

Randomized Controlled Trial of Patching vs Acupuncture for Anisometropic Amblyopia in Children Aged 7 to 12 Years

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Objective: To compare the effectiveness of 2-hour daily patching with the effectiveness of acupuncture in treating anisometropic amblyopia in children aged 7 to 12 years who have worn optimal spectacles for at least 16 weeks.

Methods: In a single-center randomized controlled trial, 88 eligible children with an amblyopic eye who had a best spectacle-corrected visual acuity (BSCVA) of 0.3 to 0.8 logMAR at baseline were randomly assigned to receive 2 hours of patching of the sound eye daily or 5 sessions of acupuncture weekly. All participants in our study received constant optical correction, plus 1 hour of near-vision activities daily, and were followed up at weeks 5, 10, 15, and 25. The main outcome measure was BSCVA in the amblyopic eye at 15 weeks.

Results: The mean BSCVA of the amblyopic eye at 15 weeks improved from baseline by 1.83 and 2.27 lines in the patching and acupuncture groups, respectively. After baseline adjustment, the mean difference of BSCVA between the 2 groups was 0.049 logMAR (95% confi-

dence interval, 0.005-0.092; $P = .03$), meeting the definition of equivalence (difference within 1 line). The BSCVA had improved by 2 lines or more in 28 (66.7%) and 31 (75.6%) eyes in the patching and acupuncture groups, respectively. Amblyopia was resolved in 7 (16.7%) and 17 (41.5%) eyes in the patching and acupuncture groups, respectively.

Conclusion: Acupuncture produced equivalent treatment effect for anisometropic amblyopia, compared with patching, and was statistically superior. Further studies are warranted to investigate its value in the treatment of amblyopia.

Clinical Relevance: Acupuncture could potentially become an alternative treatment to occlusion therapy for amblyopia.

Trial Registration: Centers for Clinical Trials Registry Identifier: CUHK_CCT00248

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AMBLYOPIA IS A LEADING cause of monocular visual impairment worldwide, with a prevalence varying from 0.3% to 5%.¹⁻⁵ Anisometropia is the major predisposing cause, contributing to approximately 30% to 50% of cases, and presents concomitantly with strabismus in another approximately 20% of cases.^{1,4,6} Recently, optimum refractive correction has been found to be effective for anisometropic amblyopia in children aged 3 to 7 years, achieving a responder rate (defined as best-corrected visual acuity [VA] in the amblyopic eye improved by ≥ 2 lines) of 77% and a resolution rate of 27%.⁷ However, in older children aged 7 to 12 years, only 30% responded to optical correction alone. Combining this with occlusion or atropine treatment of the better eye in-

creased the responder rate to 63%.⁸ However, adverse effects such as emotional problems,⁹ reversed amblyopia,¹⁰ and poor compliance can deter the use of occlusion therapy in some patients. Even with the improvement noted, many of the responders had a residual visual deficit.⁸ Hence, a more effective and convenient alternative treatment for anisometropic amblyopia is required, especially for older children.

Acupuncture is a basic component of traditional Chinese medicine and a popular treatment in alternative medicine.¹¹⁻¹⁴ It has been used for treating ophthalmic disorders such as dry eye,¹⁵ myopia,¹⁶ and amblyopia.^{17,18} In recent years, the use of functional magnetic resonance imaging has demonstrated a correlation between vision-related acupoint stimulation and visual cortical activation,^{19,20} suggesting a pos-

sible basis for the use of acupuncture in treating amblyopia. Previously, Ercolani et al¹⁷ and Pasmanik and Nizovtseva¹⁸ had reported acupuncture to be effective in treating amblyopia. However, to our knowledge, there have been no randomized controlled trials to assess acupuncture vs conventional treatments for amblyopia. We therefore conducted the present randomized controlled trial to compare acupuncture with patching in the treatment of anisometropic amblyopia in children aged 7 to 12 years.

METHODS

Our study was conducted at the Joint Shantou International Eye Center of Shantou University and The Chinese University of Hong Kong, Shantou, China. Eligible children were recruited from pediatric eye clinics during the period from December 2007 through May 2009 after written informed consent was obtained from the children and their parents. The study protocol was approved by the institutional review board and ethics committee. The tenets of the Declaration of Helsinki were followed in all study procedures.

