\pm 0.12D$ to after 12 month $2.22\pm 0.18D$ so increases in AR reading was $-0.06D$ in control groups. Subjective refraction changed from base line $2.01\pm 0.06D$ to after 12 month $2.91\pm 0.11D$ so increases in Subjective refraction was $+0.9D$ in cases at one year follow up. Subjective refraction changed from base line $2.03\pm 0.05D$ to after 12 month $3.23\pm 0.18D$ so increases in subjective refraction were $+1.2D$ in control group at one year follow up.

Conclusion: Low-dose (0.01%) topical atropine eye drops treatment was a safe and effective method for slowing down the progression of myopia in children and adolescents because it has growth suppressing influence by acting on extraretinal muscarinic receptors possible in the retinal pigment epithelium, choroid and sclera.

Keywords: Myopia, Atropine, Subjective refraction, Autorefractometer.

Introduction

Refractive error has been reported as the most common cause of reduced vision in children, affecting 2%–11% of the population below 16 years of age. It is also responsible for 60%–80% of visual impairment in children. As a single entity, myopia is the most common ocular disorder worldwide. It has been well documented that development of myopia depends both on genetic and environmental factors. In general, myopia has the trait of familial clustering. A study among Singapore Chinese preschoolers showed that family history of myopia was the strongest risk factor for offspring's myopia. Environmental risk factors such as prolonged

near work, intensive education, and limited time spent outdoors are strongly supported.¹

Atropine was first used to prevent myopia in 1920s. Since then, numerous related studies have been conducted. Different type of concentration of atropine eye drop 1%, 0.5%, 0.25%, 0.1% and 0.01% are used to prevent progression of the myopia. Both concentration and frequency of atropine have been modified to minimize the side effects while trying to maintain the benefits.²⁻³

Due to limited study was found in India we conducted this study to evaluate the efficacy & safety of topical 0.01% atropine eye drops in

slowing down the progression of myopia and axial length elongation.

Materials and Method

Study design: Hospital based case control interventional prospective study.

Inclusion Criteria:

- Age: 5 to 15 years
- Myopia ≥ 1.00 D (cycloplegic refraction; spherical equivalent)
- No prior or current treatment for preventing myopia progression (bifocals / progressive addition lenses / orthokeratology)

Exclusion Criteria:

- Best corrected visual acuity < 0.5 (6/12)
- Refractive Myopia
- Astigmatism ≥ 1.5 D
- Amblyopia
- Ocular hypertension / Glaucoma
- Prior intraocular surgery
- Allergy to atropine eye drops
- Systemic diseases associated with myopia such as Marfan syndrome, Stickler syndrome

- History of cardiac or significant respiratory diseases
- Lack of consent for participating in the study

Study Methodology:

After taking written consent of guardian of children of myopia, ages 5-15 years will be randomized to two groups. Intervention group will receive atropine 0.01% eye drop at bed time once daily in each eye for six months. Control group was receive carboxy methyl cellulose 0.5% eye drop at bed time once daily in each eye for six month. Then patients review at one year to access progression of myopia. The dose of atropine .01% is prepared from dilution of 1% atropine drop by 10ml C.M.C. (carboxy methyl cellulose).

Data Analysis:

Data was recorded as per Performa. The data analysis was computer based; SPSS-22 will be used for analysis. For categoric variables chi-square test was used. For continuous variables independent samples's *t*-test was used. *p*-value < 0.05 was considered as significant.

Results

Table 1: Socio-Demographic Profile of Patients

| Variable | Intervention group | Control group | p-value |
|---------------|--------------------|------------------|----------|
| Age in Yrs | 11.02 \pm 1.60 | 11.02 \pm 1.48 | > 0.05 |
| Male : Female | 12 : 13 | 12 : 13 | > 0.05 |

Both groups were comparable.

Table 2: Progression of Myopia

| Variable | Base line | At 6 month | At 12 month | Difference between base to 12 month |
|------------------------------|--------------------|---------------------|---------------------|-------------------------------------|
| Axial length | | | | |
| Cases | 23.92 \pm 0.82mm | 24.11 \pm 0.80 mm | 24.22 \pm 0.86 mm | +0.3 mm |
| Control | 23.77 \pm 0.76mm | 23.98 \pm 0.58 mm | 24.17 \pm 0.58 mm | +0.4 mm |
| AR | | | | |
| Cases | 2.11 \pm 0.11 D | 2.16 \pm 0.12 D | 2.09 \pm 0.12D | -0.02D |
| Control | 2.16 \pm 0.12 D | 2.20 \pm 0.17 D | 2.22 \pm 0.18 D | -0.06D |
| Subjective refraction | | | | |
| Cases | 2.01 \pm 0.06 D | 2.41 \pm 0.05 D | 2.91 \pm 0.11D | +0.9D |
| Control | 2.03 \pm 0.05 D | 2.55 \pm 0.18 D | 3.23 \pm 0.18 D | +1.2D |

