The effect of retarding myopia progression with seasonal modification of topical atropine in Chiayi area, Taiwan

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Abstract- To determine if different concentration of atropine with seasonal modification is more physiologically effective to retard myopia progression.

Methods— Two hundred and forty eyes of one hundred and twenty healthy preschool- and school-aged children were recruited. The case group (group 1) had one hundred and twenty-six eyes of sixty three children; one hundred and fourteen eyes of fifty seven children served as the control group (group 2). The mean age was 9.08 (+/-2.82) years with a mean spherical equivalent of -1.90(+/- 1.66) dipters (D) and astigmatism of -0.50 +/- 0.59 D in the case group, compared to the mean age as 9.35 (+/-2.77) years with a mean spherical equivalent of -2.09(+/- 1.67) dipters (D) and astigmatism of -0.55 +/- 0.60 D in the control group. The concentration of atropine eye drops was modified by seasonal variation and used once a day; in general, 0.1% for summers, 0.25% for springs and falls, and 0.5% for winters. Visual acuity, intraocular pressure, and eyeball axial length were evaluated.

Results— At 1-year follow-up, the mean progression 0.28 (+/- 0.75) D of myopia equivalent on atropine treatment group was significantly less than that of the control group 1.23 (+/- 0.44) D. The progression of myopia was significantly correlated with the increases of axial length in cases (r = 0.297, P =0.001) as well as in controls (r = 0.348, P=0.000); however, it was not associated with intraocular pressure (r = -0.0015, P=0.923) among the whole subjects.

Conclusion— After minimizing the photophobia symptoms to improve the medication compliance, the modified use of atropine, based on seasonal variation, is shown promising to slow down the myopia progression for preschool- to school-aged children.

I. INTRODUCTION

Myopia is a common ocular disorder, and high or pathologic myopia (myopia at least −6.0 dipters) is associated with potentially blinding complications, such as macular degeneration, retinal detachment, glaucoma, and cataract.1,4 The prevalence rate 60% to 80% of myopia in young adults in Taiwan, Hong Kong, and Singapore is higher than those 20% to 50% in the United States and Europe.1,5,7 The data released by Taiwanese National Health Bureau in 2003 showed that the prevalence rates of preschool children aged 4-5 years, 5-6 years and 6-7 years were 11.36%, 15.18% and 18.84% respectively. The progression rate, however, became very significant compared to the prevalence data in 1991-1994. At that period, the prevalence rates were only 4.79%, 5.68%, and 7.34% for each age group correspondingly. It appears to be a severe and important national health issue here in Taiwan obviously. The progression rate of myopia is highest in young children, and the average age for stabilization of myopia is approximately 16 years.7 The earlier onset of myopia, the more rapid progression. Thus, a treatment to slow down or even to arrest the progression of myopia in children can not be overemphasized. The etiopathogeneses of myopia might include genetic basis, excessive accommodation, prolonged near work, and proliferation of chondrocytes on the anterior margins of sclera.2,11

II. MATERIAL AND METHODS

Study Population

This present study was a university based, case-control study. Two hundred and forty eyes of one hundred and twenty healthy preschool- and school-aged children were recruited from October 2006 to December 2008 in Chiayi area, Taiwan. The case group (group 1) had one hundred and twenty-six eyes of sixty three children; one hundred and fourteen eyes of fifty seven children served as the control group (group 2). Those who had ocular trauma history, traumatic cataract, keratoconus, high myopia (-10 D or...
higher), high hyperopia, severe astigmatism, ocular hypertension, or glaucoma were excluded. The cases, aged 4 to 16 years with mean 9.08 (+/-2.82) years, demonstrated a mean spherical equivalent of -1.90(+-1.66) diopters (D) (range 0 to -7.63 D) and a mean astigmatism of -0.50 +/- 0.60 D (-2.50 to 0 D) (Figure 1a). The controls, aged 4 to 16 years with mean 9.35 (+/-2.77) years, demonstrated a mean spherical equivalent of -2.09(+-1.67) diopters (D) (range 0 to -7.50 D) and a mean outdoor activities. And progressive spectacles were given for those who have any difficulty in classroom.

III. Study Procedures

All eye drops of concentration 0.1%, 0.25% and 0.5% atropine were commercialized. Initial ocular examinations included uncorrected visual acuity (UCVA), best spectacle corrected visual acuity (BSCVA), intraocular pressure (IOP), and axial length (AL) of eye globe. We repeated those measures at the subjects’ on-scheduled visits every four to six weeks. We then collected every three-month data for statistical analysis. One year later, there were one hundred and eighteen eyes completed the study.

