Randomised controlled trial of treatment of unilateral visual impairment detected at preschool vision screening

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Editorial by Dutton and Cleary

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Abstract

Objectives To test the efficacy of treatment for unilateral visual loss detected by preschool vision screening and the extent to which effectiveness varies with initial severity.
Design Randomised controlled trial of full treatment with glasses and patching, if required, compared with glasses only or no treatment. Masked assessment of best corrected acuity after one year of follow up.
Setting Eight UK eye departments.
Participants 177 children aged 3-5 years with mild to moderate unilateral impairment of acuity (6/9 to 6/36) detected by screening.
Results Children in the full and glasses treatment groups had incrementally better visual acuity at follow up than children who received no treatment, but the mean treatment effect between full and no treatment was equivalent to only one line on a Snellen chart (0.11 log units; 95% confidence interval 0.050 to 0.171; $P < 0.0001$). The effects of treatment depended on initial acuity: full treatment showed a substantial effect in the moderate acuity group (6/36 to 6/18 at recruitment) and no significant effect in the mild acuity group (6/9 to 6/12 at recruitment) ($P = 0.006$ for linear regression interaction term). For 64 children with moderate acuity loss the treatment effect was 0.20 log units, equivalent to one to two lines on a Snellen chart. When all children had received treatment, six months after the end of the trial, there was no significant difference in acuity between the groups.
Conclusions Treatment is worth while in children with the poorest acuity, but in children with mild (6/9 to 6/12) unilateral acuity loss there was little benefit. Delay in treatment until the age of 5 did not seem to influence effectiveness.

Introduction

Amblyopia is a form of cerebral visual impairment caused by abnormal vision, commonly uncorrected refractive error, during a sensitive period of development.[1–4] Treatment is thought to be effective only during this sensitive period, which varies for different types of amblyopia but most commonly lasts until 7 years of age.[5–7]

Strabismic amblyopia usually presents with a visible squint, but refractive amblyopia or a small angle strabismus may not be detected until it is too late for effective treatment. Preschool vision screening became widespread in the United Kingdom and Europe during the 1970s and 1980s, with the aim of detecting unilateral amblyopia at a stage when treatment would be effective.[8–13]

Recent studies have raised concerns about the appropriateness of amblyopia as a target condition for early screening[14] and the possible adverse psychological impact of treatment weighed against the limited disability it causes.[15] A systematic review concluded that there was no robust evidence for the effectiveness of amblyopia treatment.[12] Our study arose out of the controversy generated by that review. We looked at the effectiveness of treatment by patching plus glasses or glasses alone compared with no treatment and explored the extent to which effectiveness varied with initial severity.

Methods

The study was a pragmatic, single blind, randomised controlled trial in eight UK children's eye clinics. It was designed to assess the benefits of current standard treatment of children who fail preschool vision screening tests.

Recruitment of participants—In all centres preschool vision testing was already conducted by community based orthoptists. Children were referred to dedicated recruitment clinics if, after two standard screening tests, they had 6/6 vision in one eye and 6/9 to 6/36 vision in the other. If the acuity findings were confirmed in the recruitment clinic, the child was eligible to join the trial. Consent was then requested from the carer by the trial centre ophthalmologist. If the ophthalmologist found any other ocular abnormalities the child was excluded from the trial.

Allocation to treatment—Once consent was obtained, the child was randomly allocated to a treatment group by the researchers phoning the trial centre, where allocation tickets, computer generated before the start of recruitment, were stored in numbered, sealed, opaque envelopes.

Treatment—After randomisation, all children were tested for refractive error with cycloplegic drops to eliminate artefact due to accommodation. Glasses were dispensed to children only in the full and glasses groups, who were then seen after six weeks to verify the