PARTICIPANT ENROLLMENT

Patients aged 7 to 12 years were eligible if they had anisometropic amblyopia and had worn optimal spectacles for at least 16 weeks prior to enrollment. The entry criteria included (1) anisometropia of 0.50 diopters (D) or more of the spherical equivalent and/or a 1.50-D or more difference between the eyes in astigmatism; (2) VA in the amblyopic eye of a 0.3-0.8 logMAR (equivalent to 20/40-20/125) and VA in the sound eye of 0.1 logMAR or more (equivalent to 20/25); (3) an interocular VA difference of 2 logMAR lines or more; (4) a myopic spherical equivalent of no more than -6.00 D in the amblyopic eye; (5) no measurable heterotropia in primary gaze at distance or near fixation with spectacles or no documented history of strabismus; (6) no other ocular cause for reduced acuity; and (7) no prior treatment for amblyopia except for spectacle use. The spectacles should have been worn until VA was stabilized (VA improved by <1 line compared with the previous visit at least 5 weeks earlier). Participants who showed stabilization within 16 weeks prior to the study-specified screening visit were instructed to continue wearing spectacles until after 16 weeks.

SPECTACLE PRESCRIPTION AND BASELINE EXAMINATION

At the screening visit, protocol-specified spectacles were prescribed on the basis of cycloplegic refraction using cyclopentolate, 1%. Anisometropia, astigmatism, and myopia were corrected fully, whereas hyperopia was either fully corrected or symmetrically undercorrected by no more than +1.50 D. The baseline examination was scheduled within 2 weeks of the screening visit. New spectacles were provided for all participants on the day of baseline examination. With the participant wearing the new spectacles, VA was measured in each eye by a study-certified vision examiner using the Early Treatment Diabetic Retinopathy Study (ETDRS) testing protocol presented on an electronic visual acuity tester (Jaeb Center for Health Research, Tampa, Florida).^{21,22} For each participant, the VA was measured in the amblyopic eye prior to being measured in the sound eye. Visual acuity was remeasured in the amblyopic eye after 30 minutes. The better of the 2 VA scores was used as the baseline VA to assess eligibility and to serve for subsequent analysis of VA improvement.

RANDOMIZATION AND TREATMENT PROTOCOL

After eligibility was confirmed, participants were randomly assigned to either patching or acupuncture by use of a simple randomization method²³ that consisted of a list of computer-generated random numbers. The participants were assigned by matching their serial numbers of trial enrollment to the sequence of the random numbers, with odd numbers being assigned to the patching group and even ones to the acupuncture group.

Treatments were started within 2 days after randomization. All participants were asked to wear the provided spectacles constantly and received 1 of the 2 following treatments.

Patching

Patching consisted of 2 continuous hours of daily patching of the sound eye using felt patches on the glasses. Participants were also instructed to perform near-vision activities for 1 hour during patching. The activities included writing homework assignments, reading, computer work, and other eye-hand coordination activities. As a compliance aid, parents were required to monitor their children during the time of patching and encourage them to use the nonpatched eye. They were also told to record the duration of patching and the near-vision activities every day and report orally to the investigators at every 5-week visit. The treatment was continued for the duration of the trial unless reverse amblyopia occurred in the sound eye.

Acupuncture

Acupuncture consisted of 5 treatment sessions per week. During the weekdays, acupuncture was performed after school. Needling was performed by one of us (J.Z.), a certified acupuncturist who was masked to the VA outcomes of the participants. Five acupoints, unilateral GV20 (baihui), bilateral EX-HN5 (taiyang), bilateral BL2 (cuanzhu), unilateral LI4 (hegu), and bilateral BL59 (fuyang), were selected on the basis of the theory and literature reports of traditional Chinese medicine.^{24,25} Disposable acupuncture needles (Hwato; Suzhou, China) were inserted at the acupuncture sites, manually manipulated by rotation methods to achieve a characteristic sensation known as *de Qi*, and left in place for 15 minutes. The locations of the acupoints and the manipulation methods used are shown in **Table 1** and **Figure 1**. Acupuncture treatment was continued for the duration of the study. Acupuncture-related adverse effects at any session were treated and recorded. The children in the acupuncture group were instructed to perform 1 hour per day of near-vision activities at any time of the day, similar to the children in the patching group, but without the use of a patch.

FOLLOW-UP VISITS

Follow-up visits were scheduled at weeks 5, 10, and 15, with a final visit at week 25, regardless of the VA outcomes of the participants. At each visit, a blank form with no details of the previous measurements was provided to the vision examiner who was masked as to the treatment status of the participant. To ensure masking of the observers, VA testing and acupuncture were performed on different floors of the hospital. The VA examiner met the children only on the days of follow-up visits. The children and parents were told not to bring the patch and not to inform the examiner of the assigned treatment. At the visit, VA was measured in each eye by use of the ETDRS testing protocol, with the participant wearing the prescribed spectacles. The amblyopic eye was remeasured a half an hour later. The better of the 2 VA scores was taken as the outcome measure. The sound eye

Table 1. Locations of Acupoints and Manipulation Methods Used in the Acupuncture Group