IV. Statistical Analysis

Statistical analyses were performed using standard software (SPSS, version 11.01 for Windows, SPSS Chicago, IL). Student’s t test and correlation coefficient were used for statistical analysis. Ninety-five percent confidence interval astigmatism of -0.55 +/- 0.60 D (-2.50 to 0 D) (Figure 1b). Study cases were given atropine eye drops once daily for at least 1 year with follow-up. The dose regimen of atropine eye drops including 0.1%, 0.25%, and 0.5% were modified by seasonal variation, sunlight intensity and myopia severity, one drop on each eye every night. In general, the 0.1% concentration was used in summer, the 0.25% dosage in spring and fall, and the 0.5% concentration in winter. Anti-UV sunglasses were prescribed for those who had limits were calculated for differences in mean results. A probability value of P<0.05 was considered statistically significant.

V. Results

Refractive Status

Initially, the spherical equivalent of cases ranged from 0 D to -7.63 diopters (D) (average -1.90 +/- 1.66 D) and astigmatism was -2.50 to 0 D (mean -0.50 +/- 0.60 D). After 1 year of follow-up, the mean progression was only 0.28 (+/- 0.75) D of myopia (Table 1, Figure 2a, and Figure 3a). This compares to 1.23 (+/- 0.44) D of the controls (Table 1, Figure 2b, and Figure 3b).and 1.06 (+/- 0.61) D of the national data of general population that did not receive any treatment.16

<table>
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<tr>
<th>Table 1 Mean Spherical Equivalent(D)</th>
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SD = standard deviation
VI. AXIAL LENGTH

Average axial length of cases (group 1) and controls (group 2) at the beginning of the study was 23.78 (+/- 0.94) mm and 23.92 (+/- 0.83) mm respectively. One year later, average axial length of cases (group 1) was 24.12 (+/- 0.99) compared to those of controls 24.78 (+/- 0.96) mm. Progression of myopia significantly correlated with the increases of axial length for cases (r = 0.297, p=0.001) and for controls (r = 0.348, p=0.000) as shown in Figure 4.

VII. INTRAOCULAR PRESSURE

After one-year follow-up the mean intraocular pressure was 18.06(+/- 3.37) and 18.14(+/- 3.29) mmHg of cases and controls respectively, compared to the initial mean intraocular pressure 17.39 (+/- 3.97) and 17.89(+/- 3.48) mmHg. The progression of myopia was not associated with the increase of intraocular pressure among cases (r = 0.0023, p=0.907) nor controls. (r = 0.001, p=0.907) as shown in Figure 5a. The progression of myopia was not associated with intraocular pressure either (r = -0.0015, p=0.923) as demonstrated in Figure 5b.

VIII. SAFETY

Adverse events like papillae, follicles, visual acuity decreased subjectively, and abnormality of accommodation, in general, were mild in severity. No serious adverse effects were ever reported.

IX. DISCUSSION

Saw reported in an evidence-based review article, that there is no evidence to suggest that bifocal lenses, pressure-lowering eye drops, or soft contact lenses retard the progression of myopia. Only atropine eye drops reveal level B, I. (B = moderately important recommendation; I = strong evidence supporting recommendation) and are very cost effective. Although treatment with 0.5% atropine was the most effective, children and parents usually quit the treatment owing to adverse effects, especially photophobia under strong sunlight clinically. In our series different atropine concentration of 0.1%, 0.25%, and 0.5%, based on seasonal variation and sunlight intensity, mean myopia progression(0.28+/-0.75 diopter per year (D/Y)) was more than 0.5% atropine(0.04 +/-0.63 D/Y), but less than 0.25%(0.45+/-0.55 D/Y) and 0.1%(0.47+/-0.91 D/Y). Thus adjusting the concentration of atropine is highly effective, especially in long and full sunshine area, such as area close to the Tropic of Cancer or areas of low latitudes.

Atropine, a muscarinic antagonist, acts through the mechanism of paralyzing accommodation and direct effect on scleral growth. Our results revealed that progression of myopia was significantly correlated with the increases of axial length. We thus might attribute the retardation of myopia to the slow rate of scleral growth. The adverse effects of atropine such as photophobia, visual acuity decreased subjectively, abnormality of accommodation, macular degeneration, retinal toxicity, and cataract formation due to excess ultraviolet light exposure were ever reported. We prescribed anti-UV sunglasses or suggested a sunscreen hat wearing for patients having outdoor activities.

