

The effectiveness of progressive addition lenses on the progression of myopia in Chinese children

Zhikuan Yang, Weizhong Lan, Jian Ge, Wen Liu, Xiang Chen, Linxin Chen and Minbin Yu

State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center, Sun Yat-sen University, Guangzhou 510060, China

Abstract

Purpose: To evaluate the effectiveness of progressive addition lenses (PALs), with a near addition of +1.50 D, on the progression of myopia in Chinese children.

Methods: We enrolled 178 Chinese juvenile-onset acquired myopes (aged 7–13 years, -0.50 to -3.00 D spherical refractive error), who did not have moderately or highly myopic parents, for a 2-year prospective study. They were randomly assigned to the PAL group or single vision (SV) group. Primary measurements, which included myopia progression and ocular biometry, were performed every 6 months. Treatment effect was adjusted for important covariates, by using a multiple linear regression model.

Results: One hundred and forty-nine subjects (75 in SV and 74 in PAL) completed the 2-year study. The myopia progression (mean \pm S.D.) in the SV and PAL groups was -1.50 ± 0.67 and -1.24 ± 0.56 D, respectively. This difference of 0.26 D over 2 years was statistically significant ($p = 0.01$). The lens type ($p = 0.02$) and baseline spherical equivalent refraction ($p = 0.05$) were significant contributing factors to myopia progression. Mean increase in the depth of vitreous chamber was 0.70 ± 0.40 and 0.59 ± 0.24 mm, respectively. This difference of 0.11 mm was statistically significant ($p = 0.04$). Age ($p < 0.01$) was the only contributing factor to the elongation of vitreous chamber. Different near phoria ($p < 0.01$) and gender ($p = 0.02$) caused different treatment effects when wearing SV lenses. However, there were no factors found to influence the treatment effect of wearing PALs.

Conclusions: Compared with SV lenses, myopia progression was found to be retarded by PALs to some extent in Chinese children without moderately or highly myopic parents, especially for subjects with near esophoria or females.

Keywords: clinical trial, ethnicity, myopia, progressive addition lens

Introduction

Epidemiological studies indicate that myopia is related to both environmental and genetic factors (Hammond *et al.*, 2001; Lyhne *et al.*, 2001; Saw *et al.*, 2002; Ting *et al.*, 2004). Chinese populations have the highest prevalence of myopia in the world and may be one of

the ethnicities which are the most susceptible to myopia (Fan *et al.*, 2004; He *et al.*, 2004; Lin *et al.*, 2004). It is of interest that those Chinese youngsters who were born and live overseas, still have much higher occurrence of myopia than the native population, even though they have the same educational and cultural environment (Wu *et al.*, 2001; Kleinstein *et al.*, 2003; Goh *et al.*, 2005). This strongly indicates a genetic difference between ethnicities. Therefore, it is worthwhile to look again at the effectiveness of progressive lens intervention, which has been shown to have limited therapeutic effect in Caucasians, but this time specifically in a Chinese population.

Among a variety of interventions, progressive addition lenses (PALs) are one option that has been evaluated

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Correspondence and reprint requests to: Jian Ge.

Tel.: +86 20 87330351; Fax: +86 20 87330409.

E-mail address: Cjiange@hotmail.com

across countries (Leung and Brown, 1999; Shih *et al.*, 2001; Edwards *et al.*, 2002; Gwiazda *et al.*, 2003). The rationale for this intervention was based on the capacity of the PALs to decrease accommodative lag. Lag was presumed to be similar to hyperopic retinal defocus (Gwiazda *et al.*, 2003, 2005) that is known to induce experimental myopia in animals (see review by Norton, 1999). Leung and Brown (1999) reported a statistically significantly smaller myopia progression in the PAL group compared with a single vision (SV) control group in Hong Kong Chinese children, and the effect was dose-related. However, two subsequent masked, randomized studies in the same ethnicity reported conflicting results (Shih *et al.*, 2001; Edwards *et al.*, 2002). It is known that myopia progression is influenced not only by interventions but also, for example, by other potentially confounding factors, such as ethnicity, age of onset, gender and heterophoria (Braun *et al.*, 1996; Brown *et al.*, 2002; Gwiazda *et al.*, 2004; Hyman *et al.*, 2005). Thus, results have not been conclusive due to not controlling for these important factors in these studies.