Acupoint Code (Name)	Location ^a	Direction of Insertion ^b	Depth of Insertion, mm
GV20 (baihui)	On top of the head, 7 <i>cun</i> above the occipital hairline and 5 <i>cun</i> behind the frontal hairline	Perpendicular or oblique	1-2
EX-HN5 (taiyang)	At the temporal fossa and 1 <i>cun</i> behind the midpoint of a line from the lateral end of the eyebrow to the external canthus	Perpendicular or oblique	6-10
BL2 (cuanzhu)	In the supraorbital notch and at the median end of the eyebrow	Perpendicular or oblique	2-6
LI4 (hegu)	At the dorsum of the hand and between the first and second metacarpals, midway down the second metacarpal	Perpendicular	10-15
BL59 (fuyang)	3 <i>cun</i> above the site between the Achilles tendon and lateral malleolus	Oblique	10-20

^a *Cun* is a unit of measure that is used in traditional Chinese medicine to measure the length of a certain part of the body surface for the convenience of locating acupoints.

^b The needles are inserted into the skin in a direction with respect to the skin.

was remeasured only if the VA score was found to be 1 line or more worse than any of the prior VA scores. If the VA remained unchanged, then a cycloplegic refraction was performed, and the VA was retested. If a change in optical correction did not improve the VA of the sound eye, then patching was discontinued and the participant was prescribed new spectacles and continued his or her scheduled follow-up visits until the end of the trial.

STUDY OUTCOME MEASURES

The primary outcome measure was the best spectacle-corrected VA (BSCVA) in the amblyopic eye at week 15. Other outcome measures included the BSCVA in the amblyopic eye at other follow-up visits, the VA in the sound eye at every follow-up visit, as well as the responder and resolution rates at every follow-up visit. In our study, amblyopia was considered resolved in participants achieving an interocular VA difference of 1 line or more⁷ and/or an amblyopic-eye VA of 0.1 logMAR or more. A responder was defined as a participant whose VA in the amblyopic eye improved by 2 lines or more from baseline.

STATISTICAL METHODS

This trial was designed to evaluate whether the treatment effects of 2-hour daily patching and acupuncture are equivalent in treating anisometropic amblyopia in children. A sample size of 80 participants provided 80% power and a type I error rate of 5% for an equivalence limit of 1 logMAR line based on the following assumptions derived from our previous pilot study (J. Z. and D. S. C. L., unpublished data, 2006): an SD of ± 1.5 lines for the mean 15-week VA scores and a dropout rate of 10%.

The letter scores yielded from the ETDRS testing protocol were converted to logMAR equivalents using the formula $\log\text{MAR} = 1.7 - (0.02 \times \text{letter score})$. With this conversion, a 5-letter difference in VA (1 line) is equivalent to a 0.1 difference in logMAR.²¹ The

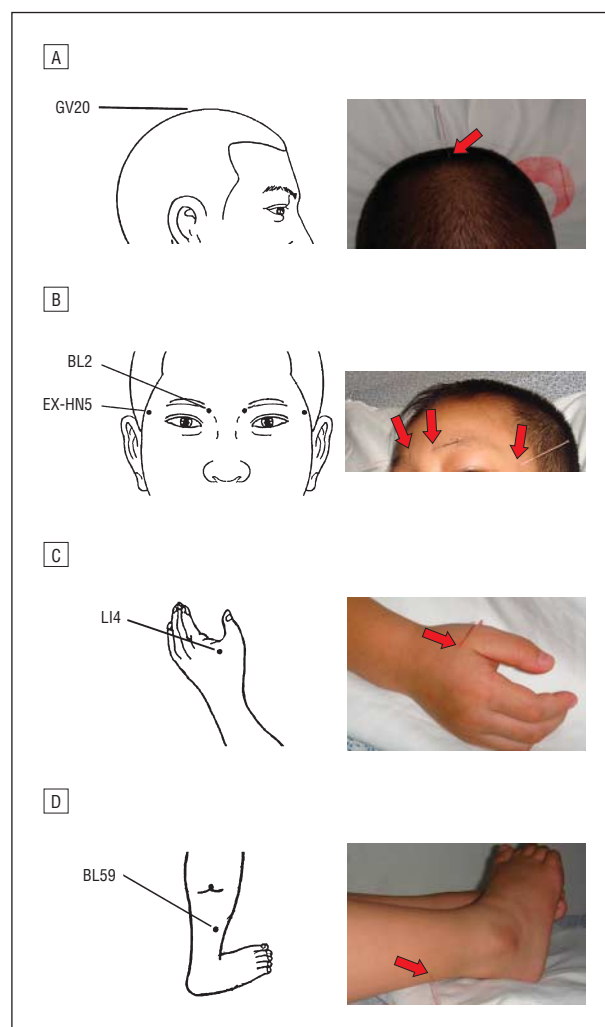


Figure 1. Schematic diagram showing the positions of the acupoints used in this study and photographs showing children receiving acupuncture. A-D, 5 Acupoints: unilateral GV20 (baihui) (A), bilateral BL2 (cuanzhu) and bilateral EX-HN5 (taiyang) (B), unilateral LI4 (hegu) (C), and bilateral BL59 (fuyang) (D). The arrows indicate the acupoints.