Siatkowski from US Pirenzepine Study Group and Tan from Asian Pirenzepine Study Group reported that 2% pirenzepine ophthalmic gel, a subtype selective M1 anti-muscarinic antagonist, used twice daily had a mean increase in myopia of 0.26 D and 0.47 D respectively over a 1-year treatment period. Their placebo-controlled groups revealed a mean increase in myopia of 0.53 D and 0.84 D correspondingly. Chua in Singapore used 1% atropine to treat myopia and reported in year 2006 that myopia progression was only -0.28+/-0.92 D in treated group compared to -1.20+/-0.69 D/Y in placebo-controlled group; Fan in Hon Kong also used topical 1% atropine eye ointment to treat myopia and get the similar result that myopic progression was significantly less (P = 0.005) in the atropine group (+0.06 +/- 0.79 D) than in the control group (-1.19 +/- 2.48 D). However, most children or their parents will quit the treatment in summer if using high concentrated atropine e.g. 0.5% or 1%.

Previous study about pressure-lowering eye drops showed no effect of retarding myopia progression. We questioned that weather increased intra-ocular pressure (IOP) could affect myopia progression or not. In this study, the result showed that progression of myopia was not associated with IOP (Figure 5). We try to understand the reason why subjects gave up the therapy in the middle of treatment. There were some reasons reported such as irritation from eye drop, over expectation of myopia control, misunderstanding or incomplete children and parental education, and too much time spent on ocular examinations. By providing a better physiologic adaptation, we should be able to improve treatment. To improve the compliance, the frequency of installation reduced to twice a week for those very low myopes (-0.75 to 0 D).

In our study, anti-UV sunglasses prescribed for those who had outdoor activities, but progressive spectacles were also given for those who have any difficulty in classroom or in reading. The trifocal lenses, not bifocal, had a better cosmetic appearance and preference for children. For those low to moderate myopes, atropine appears to retard the progression of myopia promisingly. Whether pathologic or extreme myopia could be prevented by the use of atropine or not still needs a large scale and longitudinal study.

It still remains a myth that some cases resulted in much improvement of myopia or much reduction of myopic power, for example myopia of -1.25 D back to ammetropia (0 to +0.25 D) or -2.50 D back to -1.0 D, after three- to six-month atropine treatment and became stabilized afterwards; however, it did not reveal much reduction of myopic power among controls. The axial length appeared only minimal increase after continuous atropine therapy for more than one year. The effect was attributed partially to scleral rigidity or slower scleral growth. We thus have to reconsider the
phenomenon of pseudomyopia that the power difference before and after pupil dilatation in clinic, because the mydriatic medication might not release or paralyze the accommodative power completely. More cases are needed for further analysis. We hypothesize the “trigger theory” that children born by high myopic parents were like a pistol loaded with bullets (genome) that might not do any harm if they were not triggered (risk factors); a lot of damages (complications) followed if the triggers are pulled again and again. Atropine acted as a viscous medium or damper to slow down that bullet thus reduce the damage. In Singapore, Tong et al. reported that even after stopping treatment, eyes treated with atropine demonstrated higher rates of myopia progression compared with eyes treated with placebo. However, the absolute myopia progression after 3 years was significantly lower in the atropine group compared with placebo. We thus strongly suggest that myopia should be treated intensively as early as possible in order to avoid the late complications caused by high myopia. By improving the medication compliance and reducing the complaints of photophobia, the modified use of atropine concentration of 0.1%, 0.25%, and 0.5%, based on seasonal variation and myopic severity, could effectively slow down the myopia progression in preschool- and school-aged children.

X. REFERENCES
23) Chua WH, Balakrishnan V, Chan YH, Tong L, Ling Y, Quah BL, Tan D.


Figure 3a

Figure 3b
Increases of axial length (mm)

Increase intraocular pressure (mmHg)

Figure 4
Figure 5a
XI. FIGURE LEGENDS

1) Figure 1a. The distribution of myopic status of one hundred and twenty six eyes of cases (group 1) at the study entry.

2) Figure 1b. The distribution of myopic status of one hundred and fourteen eyes of controls (group 2) at the study entry.

3) Figure 2a. The spherical equivalent (SE) of baseline, three-month follow-up, six-month follow-up, nine-month follow-up, and one-year follow-up of cases (group 1).

4) Figure 2b. The spherical equivalent (SE) of baseline, six-month follow-up, and one-year follow-up of controls (group 2).

5) Figure 3a. The 95% confidence interval (CI) of baseline, three-month follow-up, six-month follow-up, nine-month follow-up, and one-year follow-up.

6) Figure 3b. The 95% confidence interval (CI) of baseline, six-month follow-up, and one-year follow-up.

7) Figure 4. The progression of myopia was significantly correlated with the increases of axial length in cases (L1: $r = 0.297$, $P = 0.001$) and in controls (L2: $r = 0.348$, $P=0.000$).

8) Figure 5a. The progression of myopia was not associated with the increase of intraocular pressure in cases (L1: $r = 0.0023$, $P=0.907$) nor in controls (L2: $r = 0.011$, $P=0.907$).

9) Figure 5b. The progression of myopia was not associated with intraocular pressure ($r = -0.0015$, $P=0.923$) among the whole subjects.