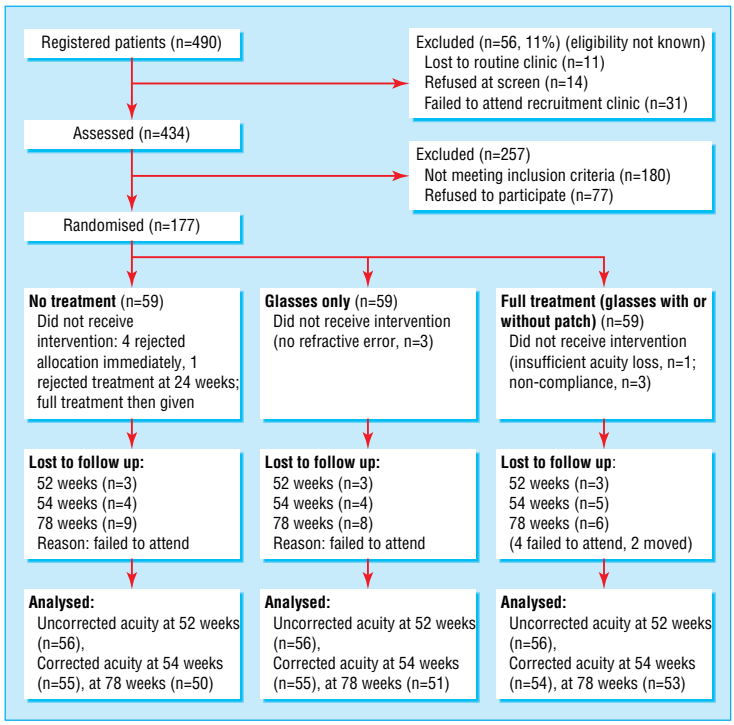

Fig 1 Participant flow through trial

glasses prescription. Children in the full treatment group then started to wear a patch if their corrected acuity remained reduced. They were reviewed every six weeks and managed by the treating orthoptist according to protocol. Children in the glasses group received no further treatment for 52 weeks. Children in the control group (no treatment) received no active treatment for 52 weeks. For those children receiving treatment, we assessed compliance using weekly parental diaries for the first 12 weeks of glasses wear and with daily diaries for the duration of patching treatment.

Measurements—A research orthoptist, who remained masked throughout to the child's treatment group, assessed vision at 24, 52, 54, and 78 weeks. At six months, if a child in the no treatment or glasses treatment groups developed manifest squint or acuity below 6/36 they were offered full treatment. After visual acuity testing at 52 weeks all children underwent refraction again and all, including the no treatment group, were prescribed glasses as required. They were then reviewed two weeks later, and best corrected visual acuity (with glasses) was measured in all three groups. Children in the no treatment and glasses treatment groups were then offered patching treatment as required. Six months later, 18 months after recruitment, we saw all the children once more and tested their best corrected (with glasses) visual acuity.

Analysis

Prestated outcome measures were uncorrected and corrected logMAR acuity, compared between the three groups at 52 and 54 week follow up. A planned subgroup analysis compared children whose acuity loss at recruitment was mild (6/12 to 6/9) with those whose acuity loss was moderate (6/36 to 6/18). LogMAR acuity was obtained with Glasgow acuity cards (marketed as LogMAR Crowded Test by Keeler, Windsor) and were used in preference to Snellen acuity values as logMAR is a continuous measure of acuity, more suited to statistical analysis.. Analysis was by intention to treat. The main planned analytical method was trend in analysis of variance between treatment groups with linear regression used to fit the interaction term for the initial acuity group.

Results

Recruitment to the trial opened in April 1999 and closed in December 2000; 12 month follow up closed in December 2001 and 18 month follow up in June 2002. We recruited and randomised 177 out of 254 eligible children. The parents of 77 children refused to participate. Participating children had a mean age of 48.1 (SD 5.0) months having been screened at a mean age of 45.6 (4.6) months. Sixty seven (38%) children were in the moderate category. The randomisation allocated 59 children to each group, with a reasonable distribution of acuity. Of the total, 173 (98%) had a significant refractive error, 127 (72%) of whom had anisometropia (significant difference in refractive error between the two eyes). Figure 1 shows the flow of participants through the trial. Compliance with glasses and with patching was reasonable. See bmj.com for more details. Follow up data at 52 weeks were available for 168 (95%) children and at 54 weeks for 164 (93%). Children in the full and glasses treatment groups had incrementally better uncorrected (without glasses) and corrected (with glasses) visual acuity at follow up compared with those in the no treatment group, but the overall treatment effect was small (table 1). The mean treatment effect between full and no treatment was equivalent to only one line on a Snellen chart (0.11 log units; 95% confidence interval 0.050 to 0.171; $P < 0.0001$).

The effect of full treatment was greater in the subgroup of children with moderate acuity loss at baseline; equivalent to one to two lines on a Snellen chart. Full treatment had no significant effect in the subgroup of children with mild acuity loss at baseline (table 2).