primary analyses for the amblyopic-eye VA involved a treatment group comparison of the 15-week VA, controlling for the baseline VA scores by using analysis of covariance (ANCOVA). The treatments were considered equivalent if the upper and lower bounds of the 2-sided 95% confidence intervals (CIs) constructed on the difference between adjusted mean VA scores for the 2 groups were contained within the interval of ± 1 line (± 0.1 logMAR). Confounding was evaluated by including covariates of interest in the ANCOVA model, and interaction between baseline factors and treatment group on the 15-week VA was assessed by including interaction terms in the model.

As secondary analyses, the time-course profiles of treatment effects were evaluated by within-group comparisons of BSCVA means using repeated-measures analysis of variance along with a post hoc Bonferroni test for all possible comparisons and treatment-group comparisons of BSCVA means at each visit using ANCOVA adjusted for baseline acuity. Treatment group comparisons for binary variables, including rates of resolved amblyopia and responder rates, were performed using a χ^2 test. All analyses followed the intention-to-treat principle. A 2-tailed *P* value of less than .05 was considered to be statistically significant. The SPSS version 16.0 software (SPSS Inc, Chicago, Illinois) was used for statistical analyses.

Table 2. Baseline Characteristics of the Participants in the Study Groups in Our Randomized Controlled Trial

Characteristic	No. (%)	
	Acupuncture Group (n=43)	Patching Group (n=45)
Female	17 (39.5)	21 (46.7)
Age at recruitment, y		
7 to <8	5 (11.6)	12 (26.7)
8 to <9	9 (20.9)	5 (11.1)
9 to <10	11 (25.6)	6 (13.3)
10 to <11	5 (11.6)	3 (6.7)
11 to <12	6 (14.0)	11 (24.4)
12	7 (16.3)	8 (17.8)
Mean (SD) age, y	9.4 (1.6)	9.4 (1.9)
BSCVA in the amblyopic eye, logMAR (Snellen fraction)		
0.8 (20/125)	1 (2.3)	2 (4.4)
0.7 (20/100)	8 (18.6)	9 (20.0)
0.6 (20/80)	3 (7.0)	6 (13.3)
0.5 (20/63)	5 (11.6)	6 (13.3)
0.4 (20/50)	13 (30.2)	9 (20.0)
0.3 (20/40)	13 (30.2)	13 (28.9)
Mean (SD) BSCVA in the amblyopic eye, logMAR	0.46 (0.16)	0.49 (0.17)
Approximate to Snellen equivalent	20/63 ⁺²	20/63
BSCVA in the sound eye, logMAR (Snellen fraction)		
0.1 (20/25)	17 (39.5)	23 (51.1)
0.0 (20/20)	22 (51.2)	16 (35.6)
-0.1 (20/16)	4 (9.3)	6 (13.3)
Mean (SD) BSCVA in the sound eye, logMAR	0.03 (0.06)	0.04 (0.07)
Approximate to Snellen equivalent	20/20 ⁻¹	20/20 ⁻²
Interocular VA difference, No. of lines		
2	10 (23.3)	8 (17.8)
3	6 (14.0)	8 (17.8)
4	10 (23.3)	8 (17.8)
5	4 (9.3)	4 (8.9)
6	6 (14.0)	10 (22.2)
≥7	7 (16.3)	7 (15.6)
Mean (SD) interocular VA difference, No. of lines	4.3 (1.9)	4.5 (1.8)
Refractive error in the amblyopic eye (spherical equivalent), D		
-6.00 to <0	4 (9.3)	4 (8.9)
0 to <1.00	8 (18.6)	4 (8.9)
1.00 to <2.00	4 (9.3)	5 (11.1)
2.00 to <3.00	3 (7.0)	3 (6.7)
3.00 to <4.00	2 (4.7)	7 (15.6)
≥4.0	22 (51.2)	22 (48.9)
Mean (SD) spherical equivalent, D	3.1 (2.8)	3.8 (2.9)
Refractive error in the sound eye (spherical equivalent), D		
-6.00 to <0	9 (20.9)	6 (13.3)
0 to <1.00	14 (32.6)	12 (26.7)
1.00 to <2.00	9 (20.9)	12 (26.7)
2.00 to <3.00	4 (9.3)	4 (8.9)
3.00 to <4.00	4 (9.3)	2 (4.4)
≥4.0	3 (7.0)	9 (20.0)
Mean (SD) spherical equivalent, D	1.2 (1.8)	1.8 (2.3)
Interocular refractive error difference (spherical equivalent), D		
<1.00	13 (30.2)	7 (15.6)
1.00 to <2.00	6 (14.0)	14 (31.1)
2.00 to <3.00	7 (16.3)	10 (22.2)
3.00 to <4.00	7 (16.3)	5 (11.1)
≥4.0	10 (23.3)	9 (20.0)
Mean (SD) spherical equivalent, D	2.5 (1.9)	2.4 (1.6)

Abbreviations: BSCVA, best spectacle-corrected visual acuity; D, diopter; VA, visual acuity.

