

Effects of Different Concentrations of Atropine on Controlling Myopia in Myopic Children

YUNG-FENG SHIH, CHIEN-HSIUNG CHEN,
AI-CHUAN CHOU, TZYY-CHANG HO,
LUKE L.-K. LIN, and POR-TYING HUNG

*Department of Ophthalmology, National Taiwan University Hospital,
Taipei, Taiwan*

ABSTRACT

Although 1% atropine effectively slows myopia progression, it is associated with adverse effects, including photophobia, blurred near vision, and poor compliance. We investigated whether lower doses of atropine would control myopia progression. One hundred and eighty-six children, from 6 to 13 years of age, were treated each night with different concentrations of atropine eye drops or a control treatment for up to 2 years. The mean myopic progression in each of the groups was 0.04 ± 0.63 diopter per year (D/Y) in the 0.5% atropine group, 0.45 ± 0.55 D/Y in the 0.25% atropine group, and 0.47 ± 0.91 D/Y in the 0.1% atropine group. All atropine groups showed significantly less myopic progression than the control group (1.06 ± 0.61 D/Y) ($p < 0.01$). Our study also showed that 61% of students in the 0.5% atropine group, 49% in the 0.25% atropine group and 42% in the 0.1% atropine group had no myopic progression. However, 4% of children in the 0.5% atropine group, 17% in the 0.25% atropine group, and 33% in the 0.1% atropine group still had fast myopic progression (> 1.0 D/Y). In contrast, only 8% of the control group showed no myopic progression and 44% had fast myopic progression. These results suggest that all three concentrations of atropine had significant effects on controlling myopia; however, treatment with 0.5% atropine was the most effective.

INTRODUCTION

Myopia can be a serious ocular problem. It may result in many complications, such as retinal break, retinal detachment, and myopic retinopathy, which deteriorate vision. In Taiwan, more than 90% of college students suffer from myopia (1). Thus, finding an effective method of controlling myopic progression is critical.

Many studies have shown that daily instillation of 1% atropine markedly reduces the progression rate of myopia (2-9). One study in Taiwan showed that 1% atropine can significantly slow myopic progression. The mean progression was 0.22 diopters per year in the 1% atropine group and 0.91 diopters per year in the control group (10). Unfortunately, systemic or ocular side effects, such as blurred near vision, photophobia, allergic dermatitis, possible UV-related retinal damage

make long-term use of 1% atropine impractical (7). Therefore, we tried to lower the concentration to reduce the side effects. Our previous study (11) showed that 0.5% atropine was effective in slowing myopic progression, even in children with high myopia. The mean myopic progression was 0.01 diopters per month in the atropine group and 0.14 diopters/month in the control group (11). Based on this finding, we felt that lower concentrations might still have an effect on controlling myopia. In this study, we investigated the effects of 0.5%, 0.25%, and 0.1% atropine eye drops in controlling myopic progression in children.

MATERIALS AND METHODS

A total of 200 myopic children, age 6 to 13 years, without tropia or amblyopia, were recruited from the vision care center of National Taiwan University Hospital in 1994. The children were randomly given different concentrations of atropine (0.5, 0.25, or 0.1%) or a control treatment (0.5% tropicamide). Medications were given as eye drops, once per night. At the time of enrollment, the refractive status was -0.50 to -6.75D, and astigmatism was less than -2.0D and anisometropia was less than 2.0D. The refractive status was assessed by cycloplegic refraction before the study began and every three months for two years. All subjects' guardian gave informed consent for participation in the study. Fourteen children were excluded from the study due to loss of follow-up, nine children from the 0.5% atropine group, three children from the 0.25% atropine group, one child from the 0.1% atropine group, and one child from the control group. Thus, 186 children were treated with atropine 0.5% (n=41), 0.25% (n=47), or 0.1% (n=49), or tropicamide (n=49).

All children had complete ophthalmologic examinations before enrollment, including best corrected vision, cycloplegic refraction, funduscopy, slit-lamp biomicroscopy. Cycloplegic refraction was measured with three successive drops of 1% tropicamide at 5-minute intervals. The measurements were taken 30 minutes after the last drop was given. Cycloplegic refractive status was measured with an autorefractometer (Topcon RK-3000, Japan) and rechecked with retinoscopy (Neitz RX). The average values of the spherical equivalent of refractive status from the autorefractometer were used in our calculations. Follow-up examinations were performed every three to four months. These examinations included visual acuity with correction, cycloplegic refraction, fundoscopic examination, slit-lamp biomicroscopy and intraocular pressure when indicated. Each patient received a 1% tropicamide cycloplegic agent during visit at the clinic.