The Correction of Myopia Evaluation Trial (COMET), a well-conducted study, recently reported a 0.20 D difference between PAL and SV groups at the 3-year visit, which was statistically but not clinically significant (Gwiazda *et al.*, 2003). Furthermore, COMET found myopes with a large accommodative lag and some other related factors had a larger treatment effect using PALs (Gwiazda *et al.*, 2003, 2004; Hyman *et al.*, 2005). Nevertheless, COMET participants were ethnically diverse with the Asian race only accounting for approximately 8% of 469 enrolled children. As a result, the test power was not large enough to evaluate the potential treatment effect specifically in the Asian race, such as in Chinese children (Gwiazda *et al.*, 2003). The results, therefore, cannot necessarily be applied to Chinese children.

For this reason, a 2-year prospective, randomized and double-masked clinical study was conducted to address the effectiveness of PALs on myopia progression in Chinese children.

Methods

All experimental protocols and procedures met the tenets of the Declaration of Helsinki and were approved by the local institutional review board. Consent was obtained from enrolled children and their parents, after verbal and written explanation of the nature and possible consequences of the clinical trial.

We calculated that a sample size of at least 138 would be powerful enough in this study (Zar, 1999) based on the following assumptions:

- (1) two-tailed $\alpha = 0.01$,
- (2) power = 90% ($\beta = 0.10$)

- (3) an overall standard deviation (S.D.) of 0.75 D in the cumulative 2-year follow-up measurements of refractive change, which is based on similar research on Chinese Hong Kong myopes (Edwards *et al.*, 2002).

- (4) an expected difference of 0.50 D in the 2 years' cumulative myopia progression between the two groups, based on the findings in Hong Kong Chinese (Lam *et al.*, 1999) and our clinical observations (-0.75 to -1.00 D per year myopic shift in Guangzhou myopes).

Given the possibility of dropout, which was set at a maximum rate of 20%, we aimed to enrol no less than 166 subjects.

We enrolled 7–13 year old urban myopes from Guangzhou city, who had approximately the same living habits and educational environment. The ophthalmic and non-ophthalmic criteria were as followed:

Ophthalmic criteria (in both eyes):

- (1) Spherical refractive error of -0.50 to -3.00 D (measured under cycloplegia)
- (2) Astigmatism of not more than 1.50 D
- (3) Anisometropia of not more than 1.00 D
- (4) Best corrected visual acuity of not less than 6/6
- (5) No strabismus
- (6) Normal intraocular pressure (measured with Goldman tonometer)
- (7) No ocular conditions that are known to affect refractive development

Non-ophthalmic criteria:

- (1) No moderately or highly myopic (< -3.00 D) parents, assessed by non-cycloplegic autorefractometry
- (2) Birth weight of more than 1250 g
- (3) Willingness to wear glasses constantly for a minimum of 2 years
- (4) Understanding random assignment and willingness not to apply other medications
- (5) No systemic conditions or use of medications that affect refractive development
- (6) No prior use of contact lenses, bifocals or PALs

All statistical analysis was carried out independently by an experienced statistician using the software SPSS 11.0 (SPSS Inc., Chicago, IL, USA). Study results are expressed as mean \pm S.D. Data analysis was conducted in the following steps. First, dropouts and retained subjects were compared on baseline ocular and demographic characteristics. Meanwhile, the equivalence of these important characteristics was also tested between the two study groups. Next, a multiple linear regression model with all potential confounding covariates, including the types of lenses, near lag, baseline spherical equivalent refraction (SER), workload, gender, age and near phoria, was employed to find out which contributed to the refractive development. Finally, this method

was used again in the two study groups separately to estimate the possible differential effect of the two kinds of lens among the above important covariates.