RESULTS

STUDY COHORT AND BASELINE CHARACTERISTICS

Between December 2007 and May 2009, 88 Chinese children (38 girls and 50 boys with a mean [SD] age of 9.4

[1.8] years) who had VA in the amblyopic eye of 0.3 to 0.8 logMAR (mean, 0.48; approximately 20/60) and an interocular VA difference of 2 lines or more (mean, 4.4 lines) were enrolled and randomly assigned to the patching group (n=45) or the acupuncture group (n=43). The participants' baseline characteristics were similar between groups (**Table 2**).

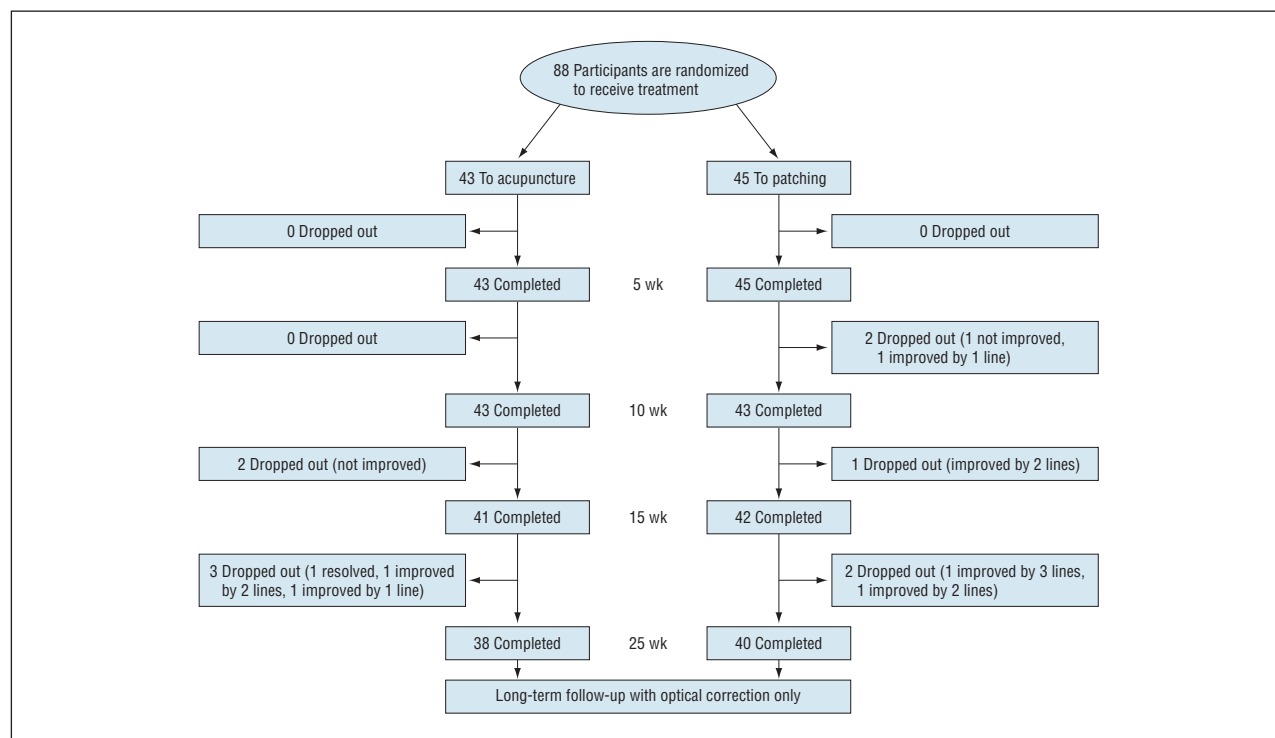


Figure 2. Flowchart showing the progress of participants in each treatment group of our randomized controlled trial. The term *not improved* is defined as a lack of improvement in visual acuity (VA) of the amblyopic eye for at least 1 logMAR line from baseline. An improvement of 1 line or more is defined as improvement in the VA of the amblyopic eye of 1 line or more than the baseline VA score.