Only children treated with 0.5% atropine were suggested to wear bifocal spectacles (add +2.0D). Children treated with 0.25% atropine were suggested to wear slightly undercorrective (-0.75D) regular glasses, and children using 0.1% atropine were suggested to wear fully corrective glasses. All children were advised to wear sunglasses with UV protection when exposed to bright light. The median duration for the tropicamide group treatment was 23.1 months, for the 0.5% atropine group treatment was 20.5 months, for the 0.25% atropine group treatment was 20.3 months, and for the 0.1% atropine group treatment was 20.1 months.

The rate of myopic progression was calculated by the change of diopters per year (D/Y); the myopic progression of more than -1.0 D/Y was defined as fast progression, and myopic change of less than -0.25D per year was defined as no progression. Data were analyzed using analysis of variance tests to evaluate the differences between the different therapies.

RESULTS

The baseline refractive status was $-4.89 \pm 2.06D$ (median, -5.12D) in the 0.5% atropine group, $-4.24 \pm 1.74D$ (median, -4.64D) in the 0.25% atropine group, $-4.41 \pm 1.47D$ (median, -4.68D) in the 0.1% atropine group and $-4.5 \pm 1.86D$ (median, -4.79D) in the control group. The mean age of each group was 9.8 years in the 0.5% atropine group; 9.7 years in the 0.25% atropine group; 8.9 years in

the 0.1% atropine group; and 8.3 years in the control group. There were no significant differences among each group.

The mean rate of myopic progression was 0.04 ± 0.63 D/Y in the 0.5% atropine group, 0.45 ± 0.55 D/Y in the 0.25% atropine group, and 0.47 ± 0.91 D/Y in the 0.1% atropine group. The rate of myopic progression of all atropine groups was significantly less than in the tropicamide group (1.06 ± 0.61 D/Y) ($p < 0.01$). The difference in the myopia progression rate between the 0.1% and 0.25% atropine groups was not significant ($p = 0.9$) (Fig. 1). During the 2 year follow-up, 61% of children in the 0.5% atropine group, 49% in the 0.25% atropine group, and 42% in the 0.1% atropine group had no progression of myopia. In contrast, only 8% had no myopic progression in the control group ($p < 0.01$). However, 4% of the 0.5% atropine group and 17% of the 0.25% atropine group had fast myopic progression (more than 1.0D/Y). It was significantly less than the control group; 44% had fast myopic progression ($p < 0.01$). In the 0.1% atropine group, 33% had fast myopic progression; it was also less than the control group ($p < 0.05$) (Table 1).

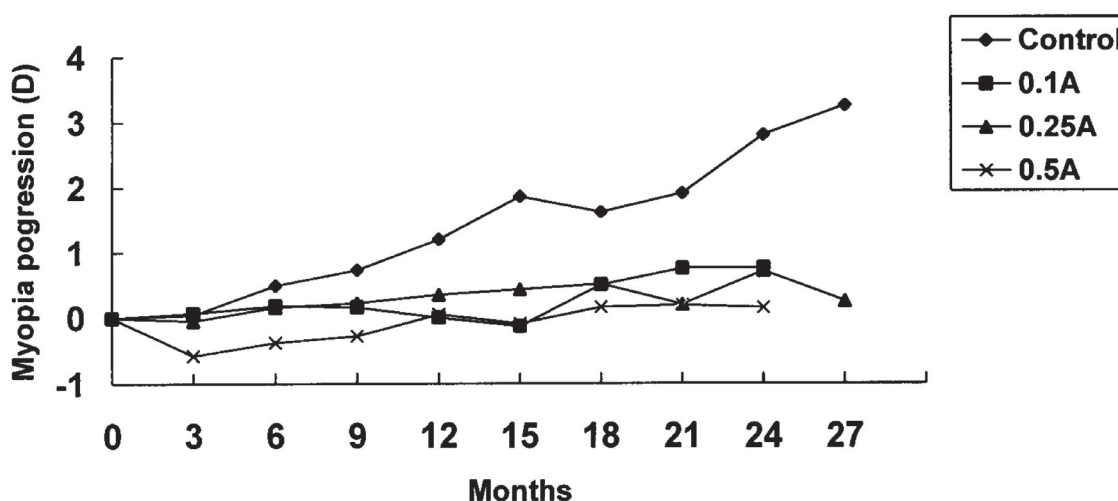


FIGURE 1. Long-Term Effects of Different Concentrations of Atropine (A) Compared with 0.5% Tropicamide Treatment on the Control of Myopic Progression. Three cases of the 0.5% atropine group quit the study at 12 months follow-up, 4 cases quit at 15 months, one case at 18 months. For the 0.25% atropine group, 2 cases quit at 15 months and one case at 18 months. Also, one case of the 0.1% atropine group and one case of the control group quit the study at 18 months.