Table 1 Visual acuity after follow up to trial end point and six months after trial, by treatment group

	No treatment	Glasses		Full		
LogMAR acuity	Mean (SD) logMAR	Mean (SD) logMAR	Mean difference (95% CI) from no treatment	Mean (SD) logMAR	Mean difference (95% CI) from no treatment	P value for trend (ANOVA)
At trial end point						
Uncorrected acuity (n=168)	0.424 (0.24) (n=56)	0.381 (0.23) (n=56)	0.043 (–0.05 to 0.13)	0.336 (0.20) (n=56)	0.088 (0.01 to 0.17)	0.041
Best corrected acuity (n=164)	0.301 (0.20) (n=55)	0.216 (0.17) (n=55)	0.085 (0.02 to 0.15)	0.193 (0.12) (n=54)	0.109 (0.05 to 0.17)	0.001
Six months after trial end						
Best corrected acuity (n=154)	0.170 (0.15) (n=50)	0.197 (0.16) (n=51)	0.03 (–0.09 to 0.03)	0.170 (0.13) (n=53)	0.0004 (–0.06 to 0.05)	0.996

ANOVA=analysis of variance.

Table 2 Visual acuity after follow up to trial end point and six months after trial, by treatment group and initial acuity

	No treatment	Glasses		Full		
	Mean (SD) logMAR	Mean (SD) logMAR	Mean difference (95% CI) from no treatment	Mean (SD) logMAR	Mean difference (95% CI) from no treatment	P value for trend (ANOVA)
At end of trial						
Mild* acuity loss (n=101)	0.22 (0.17) (n=33)	0.16 (0.14) (n=35)	0.058 (–0.02 to 0.13)	0.18 (0.11) (n=33)	0.045 (–0.02 to 0.11)	0.11
Moderate† acuity loss (n=63)	0.42 (0.19) (n=22)	0.31 (0.17) (n=20)	0.112 (–0.002 to 0.23)	0.22 (0.13) (n=21)	0.203 (0.10 to 0.30)	0.0002
Six months after end of trial						
Mild* acuity loss (n=91)	0.13 (0.08) (n=28)	0.13 (0.12) (n=31)	0.00 (–0.06 to 0.05)	0.16 (0.12) (n=32)	–0.03 (–0.08 to 0.03)	0.327
Moderate† acuity loss (n=63)	0.22 (0.20) (n=22)	0.30 (0.18) (n=20)	–0.08 (–0.19 to 0.04)	0.19 (0.14) (n=21)	0.03 (–0.07 to 0.14)	0.575

*6/9 or 6/12 at presentation.
†6/18 to 6/36 at presentation.

After 54 week follow up, children in the no treatment and glasses treatment groups received treatment according to the protocol for the full treatment group. In the no treatment group, seven (13%) had normal acuity and received no treatment. Twenty four (44%) achieved normal acuity with glasses correction only, and 24 (44%) required patching in addition to glasses. In the glasses group, 20 (36%) needed treatment with patching. In addition, seven children in the full group required further treatment with patching at this point.

At 78 weeks' follow up, six months after the formal end point of the trial, 154 (87%) children attended and there was no significant difference in acuity between the three treatment groups (tables 1 and 2).

Discussion

Previous studies in humans and animals have claimed that amblyopia can, with good compliance, be improved with treatment.[16–19] However, it is not known what level of loss of acuity merits treatment as no previous study has included an untreated control group and many have excluded children with milder acuity loss. We also specifically evaluated the treatability of children identified by standard screening programmes.

Avoiding bias

Our trial was designed to minimise possible sources of bias. Allocation to treatment was managed centrally, outcomes were assessed masked, and different testing methods were used for the trial to reduce practice effects. It was not feasible to test all children with the same frequency as those in the full treatment group, so we cannot rule out the possibility that these children may have become generally more proficient at vision testing. The analysis was by intention to treat. The results of the trial should be generalisable to any centre treating children with unilateral visual impairment as we used standard screening criteria, recruited over two thirds of eligible children, and included a wide range of initial acuity levels. Although the age range in the trial was narrow, the effect of deferred treatment in the no treatment group indicates that these findings are also applicable to children identified at school entry.