PARTICIPANT FOLLOW-UP AND TREATMENT

At 15 weeks, the primary outcome data were collected from 42 participants (93.3%) in the patching group and 41 (95.3%) in the acupuncture group. By week 25, an additional 2 participants in the patching group and an additional 3 participants in the acupuncture group had dropped out of the study. Of the 10 participants who dropped out, 6 had moved from the study area to another city in China, and 4 dropped out for unknown reasons. The treatment effects of these participants are described in **Figure 2**. During follow-up, none of the participants (or their parents) requested to alter the assigned treatment. In the patching group, no parent reported at any visit that their child had performed less than 2 hours of patching at any time. In the acupuncture group, 39 children (90.7%) had received a total of 125 assigned acupuncture sessions and 4 children (9.3%) received at least 80 (range, 80-120) assigned acupuncture sessions.

VISUAL ACUITY IN THE AMBLYOPIC EYE

At the 15-week primary outcome visit, the mean BSCVA in the patching group had improved from 0.49 logMAR at baseline to 0.30 logMAR, with a mean improvement of 1.83 lines. In the acupuncture group, the mean BSCVA had improved from 0.46 logMAR at baseline to 0.23 logMAR, with a mean improvement of 2.27 lines (**Table 3**). After controlling for the baseline VA, the mean difference in VA between groups was 0.049 logMAR (95% CI, 0.005-0.092; $P = .03$). Based on the CI, this difference met the predefined criteria for equivalence (ie, the upper and

lower bounds of the CI are within ± 0.1 logMAR or ± 1 line), although the difference is statistically significant. At week 15, VA in the amblyopic eye had improved by at least 2 lines in 28 of 42 participants (66.7%) in the patching group and 31 of 41 participants (75.6%) in the acupuncture group ($P = .37$). The number of participants fulfilling the criteria for resolution of amblyopia was 7 of 42 (16.7%) in the patching group and 17 of 41 (41.5%) in the acupuncture group ($P = .01$). There was no significant interaction between treatment group and baseline VA ($P = .82$), baseline refractive error ($P = .34$), age at enrollment ($P = .17$), or sex ($P = .12$) with regard to the 15-week outcome VA in the amblyopic eye. Subgroup analyses by age showed VA improvement in all age groups (data not shown).

At weeks 5, 10, and 25, the 95% CIs of mean difference in VA between groups were completely contained within the interval of ± 1 line (Table 3). By 25 weeks, the mean BSCVA was 0.28 logMAR in the patching group and 0.22 logMAR in the acupuncture group ($P = .06$). The resolved rate was similar between groups (30% in the patching group vs 42.1% in the acupuncture group, $P = .27$).

Serial comparisons of the mean BSCVA in the amblyopic eye between the 2 groups showed that the BSCVA had significantly improved every 5 weeks ($P < .001$), except during the last visit at week 25, compared with the visit at week 15 ($P > .10$). From weeks 15 to 25, 8 of 42 participants (19%) in the patching group and 7 of 41 participants (17%) in the acupuncture group had at least 1 line of additional VA improvement.