Outcome measurements and procedures

At each visit, objective refractive error was measured by cycloplegic autorefractometry (RM 8800; Topcon, Tokyo, Japan), which was performed 30 min after the third administration (5 min apart) of Mydrin-P (0.5% tropicamide + 0.5% phenylephrine hydrochloride; Santen Pharmaceuticals, Osaka, Japan). Mydrin-P has been proved to be an acceptable and useful cycloplegic agent in Asian schoolchildren with a wide range of myopic refractive errors (Hamasaki *et al.*, 2007). The average of three reliable readings was taken as the objective refractive error and was expressed as the spherical equivalent refractive error (SER, i.e. spherical error plus half of the cylinder error).

The depth of the vitreous chamber was chosen for evaluating the change in ocular biometry, because it was known to be highly correlated with myopia progression, and more predictable and repeatable than axial length measures. At each visit, the depth of the vitreous chamber was determined by A-scan ultrasonography using an 11 MHz probe (Axis-II; Quantel Medical, Clermont-Ferrand, France) after cycloplegic autorefractometry. Readings were accepted when anterior and posterior lens reflections were observed and a sharp retinal spike was visible. The average of 10 reliable readings in each eye was taken for analysis.

After determination of the spectacle prescription, horizontal heterophoria was measured at distance (5 m) and near (33 cm) by means of the cover test with a step-prism bar. Children were instructed to fixate on the projected words of 5/6 size, and words in N10 size in books, for the distant and near measurements, respectively. The end-point of the cover test was defined as the first neutral point. Esophoria was shown as a positive value and exophoria was shown as a negative value.

Accommodative response was measured using an open-field autorefractor (SRW-5001k; Shin-Nippon, Tokyo, Japan). Subjects, with a trial frame fitted with the SER prescription in place, were instructed to fixate binocularly at distance (5 m, a red star provided by the manufacturer) and at near (33 cm, a 5 × 5 array of Chinese characters in N10 size) and keep it clear. The average of three readings was used to calculate the accommodative response, and the calculation method used was from Gwiazda *et al.* (1993).

Near workload was assessed, at every follow-up visit, by a detailed questionnaire on near work outside school hours, which was filled out by both children and their parents. The questionnaire was adapted for this study from the one used by Saw *et al.* (1999). Near workload

was averaged for the four follow-up visits and expressed as accommodative demand (D) multiplied by hours per day (H). Questions of compliance and adherence to the assigned spectacles were also included in the questionnaire at the last visit. They included the wearing time of the spectacles (constantly; no less than half of awake time per day; or less than half of awake time per day) and whether they viewed near objects through the lower part of the lenses. Only children who reported constantly wearing the spectacles and viewing objects through the correct area of the spectacle lens were considered to have good compliance and adherence.

Figure 1 shows the flow diagram of the procedure. Enrolled subjects were assigned randomly to either the SV group or PAL group. The PALs we used were the MC lenses (Sola Optical, Guangzhou, China) with +1.50 D near addition. Spectacle prescription was determined by subjective refraction, with an end-point of minimum minus dioptric power for best visual acuity. The criterion for a change in spectacles was myopia progression larger than 0.50 D or as clinically indicated.

Throughout the study, every measurement was made by the same investigator using the same instrument, to diminish person and instrument bias. Meanwhile, we emphasized the importance of full-time proper wear of the assigned spectacles, as if they were wearing PALs, to enrolled subjects and their parents at every visit. As for the masking, except for investigator C and investigator D (unmasked investigator), investigator A and investigator B (masked investigator) and all the enrolled subjects were unaware of their group allocation. All subjects had their frame selection, adjustment, parameter measurement and optical dispensing as if for PALs, regardless of group allocation. Finally, subjects were informed to consult investigator D, rather than to consult anybody else, if they encountered any problems with frames, lenses, visual symptoms or any safety concerns, between regular visits.

Results

From July 2004 to March 2005, we enrolled 178 eligible subjects (male 53%): 89 in the SV group and 89 in the PAL group. After the 2-year visit, there were 29 dropouts (16.3%).