All children in the 0.5% atropine group accepted the bifocal spectacles very well. However, photophobia was still the main complaint at the beginning in the 0.5% atropine group. Most of the children (78%) in the 0.5% atropine group had no complaints about light sensitivity after 3 months. Nine children (15%) from the 0.5% atropine group were excluded from this study; two children suffered from intolerable photophobia; two children were afraid of long-term side effects; one child had recurrent allergic blepharitis; and four children had no patience for giving the eye drops every night. In addition, three children (5%) from the 0.25% atropine group, one child (1.7%) from the 0.1% atropine group and one child (1.7%) from the control group withdrew from the study because the child had no patience for giving the eye drops every night. No systemic or ocular complications were observed during the 0.25% or 0.1% atropine therapy in this study. All (100%) of the children in the 0.1% atropine group and 93% of the children in the 0.25% atropine group had no complaints of photophobia or near work problems after 4 weeks.

TABLE 1.
Effects of Different Concentrations of Atropine (0.5%, 0.25%, and 0.1%) Compared with 0.5%
Tropicamide Treatment for Control of Myopic Progression.

	MP $\leq$ 0.25	0.25 < MP < 1.0	MP $\geq$ 1.0
0.5% Atropine (N=41)	61%	35%	4%
0.25% Atropine (N=47)	49%	34%	17%
0.1% Atropine (N=49)	42%	25%	33%
0.5% Tropicamide (N=49)	8%	48%	44%

MP: myopic progression (diopters per year)

DISCUSSION

In this study we assessed the beneficial and adverse effects of low (0.5%, 0.25%, 0.1%) concentrations of atropine in children with myopia. All concentrations of atropine had more significant effects on preventing myopic progression than that of the control group; however, treatment with 0.5% atropine was the most effective, 61% of students in the 0.5% atropine group having no myopic progression during the 2-year study. The other groups also had patients with no myopic progression, 49% in the 0.25% atropine group, 42% in the 0.1% atropine group, and 8% in the control group. Indeed, 0.5% atropine seems to be more effective than 0.25% and 0.1%, but the dropout rate (16%) in 0.5% atropine group was also higher than in the other groups.

In this study, we defined the failure of treatment by myopia progression more than -1.0D/year. This data was based on the our previous longitudinal study on the myopia progression rate of myopic children in Taiwan (10). Thus, we decided to evaluate the myopia progression by how many diopters per year, not per month. In the control group, 44% of the children had fast myopic progression. However, only 4% of the 0.5% atropine group, 17% of the 0.25% atropine group and 33% of the 0.1% atropine had fast myopic progression. No significant difference was found between 0.1% (-0.47 D/Y) and 0.25% (-0.45 D/Y) atropine in preventing myopia. This may be due to the fact that the follow-up period was too short to show effectiveness in the 0.25% atropine group. However, the fast myopic progression rate in the 0.25% atropine group (17%) was less than that in the 0.1% atropine group (33%), thus 0.25% atropine was still more effective than 0.1%.

The possible side effects of atropine, including retinal light damage (13) and accommodative problems could be less after lowering the concentration. Daily 0.1% and 0.25% atropine drops were tolerated quite well in this study with occasional complaints of light sensitivity. More than 90% of the children in the 0.25% atropine group had no complaints of photophobia or near work problems after 4 weeks. No complaints of near work problems and no systemic or ocular complications were observed from two years use of atropine in the dosages cited among this age group. However, we are closely following up the retina and the accommodative patterns of these children.

In summary, the results of our study show that all three concentrations of atropine had significant effects on controlling myopia. How do the low concentrations of atropine slow the myopic progression? It could be due to the level of accommodation blockage, or it may act directly on the sclera; or it could inhibit the release of growth factors from the retina, thereby indirectly inhibiting myopic scleral growth (14-20). However, this needs further investigation. Although 0.5% atropine was the most effective, the drop out rate may have reduced the effectiveness of 0.5% atropine. Therefore, we suggested that 0.1% or 0.25% atropine be used in the beginning to control myopia progression in children who have fast myopic progression or who have a tendency to become highly myopic, such as in early onset myopia.

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Reprint Requests: Yung-Feng Shih, M.D.
Department of Ophthalmology
National Taiwan University Hospital
7, Chung Shan South Road
Taipei, Taiwan 100, Republic of China

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