Table 3. Outcome Measures of the Amblyopic Eye at Every Follow-up Visit

	Participants, No (%)							
	5 wk		10 wk		15 wk ^a		25 wk	
	Acupuncture (n=43)	Patching (n=45)	Acupuncture (n=43)	Patching (n=43)	Acupuncture (n=41)	Patching (n=42)	Acupuncture (n=38)	Patching (n=40)
BSCVA, logMAR								
≥0.7	2 (4.7)	6 (13.3)	1 (2.3)	3 (7.0)	0 (0.0)	1 (2.4)	0 (0.0)	1 (2.5)
0.6	5 (11.6)	7 (15.6)	2 (4.7)	2 (4.7)	3 (7.3)	1 (2.4)	2 (5.3)	1 (2.5)
0.5	2 (4.7)	4 (8.9)	4 (9.3)	9 (20.9)	2 (4.9)	7 (16.7)	2 (5.3)	7 (17.5)
0.4	8 (18.6)	6 (13.3)	5 (11.6)	3 (7.0)	2 (4.9)	5 (11.9)	2 (5.3)	4 (10.0)
0.3	13 (30.2)	13 (28.9)	11 (25.6)	12 (27.9)	9 (22.0)	7 (16.7)	8 (21.1)	6 (15.0)
0.2	10 (23.3)	6 (13.3)	16 (37.2)	10 (23.3)	10 (24.4)	15 (35.7)	10 (26.3)	10 (25.0)
0.1	3 (7.0)	3 (6.7)	3 (7.0)	4 (9.3)	12 (29.3)	6 (14.3)	11 (28.9)	10 (25.0)
0.0	0 (0.0)	0 (0.0)	1 (2.3)	0 (0.0)	3 (7.3)	0 (0.0)	3 (7.9)	1 (2.5)
Mean (SD) BSCVA, logMAR	0.35 (0.17)	0.41 (0.19)	0.30 (0.15)	0.35 (0.18)	0.23 (0.16)	0.30 (0.15)	0.22 (0.15)	0.28 (0.17)
Within-group comparison, ^b <i>P</i> value	1.2 × 10 ⁻⁹	3.2 × 10 ⁻⁶	3.3 × 10 ⁻⁴	3.3 × 10 ⁻⁵	3.3 × 10 ⁻⁴	6.9 × 10 ⁻⁵	1.0	0.19
Treatment group comparison, <i>P</i> value	.06		.12		.03		.06	
Difference in mean VA between groups (95% CI), ^c logMAR	0.034 (-0.02 to 0.070)		0.031 (-0.008 to 0.071)		0.049 (0.005-0.092)		0.043 (-0.002 to 0.088)	
Line change from baseline								
≤-1	1 (2.3)	1 (2.2)	0 (0.0)	1 (2.3)	0 (0.0)	1 (2.4)	0 (0.0)	1 (2.5)
0	8 (18.6)	16 (35.6)	4 (9.3)	6 (14.0)	1 (2.4)	2 (4.8)	1 (2.6)	1 (2.5)
1	20 (46.5)	20 (44.4)	18 (41.9)	17 (39.5)	9 (22.0)	11 (26.2)	6 (15.8)	9 (22.5)
2	12 (27.9)	7 (15.6)	13 (30.2)	16 (37.2)	17 (41.5)	18 (42.9)	14 (36.8)	18 (45.0)
3	2 (4.7)	1 (2.2)	5 (11.6)	3 (7.0)	7 (17.1)	9 (21.4)	12 (31.6)	8 (20.0)
4	0 (0.0)	0 (0.0)	3 (7.0)	0 (0.0)	6 (14.6)	1 (2.4)	4 (10.5)	3 (7.5)
≥5	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	0 (0.0)	1 (2.6)	0 (0.0)
Mean (SD) line change	1.14 (0.86)	0.80 (0.81)	1.65 (1.04)	1.33 (0.89)	2.27 (1.12)	1.83 (0.99)	2.39 (1.05)	2.0 (1.04)
Responders	14 (32.6)	8 (17.8)	21 (48.8)	19 (44.2)	31 (75.6)	28 (66.7)	31 (81.6)	29 (72.5)
Treatment group comparison, <i>P</i> value	.11		.67		.37		.34	
Resolved cases	8 (18.6)	5 (11.1)	11 (25.6)	5 (11.6)	17 (41.5)	7 (16.7)	16 (42.1)	12 (30.0)
Treatment group comparison, <i>P</i> value	.32		.10		.01		.27	

Abbreviations: BSCVA, best spectacle-corrected visual acuity; CI, confidence interval; VA, visual acuity.

^aPrimary outcome visit.

^b*P* values from post hoc comparisons of the mean BSCVA in the amblyopic eye at 2 consecutive visits in the repeated-measures analysis of variance model, adjusted for multiple comparisons by use of the Bonferroni test.

^cControlling for baseline VA.

VISUAL ACUITY IN THE SOUND EYE AND ADVERSE EFFECTS

By the end of the trial, the BSCVA in the sound eye had improved by a mean of 0.40 lines in the patching group and by a mean of 0.28 lines in the acupuncture group. Twenty of 45 participants (44.4%) in the patching group and 19 of 43 participants (44.2%) in the acupuncture group had at least 1 line of VA improvement from baseline. No participants were found to have their VA in the sound eye decrease by more than 1 line.

In the acupuncture group, most children received treatment well and felt only mild discomfort. However, 2 of 41 participants (4.9%) in the acupuncture group reported having moderate pain during 4 acupuncture sessions. The pain was fully relieved after removing the needles. Rneedling at the same session was successful after the participant was reassured and well rested. No acupuncture-related infection or other adverse events occurred.

COMMENT

We evaluated the effectiveness of acupuncture vs 2 hours of daily patching plus 1 hour of near-vision activity in

the treatment of anisometropic amblyopia in children aged 7 to 12 years who had received optimal optical corrections for at least 16 weeks before enrollment in our trial. Up to the 15-week primary outcome visit, the acupuncture group had improved by a mean of approximately 0.5 lines more than the patching group (95% CI, 0.05-0.92 lines; *P* = .03). On the basis of the CI of the difference in mean change, the predefined criterion for equivalence (ie, the upper and lower bounds of the 95% CI contained within 1 line) was met. Equivalence was also found at other visits. By 15 weeks, the proportion of responders in both groups was similar (75.6% in the acupuncture group vs 66.7% in the patching group; *P* = .37), whereas the resolution rate was significantly higher in the acupuncture group (41.5%) than in the patching group (16.7%) (*P* = .01). However, the resolution rates were similar by 25 weeks. These results suggest that the treatment effect of acupuncture is equivalent to that of patching for anisometropic amblyopia in older children.