The distributions of the change in refractive error, the change in the depth of the vitreous chamber and covariates of near lag, baseline refractive error and workload were found to be normally distributed (all $p > 0.05$). However, the covariates of near phoria and age were found to be non-normally distributed. Therefore, near phoria was classified as esophoria ($> +2$), ortho (-1 to 1), exophoria (≤ -2) and age was classified as younger age (7–10 years) and older age (11–13 years), determined by the median.

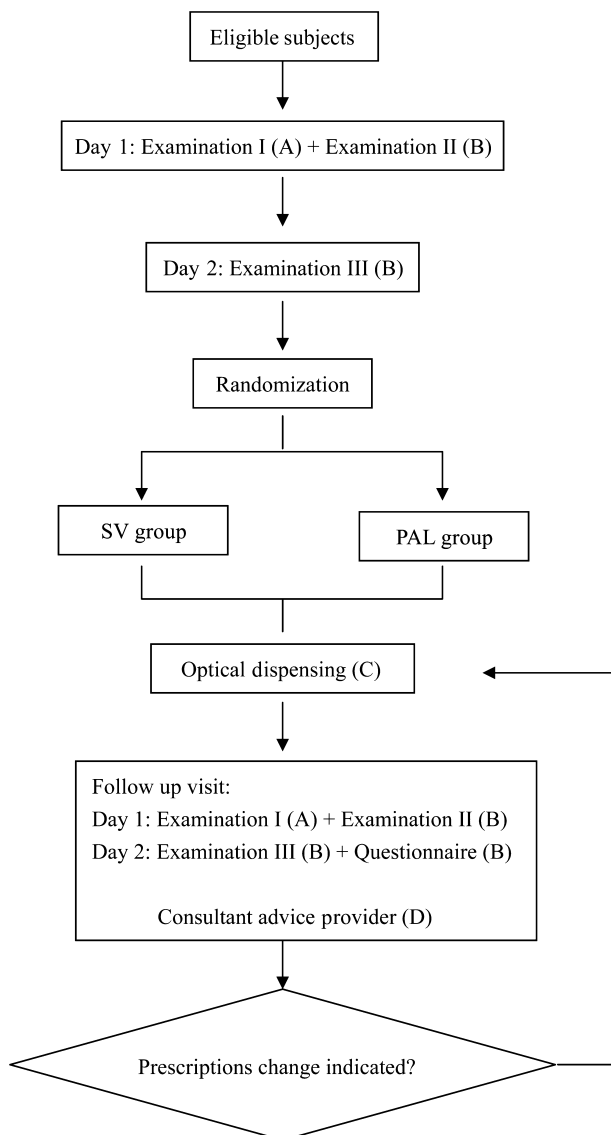


Figure 1. Flow diagram of procedure. Examination I: A-Scan + auto refraction; examination II: retinoscopy; examination III: subjective refraction + accommodative response + cover test. Investigator A and investigator B (masked investigators); investigator C and investigator D (unmasked investigators).

Table 1 shows the baseline demographic and ocular characteristics for the retained subjects vs dropouts. Comparisons of these important characteristics indicated no significant differences between these groups, except that the dropouts had a more myopic initial cycloplegic SER than those retained ($p = 0.01$).

Baseline data of retained subjects

For the 149 subjects (75 in SV and 74 in PAL), their baseline characteristics were 10.96 ± 1.59 years old; SER -1.69 ± 0.67 ; near lag 0.78 ± 0.28 D; near phoria -1.23 ± 5.38 Δ. The baseline SER and depth of the vitreous chamber in the SV and PAL group were

-1.78 ± 0.68 D v.s -1.60 ± 0.63 D ($p = 0.10$) and 17.00 ± 0.88 mm v.s 16.81 ± 0.61 mm ($p = 0.14$), respectively. There was no statistically significant difference in other characteristics between the two study groups (Table 2).

Change in refractive error between groups

The final refractions at 24 months in the SV and PAL group were -3.28 ± 0.92 and -2.84 ± 0.77 D, respectively. Thus, average myopia progression in the SV and PAL group was -1.50 ± 0.67 and -1.24 ± 0.56 D (unpaired t -test, $p = 0.01$), respectively. Figure 2a shows the myopic change over time.