Axial length changed from baseline $23.92\pm 0.82\text{mm}$ to after 12 month $24.22\pm 0.86\text{mm}$ so increases in Axial length was $+0.3\text{ mm}$ in cases at one year follow up. Axial length changed from baseline $23.77\pm 0.76\text{mm}$ to after 12 month $24.17\pm 0.58\text{mm}$ so increases in Axial length was $+0.4\text{ mm}$ in control group at one year follow up. Although increase in Axial length was less in interventional group as compare to control group but it was not statistically significant. (p value-0.568)

Autorefractometer (AR) reading changed from baseline $2.11\pm 0.11\text{D}$ to after 12 month $2.09\pm 0.12\text{D}$ so increases in AR was -0.02D in cases at one year follow up. AR reading changed from baseline $2.16\pm 0.12\text{D}$ to after 12 month $2.22\pm 0.18\text{D}$ so increases in AR -0.06D in control group at one year follow up. Although increases in AR reading was less in interventional group as compare to control group but it was not statistically significant. (p value-0.714)

Subjective refraction changed from baseline $2.01\pm 0.06\text{D}$ to after 12 month $2.91\pm 0.11\text{D}$ so increases in Subjective refraction was $+0.9\text{D}$ in cases at one year follow up. Subjective refraction from baseline $2.03\pm 0.05\text{D}$ to after 12 month $3.23\pm 0.18\text{D}$ so increases in Subjective refraction was $+1.2\text{D}$ in control group at one year follow up. Although increases in subjective refraction was less in interventional group as compare to control group but it was not statistically significant. (p value-0.701)

There was no significant difference noted in macular thickness in OCT, after one year of 0.01% atropine eye drop usage (p-value=0.3).

One child had occasional glare and one child had occasional photophobia, not requiring any treatment for the same. One child had progression of 1.0D over six month period while on atropine 0.01% eye drops.

Discussion

In our study, Axial length changed from baseline $23.92\pm 0.82\text{mm}$ to after 12 month $24.22\pm 0.86\text{mm}$ so increases in AL was $+0.3\text{mm}$ in cases at one

year of follow up. Axial length change from baseline $23.77\pm 0.76\text{mm}$ to after 12 month $24.17\pm 0.58\text{mm}$ in control group which was increases to $+0.4\text{mm}$. Although increase in axial length was less in interventional group as compare to control group but it was not statistically significant. (p value-0.568)

Autorefractometer (AR) readings changed from baseline $2.11\pm 0.11\text{D}$ to after 12 month was $2.09\pm 0.12\text{D}$ so increases in AR reading was -0.02D in interventional group at one year follow up. AR changed from baseline $2.16\pm 0.12\text{D}$ to after 12 month was $2.22\pm 0.18\text{D}$ so increases in AR reading was -0.06D in control group at one year follow up. Although increases in AR reading was less in interventional group as compare to control group but it was not statistically significant. (p value-0.714)

Subjective refraction changed from baseline $2.01\pm 0.06\text{D}$ to after 12 month $2.91\pm 0.11\text{D}$ so increases in subjective refraction was -0.9D in cases at one year follow up. Subjective refraction changed from baseline $2.03\pm 0.05\text{D}$ to after 12 month $3.23\pm 0.18\text{D}$ so increases in subjective refraction was $+1.2\text{D}$ in control group at one year follow up. Although increases in subjective refraction was less in interventional group as compare to control group but it was not statistically significant. (p value-0.701)

UCVA had not much changes upto 1 year follow up. BCVA was maintained from baseline to after one year in both interventional and control groups. There was no significant difference noted in macular thickness in OCT after one year follow up.

Similar results were found by Yen *et al.* (1989) who reported that topical atropine 1% eye drops had more successful effect on slowing down myopia progression compared with topical cyclopentolate 1% eye drops and placebo. They also reported that photophobia was a marked symptom in 64% of the cases, which was related to the high concentration of atropine used (1%).

However, the much lower concentration of atropine (0.01%) used, in the our study, was not associated with significant photophobia.⁴

Shih *et al.* (1999) compared 0.25, 0.5, or 0.1% atropine drops with 1% tropicamide eye drops in children aged between 6 and 13 years old. They concluded that atropine is an effective drug in controlling progression of myopia. According to them, children aged 6–13 years who had received tropicamide 1% were considered as the control group, in comparison with the children who had received 0.5, 0.25, or 0.1% atropine eye drops. After 2 years of follow-up, the children who received atropine with all concentrations showed a significant effect on reducing progression of myopia. Overall, 61% of the children who received 0.5% atropine had significant reduction of myopic progression, whereas 4% only had rapid progression. A lower percentage of eyes having significant reduction of myopia progression was observed in the control group compared with the atropine groups (49, 42, and 8% in the 0.25% atropine, 0.1% atropine, and control group, respectively). Concurrently, a higher percentage of children with rapid progression was observed in the control group compared with the atropine treated children (17, 33, and 44% in the 0.25% atropine, 0.1% atropine, and the control group, respectively)⁵