The use of occlusion, mainly by patching simultaneously with optical correction, remains the mainstream therapy for anisometropic amblyopia in older children. As a control, the patching group in our study was treated with optical correction plus 2 hours of daily patching and 1 hour

of near-vision activity, and this type of treatment was found to show a mean of 1.83 lines of improvement in VA in the amblyopic eye. A study conducted by the Pediatric Eye Disease Investigator Group (PEDIG) demonstrated that continued spectacle correction led to an average of approximately 0.5 lines of additional VA improvement in children who wore optimal spectacles for 16 weeks or longer.²⁶ In our study, some of the treatment effect observed may have resulted from continued optical correction. In a PEDIG trial, 2 hours of daily patching resulted in an average of 2.2 lines of improvement in best-measured VA in children aged 3 to 7 years with amblyopia from different causes.²⁶ In another PEDIG trial involving children aged 7 to 12 years, patching led to a 2-line VA improvement in the subgroup of anisometropic amblyopia at 17 weeks.²⁷ Therefore, the magnitude of VA improvement in the patching group in our study is similar to that of other well-conducted randomized trials, although the characteristics of the participants and the study designs are not exactly the same. It has been reported that 2 hours or 6 hours of daily patching produced similar VA improvements in treating moderate amblyopia.²⁸ In our setting, we do not know whether an increase of patching time in some children would have led to better VA outcomes. However, because our study was not designed to evaluate the maximum effect of patching, we did not adjust the duration of patching. Another concern is the efficiency of using a felt patch. As a compliance aid, we requested parents to monitor and encourage their children to use the nonpatched eye during patching. In view of the findings that the 15-week VA outcome was comparable with those in previous studies,^{26,27} we believe that the patching regimen used in our study was adequate.

To our knowledge, this is the first randomized clinical trial comparing the effectiveness of acupuncture as treatment for amblyopia with the effectiveness of patching as treatment for amblyopia. Although acupuncture has been used as treatment for amblyopia,^{17,18} information about its therapeutic effect is limited. Our data demonstrated that acupuncture led to a substantial VA improvement in the amblyopic eye in older children within a period of 25 weeks. In our study, we chose the 15-week point as the primary outcome because VA is expected to have stabilized in most patients at around this period.⁸ At this visit, the acupuncture group had a mean of 2.27 lines of VA improvement from baseline. The time-course profiles showed that the mean BSCVA in the amblyopic eye had continuously improved until week 15 and remained stable afterward (Table 3). These results suggest that most participants had achieved a maximum VA within the first 15 weeks of treatment. For amblyopia, age is an essential factor affecting treatment efficacy. In our study, the mean age was similar between groups at randomization, and there was no significant interaction between treatment group and age with regard to the 15-week outcome VA ($P = .17$), which suggests that the treatment equivalence was not likely due to age difference between groups.

Although the treatment effect of acupuncture appears promising, the mechanism underlying its success as a treatment for amblyopia remains unclear. Acupuncture at vision-related acupoints may modulate the activity of the visual cortex.^{19,20,29} Moreover, acupuncture has been shown to be

effective in increasing blood flow to the cerebral and ocular vasculatures (including the choroid),³⁰⁻³³ stimulating the expression of retinal nerve growth factors³⁴ and leading to metabolic changes in the central nervous system.^{33,35-37} In amblyopia, microscopic anatomical and structural abnormalities have been found in the retina, lateral geniculate bodies, and visual cortex.⁵ For treatment purposes, we selected 5 acupoints on the basis of the theory and recent literature of traditional Chinese medicine.^{24,25} These acupoints are located on the meridian with the visual-related acupoints (VA1-VA8) or at sites surrounding the eyes. Thus, acupuncture may exert its effect on amblyopia through combined modulation of both the central visual system and the eyes; however, this hypothesis has yet to be confirmed. We did not include a sham acupuncture group in our study, mainly because of its poor acceptance by patients and their parents, which, in turn, would have substantially increased the difficulty in recruiting patients.

In our study, both treatments were well tolerated. No compliance problems were reported by the parents in the patching group, and no serious adverse effects were found in either the patching group or the acupuncture group. To allay concerns that frequent administration of acupuncture during weekdays would compromise the education of the school-aged children, we performed acupuncture after school. No participant complained about interruption of schooling. Whether a reduced dose of acupuncture will lead to a similar treatment effect is yet to be investigated.

With regard to translating the results into clinical practice, the findings from this report indicate that the treatment effect of acupuncture for amblyopia is equivalent to the treatment effect of patching for amblyopia. However, only patients with anisometropic amblyopia were involved in our study and the follow-up period was relatively short. Additional multicenter studies on different types of amblyopia and a longer period of follow-up are warranted. Moreover, acupuncture itself is a very complicated system of therapy. Differences exist among acupuncturists, and there are divergent manipulation modes, stimulation parameters, treatment styles, and subjective sensations evoked by acupuncture stimulation. Because of the good results obtained in our study, the acupoints that we used could be considered for use in clinical practice. Other methods require additional studies.

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