The unadjusted correlations between the myopia progression vs the baseline SER, near lag and workload were -0.08 , 0.06 and -0.01 , respectively (all $p > 0.05$). The unadjusted myopia progression between subgroups in categorical variables is shown in Table 3. These unadjusted results showed that only the covariates of group and gender had significant effect on the change in refractive error. On the basis of previous findings (Brown *et al.*, 2002; Gwiazda *et al.*, 2004; Hyman *et al.*, 2005), we considered age, near lag, baseline SER, workload and near phoria as covariates as well, in the multiple linear regression analysis, to explore further which covariates contributed to myopia progression.

After adjusting other covariates, only the covariates of group ($p = 0.02$) and baseline SER ($p = 0.05$) were found to have statistically significant effect on myopia progression. The unstandardized coefficients were 0.32 and -0.29 , respectively.

Change in depth of the vitreous chamber

The final depth of the vitreous chamber at 24 months in the SV and PAL group was 17.69 ± 0.88 and 17.40 ± 0.65 mm, respectively. Thus, average increases in depth of the vitreous chamber in the SV and PAL group were 0.70 ± 0.40 and 0.59 ± 0.24 mm (unpaired t -test, $p = 0.04$), respectively. Figure 2b shows the change in the depth of vitreous chamber over time.

In multiple linear regression analysis including all the above covariates, only the covariate of age ($p < 0.01$) was found to have a statistically significant effect on the change in the depth of the vitreous chamber. The unstandardized coefficient was -0.21 . The covariate of 'group' only had a borderline significant contributing effect to the elongation of the vitreous chamber ($p = 0.07$).

Differential treatment effect of the two kinds of lens related to the important covariates

When the multiple linear regression analysis was performed in the two groups separately, we found that

Table 1. Comparison of baseline demographic and ocular characteristics between retained subjects and dropouts

		Retained subjects <i>n</i> = 149		Dropouts <i>n</i> = 29		<i>p</i>
		<i>n</i>	$\bar{X} \pm \text{S.D.}$	<i>n</i>	$\bar{X} \pm \text{S.D.}$	
Gender*	Male	78		14		0.69
	Female	71		15		
Group*	SV	75		15		0.89
	PAL	74		14		
Age* (years)	7–10	56		9		0.50
	11–14	93		20		
Near phoria* (Δ)	≤ -2	60		7		0.25
	-1 to 1	54		14		
	≥ 2	35		8		
Near lag [†] (D)			0.78 \pm 0.28		0.66 \pm 0.31	0.12
Baseline SER [†] (D)			-1.69 \pm 0.67		-2.06 \pm 0.86	0.01

*Categorical variables, analysed by chi-squared test.

[†]Continuous variables, analysed by unpaired *t*-test

Table 2. Comparison of demographic and ocular characteristics between study groups

		SV group <i>n</i> = 75		PAL group <i>n</i> = 74		<i>p</i>
		<i>n</i>	$\bar{X} \pm \text{S.D.}$	<i>n</i>	$\bar{X} \pm \text{S.D.}$	
Gender*	Male	44		34		0.14
	Female	31		40		
Age*(years)	7–10	27		29		0.74
	11–14	48		45		
Near phoria* (Δ)	≤ -2	29		31		0.22
	-1 to 1	24		30		
	≥ 2	22		13		
Near lag [†] (D)			0.76 \pm 0.26		0.80 \pm 0.30	0.57
Number of mild myopic parents* (<i>n</i>)	None	55		53		0.70
	One	18		17		
	Both	2		4		

*Categorical variables, analysed by chi-squared test.

[†]Continuous variables, analysed by unpaired *t*-test.