Tong *et al.* (2018) studied the effects of atropine on the progression of myopia. They studied the effect of atropine on 400 school-aged children with myopia (SE between -1.00 and -6.00 D) with low astigmatism (≤ 1.5 D) in a double-masked trial in which 50% of the children had received 1% atropine in one eye at night and the other 50% had received lubricant eye drops as a placebo. After 2 years of follow-up, the mean rate of progression of myopia was significantly lower in the 1% atropine group (-0.28 ± 0.92 D) compared with the placebo group (-1.20 ± 0.69 D). After the follow-up period, the children were observed for another 12 months. During this period, myopic rebound was observed, which

was more marked in the atropine group (-1.14 ± 0.80 D) than in the placebo group (-0.38 ± 0.39 D). Despite the rebound, the overall progression of myopia was still significantly lower in the eyes that received atropine in comparison with placebo, over the whole 3-year period.⁷

The previous results were consistent with the current study results concerning the effectiveness of atropine. However, the very low concentration (0.01%) used in the present study had significantly improved patient tolerability to the long-term atropine use. In the our study, the rebound effect was not observed after stoppage of atropine, which is left for further research. The use of atropine eye drops has some ocular and systemic adverse effects. The most common ocular adverse effect is photophobia, which is strongly related to the concentration of topical atropine. When the concentration of 1% was used,⁶ a large proportion of patients (64%) had reported photophobia, leading to marked drop-out during the study, whereas it was reported in only 7% of the patients when the concentration was reduced to 0.25%. In addition, blurring of vision was reported even with low concentrations down to 0.1%. However, with reduction of the concentration to 0.01%, no cases of photophobia were reported, with selectivity of the effect of atropine on the progression of myopia, as reported by other studies,⁸⁻¹¹ which encountered no adverse effects or complications with this very low concentration. Similar results were reported by the current study, as we found no complications or adverse effects with 0.01% topical atropine in group A.⁶

In our study, the low dose atropine eye drops (0.01%) was an effective method to slow down the progression of myopia. Similar results were reported in the Cochrane database review of 2011, which found that the antimuscarinic agents were considered as an effective method to slow down the progression of myopia, with atropine being the most effective antimuscarinic agent.

In our study, after 1 year of follow up, it was found that the progression of myopia in patients receiving topical atropine eye drops (0.01%) was slower than those in the control group, as progression

Conclusion

Low-dose (0.01%) topical atropine eye drops treatment was a safe and effective method for slowing down the progression of myopia in children and adolescents because it has growth suppressing influence by acting on extraretinal muscarinic receptors possible in the retinal pigment epithelium, choroid and sclera.

References

1. Padhye AS, Khandekar R, Dharmadhikari S, Dole K, Gogate P, Deshpande M. Prevalence of uncorrected refractive error and other eye problems among urban and rural school children. *Middle East Afr J Ophthalmol* 2009;16:69-74.
2. Dirani M, Chan YH, Gazzard G, Hornbeak DM, Leo SW, Selvaraj P, et al. Prevalence of refractive error in Singaporean Chinese children: The strabismus, amblyopia, and refractive error in young Singaporean Children (STARS) study. *Invest Ophthalmol Vis Sci* 2010;51:1348-55.
3. Dandona R, Dandona L, Srinivas M, Sahare P, Narsaiah S, Muñoz SR, et al. Refractive error in children in a rural population in India. *Invest Ophthalmol Vis Sci* 2002;43:615-22
4. Chia, A., Lu, Q.S., and Tan, D. Five-year clinical trial on atropine for the treatment of myopia 2: myopia control with atropine 0.01% eyedrops. *Ophthalmology*. 2016; 123: 391–399
5. Huang, J., Wen, D., Wang, Q. et al. Efficacy comparison of 16 interventions for myopia control in children: a network meta-analysis. *Ophthalmology*. 2016; 123: 697–708
6. Gong, Q., Janowski, M., Luo, M. et al. Efficacy and adverse effects of atropine in childhood myopia: a meta-analysis. *JAMA Ophthalmol*. 2017; 135: 624–630
7. Jain IS, Jain S, Mohan K. The epidemiology of high myopia: Changing trends. *Indian J Ophthalmol*. 1983;31:723–8.
8. Murthy GV, Gupta SK, Ellwein LB, Muñoz SR, Pokharel GP, Sanga L, et al. Refractive error in children in an urban population in New Delhi. *Invest Ophthalmol Vis Sci*. 2002;43:623–31.
9. Mohan M. NPCB-WHO Report. New Delhi: Ministry of Health and Family Welfare, Government of India; 1989. National survey of blindness-India.
10. Murthy GV, Gupta SK, Bachani D, Jose R, John N. Current estimates of blindness in India. *Br J Ophthalmol*. 2005;89:257–60.
11. Morgan IG, Rose KA, Ellwein LB Refractive error study in children survey group. Is emmetropia the natural endpoint for human refractive development? An analysis of population-based data from the refractive error study in children (RESC) *Acta Ophthalmol*. 2010;88:877–8.