Responses to treatment

The overall response to treatment was disappointing: an increase equivalent to one line on a Snellen chart. However, children with moderate initial acuity loss improved with full treatment from 6/18 or worse to a mean acuity close to 6/9, while those in the mild group were essentially unchanged. The benefit to acuity from 12 months of wearing glasses compared with no treatment suggests that the treatment effect from glasses alone is limited.[20] The most striking effect was the additive effect of patching in the moderate group.

As in all trials, there is the possibility that those left untreated may suffer, but the no treatment group in fact showed a tendency to spontaneous improvement. Currently, continual wearing of glasses is recommended until the age of 7, even if acuity improves to normal, to prevent the development of refractive amblyopia.[21] Results in the untreated group, however, suggest that the risk of subsequently developing amblyopia is slight.

In many districts without preschool screening children are not detected or treated until school entry, the age at which our untreated group completed the trial and were offered treatment. The post-trial follow up shows that deferring their treatment did not limit their potential for improvement and nearly halved the proportion of children needing patching at all. This is consistent with another study that showed that presenting acuity, rather than age, is the most important determinant of outcome.[6] The late results in the full group also suggest that the treatment effects persist well after most patching treatment has ceased.

Conclusions

Amblyopia and refractive error are common worldwide, and many countries have screening programmes to detect asymptomatic visual defects in children. Thus the implications of our findings are considerable and should provide helpful evidence for future service planning. Children with a moderate acuity loss of 6/18 or worse showed a clear cut response to treatment, which itself arguably justifies screening to identify and treat these children. In contrast, children with mild acuity loss, who represent over half those identified with unilateral acuity impairment at screening in this and other studies,[22] received little benefit from either treatment. This level of impairment, though often excluded from studies,[16 18] is still commonly treated in routine clinical practice. We argue that children with 6/9 in only one eye should no longer constitute screen failures and do not justify treatment, even with glasses.

Nearly 40% of the children referred for treatment by community orthoptists did not in fact have the target condition, and were excluded from our trial. This was despite two tests in the community and presumably reflects difficulties in testing preschool children. This, together with the good response seen in those whose treatment was deferred, supports the use of relatively later screening, as recently suggested.[23]

The members of the data monitoring committee are listed on bmj.com.

What is already known on this topic

Preschool vision screening aims to detect amblyopia at a stage when treatment is effective

Amblyopia has conventionally been treated with glasses, supplemented by patching of the better eye if necessary

Treated children tend to improve over time, but no study has included an untreated control group or compared outcomes for different levels of acuity at presentation

What this study adds

Treatment of children with considerably reduced acuity (6/18 and worse) can result in a mean acuity equivalent to 6/9 on the Snellen chart

Children with 6/9 or 6/12 initial acuity show little benefit from treatment

Children whose treatment is deferred from age 4 until age 5 have the same acuity after treatment, but fewer need patching treatment at all

Over a third of children thought to require treatment after repeat screening do not have acuity loss

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Randomised controlled trial of smoking cessation intervention after admission for coronary heart disease

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Abstract

Objective To determine whether a nurse led smoking cessation intervention affects smoking cessation rates in patients admitted for coronary heart disease.

Design Randomised controlled trial.

Setting Cardiac ward of a general hospital, Norway.

Participants 240 smokers aged under 76 years admitted for myocardial infarction, unstable angina, or cardiac bypass surgery. 118 were randomly assigned to the intervention and 122 to usual care (control group).

Intervention The intervention was based on a booklet and focused on fear arousal and prevention of relapses. The intervention was delivered by cardiac nurses without special training. The intervention was initiated in hospital, and the participants were contacted regularly for at least five months.

Main outcome measure Smoking cessation rates at 12 months determined by self report and biochemical verification.

Results 12 months after admission to hospital, 57% (n = 57/100) of patients in the intervention group and 37% (n = 44/118) in the control group had quit smoking (absolute risk reduction 20%, 95% confidence interval 6% to 33%). The number needed to treat to get one additional person who would quit was 5 (95% confidence interval, 3 to 16). Assuming all dropouts relapsed at 12 months, the smoking cessation rates were 50% in the intervention group and 37% in the control group (absolute risk reduction 13%, 0% to 26%).

Conclusion A smoking cessation programme delivered by cardiac nurses without special training, significantly reduced smoking rates in patients 12 months after admission to hospital for coronary heart disease.