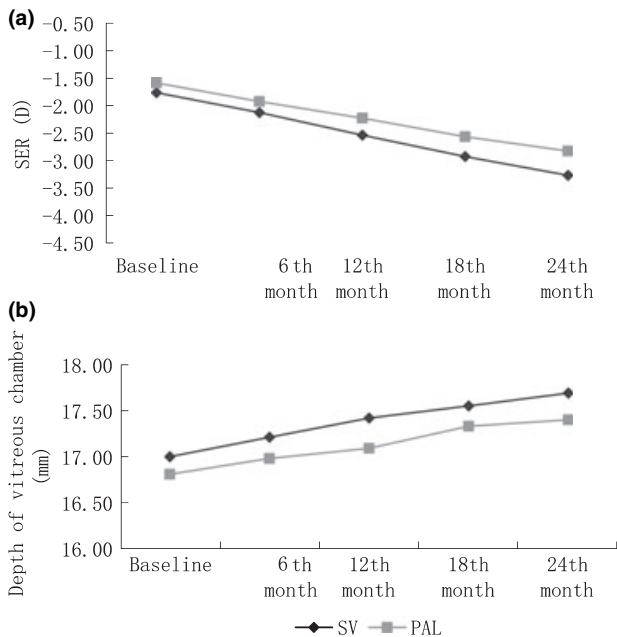


Figure 2. (a) Mean spherical equivalent refraction (SER) and (b) mean vitreous chamber depth for the two study groups at each visit.

the covariates of near phoria (unstandardized coefficient = -0.34, *p* < 0.01) and gender (unstandardized coefficient = -0.49, *p* = 0.02) contributed to myopia progression in the subjects wearing SV lenses. This meant that esophoric and female subjects progressed faster than others when they wore SV lenses. In the subjects wearing PALs, there were no factors found to

Table 3. Comparison of unadjusted myopia progression between subgroups in categorical variables

		<i>n</i>	$\bar{X} \pm \text{S.D.}$	<i>p</i>
Group*	SV	75	-1.50 \pm 0.67	0.01
	PAL	74	-1.24 \pm 0.56	
Gender*	Male	78	-1.28 \pm 0.59	0.05
	Female	71	-1.48 \pm 0.66	
Age* (years)	7–10	56	-1.49 \pm 0.65	0.09
	11–13	93	-1.30 \pm 0.61	
Near phoria [†] (Δ)	≤ -2	60	-1.40 \pm 0.62	0.89
	-1 to 1	54	-1.34 \pm 0.60	
	≥ 2	35	-1.37 \pm 0.65	

*Comparison between subgroups, analysed by unpaired *t*-test.

[†]Comparison between subgroups, analysed by one-way ANOVA test.

Table 4. Unadjusted difference of treatment effect between the two study groups

		SV Group n = 75		PAL Group n = 74		p
		n	$\bar{X} \pm \text{S.D.}$	n	$\bar{X} \pm \text{S.D.}$	
Gender*	Male	44	-1.39 ± 0.56	34	-1.13 ± 0.60	0.06
	Female	31	-1.67 ± 0.79	40	-1.33 ± 0.52	0.04
Near phoria* (Δ)	≤ -2	29	-1.48 ± 0.75	31	-1.33 ± 0.49	0.41
	-1 to 1	24	-1.48 ± 0.51	30	-1.23 ± 0.64	0.17
	≥ 2	22	-1.65 ± 0.76	13	-0.88 ± 0.51	<0.01

*Comparison between subgroups, analysed by unpaired *t*-test.

influence the treatment effect, although baseline SER had an effect with borderline significance ($p = 0.06$). Table 4 shows the unadjusted difference of treatment effect between the two study groups in relation to gender and near phoria, respectively.

Compliance and adherence

Self-reported compliance and adherence to spectacle wear were good, as assessed by answers to questionnaires administered to both children and their parents. Overall, 130 (87%) of 149 reported constant wearing of their glasses and viewing things through the appropriate areas of the lenses.

Discussion

In this study, we evaluated the effectiveness of PAL on myopia progression in Chinese children. Although there is no gene which has been found to be correlated with school myopia until now, one cannot deny the effect of genetic background on the occurrence of myopia and its development. Saw *et al.* (2001) reported a positive association between parental myopia and the rate of myopia progression in school children. However, the effect of genetic background is very difficult to measure and quantify. Thus, limiting enrolment of children who have parents with little or no myopia in this study facilitated the evaluation of the optical intervention on myopia progression.

Over the 2-year period, losses to observation were relatively low at approximately 16%. The comparisons of the baseline demographic and ocular characteristics showed that there were no significant differences between subjects who completed the study and those lost to observation, except that the dropouts were initially more myopic than those retained. It is possible that these dropouts with higher myopia were more worried about their condition than those less myopic subjects, and opted for other forms of myopia treatment. It seems unlikely that this has biased the samples significantly. Our randomized allocation led to good

similarity between the two study groups (Table 2): the adoption of a multiple regression model made it possible to explore the potential confounding factors on myopia progression rate, which was especially useful for some factors, like the workload, that could not be determined at baseline.

We found myopia progression (mean ± S.D.) of -1.50 ± 0.67 D in the SV group and -1.24 ± 0.56 D in the PAL group. The unadjusted difference of 0.26 D between the two groups was statistically significant. Further, the adjusted treatment effect of PALs was found to be 0.32 D, after controlling for all the other potentially confounding covariates. Edwards *et al.* (2002) found a myopia progression of -1.26 ± 0.74 D in the SV group and -1.12 ± 0.67 D in the PAL group in Hong Kong Chinese children over a 2-year period. The two studies were very similar in regards to the ethnicity, culture, educational background and study period: the same lens was also used, the Sola MC lens with +1.50 D addition and a short corridor. Thus, the results of these two studies ought to be comparable. Nevertheless, their results show no statistically significant treatment effect of PALs. One of the differences between the samples of the two studies was that the initial average SER was -1.69 D in this study, compared with approximately -2.85 D in the earlier study. Since we found a significant and negative association between the baseline SER and myopia progression, this may explain the reason for higher myopia progression in this study for both groups and explain the reason, at least in part, for the smaller difference that they found.

Like this study, the COMET study, which also used a multiple regression model, also found a statistically significant treatment effect in their population of diverse ethnicity (Gwiazda *et al.*, 2003, 2004). Nevertheless, they found myopes with larger near lags in combination with near esophoria benefited more from PALs. Although we also found that near esophoric myopes benefitted from PALs, compared with SV lenses, we did not find near lag a differential treatment factor in this study. This indicates that those Chinese children with a large near lag do not necessarily have a slower progression rate than those with a low near lag when wearing PALs. A very recent study reported differences in near lag as a function of ethnicity (Mutti *et al.*, 2006). One possible explanation could be that near lag might play a weaker role during myopia development in Chinese than in Caucasians, which remains to be confirmed. Another differential treatment factor, baseline SER, found to be significant in the COMET study ($p = 0.04$), also had a borderline significance ($p = 0.06$) in this study. One of the reasons for the relatively lower statistical significance of the baseline SER could be that the range of initial SER was much lower in this study, which was 2.50 D compared with 3.25 D in COMET study. We also found

females had a faster progression rate than the males when wearing SV lenses, which was consistent with COMET study (Hyman *et al.*, 2005).

Leung and Brown (1999) found that subjects using PALs with +2.00 D addition had a slower progression rate than those using PALs with +1.50 D. However, the treatment effect was approximately equal between the present study with +1.50 D and the second year results in COMET with +2.00 D. Rosenfield and Carrel (2001) measured the accommodative response in subjects who viewed a near target through their distance refractive error combined with a +0.75, +1.50, +2.00 and +2.50 D near add. They found the additional lens power required to reduce the accommodative error to zero correlated significantly with the individual initial accommodative error. It is difficult, therefore, to predict the amount of treatment effect when comparing PALs with different near additions.

Limitations

Given the increasing prevalence and severity of myopia in Asia, there is increasing risk for the current myopic children to be parents with moderate or high myopia in the future. Results in this study can only be applied to the treatment effect of PALs on the children without obvious genetic background and this limits the ability to generalize these results to the Chinese population as a whole. It is of interest to find that children with two myopic parents benefited most from the treatment with PALs, compared with those without, or with only one myopic parent (Kurtz *et al.*, 2007). Therefore, it is necessary to carry out parallel studies specifically on these genetically susceptible subjects in China.

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Competing interest

The authors have no financial interest in the outcome of this study.

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