

Amblyopia treatment outcomes after screening before or at age 3 years: follow up from randomised trial

C Williams, K Northstone, R A Harrad, J M Sparrow, I Harvey, ALSPAC Study Team



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Abstract

Objective To assess the effectiveness of early treatment for amblyopia in children.

Design Follow up of outcomes of treatment for amblyopia in a randomised controlled trial comparing intensive orthoptic screening at 8, 12, 18, 25, 31, and 37 months (intensive group) with orthoptic screening at 37 months only (control group).

Setting Avon, southwest England.

Participants 3490 children who were part of a birth cohort study.

Main outcome measures Prevalence of amblyopia and visual acuity of the worse seeing eye at 7.5 years of age.

Results Amblyopia at 7.5 years was less prevalent in the intensive group than in the control group (0.6% *v* 1.8%; $P=0.02$). Mean visual acuities in the worse seeing eye were better for children who had been treated for amblyopia in the intensive group than for similar children in the control group (0.15 *v* 0.26 LogMAR units; $P<0.001$). A higher proportion of the children who were treated for amblyopia had been seen in a hospital eye clinic before 3 years of age in the intensive group than in the control group (48% *v* 13%; $P=0.0002$).

Conclusions The intensive screening protocol was associated with better acuity in the amblyopic eye and a lower prevalence of amblyopia at 7.5 years of age, in comparison with screening at 37 months only. These data support the hypothesis that early treatment for amblyopia leads to a better outcome than later treatment and may act as a stimulus for research into feasible screening programmes.

Introduction

Preschool screening of vision is carried out to detect amblyopia (reduced visual acuity that is not instantly alleviated by wearing spectacles, in an otherwise apparently healthy eye). It is treated by long term wearing of spectacles when appropriate and by temporarily patching the better seeing eye. A recent systematic review discussed the poor clinical evidence base underpinning these programmes and emphasised the lack of evidence that treatment for amblyopia is better than placebo or that early treatment is more effective than later treatment.¹⁻⁴ We present the follow up results from a population based randomised controlled trial, which was nested within a birth cohort study.

Methods

Participants—The participants were part of the ongoing Avon longitudinal study of parents and children (ALSPAC).^{5,6} Further details are given on bmj.com. The nested randomised controlled trial reported here was open to all children in the cohort

born during the last six months of the study period. We excluded children whose parents had declined to continue with the study or had more than one participating child.

Routine services provided in the study area—One institution provides hospital eye services for all children in the study area. All children received the usual recommended surveillance by their general practitioners and health visitors and were offered screening for reduced visual acuity by a school nurse at school entry (4-5 years).

Randomisation, assignment, and masking—We allocated children into different arms of the study by a “pseudo-random” process according to the last digit in the day of the mother’s date of birth: 1, 3, and 5 for the intensive group, and 2 and 4 for the control group. The orthoptists carrying out the vision tests had no knowledge of the mothers’ dates of birth, the rules determining allocation into the different groups, or the screening history of the children.

Protocols—In the intensive group, children were invited to attend a research clinic at 8, 12, 18, 25, 31, and 37 months, where an orthoptist examined them and carried out a battery of tests appropriate to the age of the child (see bmj.com). The children in the control group were offered similar testing by an orthoptist at 37 months only. Any child failing the acuity test or cover test in either of the groups was referred to the hospital eye service.

Final assessment—We invited all children to a vision assessment at 7.5 years, including measurement of visual acuity both with and without a pinhole (with pinhole as a proxy for correction by spectacles). We sent out a questionnaire on family history and previous treatment with patching beforehand.

Statistical analysis—We analysed the data according to the principle of intention to treat. The outcomes were the prevalence of amblyopia and the visual acuity in the worse seeing eye for children after treatment with patching at 7.5 years. The visual acuity result used for each eye was the better of the results obtained with and without pinhole. We defined amblyopia in advance in two ways to allow comparisons with other studies: amblyopia A, where the interocular difference in acuity was 0.2 LogMAR (two lines on the chart) or more⁷; and amblyopia B, where the visual acuity in the amblyopic eye was worse than 0.3 LogMAR.⁸ We compared proportions with the χ^2 test or Fisher’s exact test. We analysed continuous data by using analysis of variance or multivariate analysis.

Results

Of the 3490 children in the trial, 1929 attended the final examination. Fifteen children had organic ocular pathology or were developmentally delayed and were excluded from further analysis, leaving 1914 children—1088/2029 (54%) of the intensive group and

Division of Child Health, University of Bristol, Bristol BSS 1TQ

C Williams
consultant ophthalmologist
K Northstone
research fellow in statistics

Bristol Eye Hospital, Lower Maudlin St, Bristol BS1 2LX

R A Harrad
consultant ophthalmologist
J M Sparrow
consultant ophthalmologist

School of Medicine, Health Policy and Practice, University of East Anglia, Norwich NR4 7TJ

I Harvey
professor of epidemiology and public health

Correspondence to: C Williams
Cathy.Williams@bristol.ac.uk

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826/1490 (55%) of the control group as originally randomised.

Prevalence of amblyopia at 7.5 years of age—Amblyopia was found less often at 7.5 years in the intensive group than in the control group. The prevalence of amblyopia A was 1.5% (95% confidence interval 0.9% to 2.4%) in the intensive group and 2.7% (1.8% to 4.0%) in the control group ($\chi^2=3.4$, $df=1$, $P=0.06$). The prevalence of amblyopia B was 0.6% (0.3% to 1.3%) in the intensive group and 1.8% (1.1% to 3.0%) in the control group ($\chi^2=5.6$, $df=1$, $P=0.02$).

Prevalence of residual amblyopia at 7.5 years after patching treatment—Residual amblyopia was more likely to be present despite previous treatment in the control group (10/40) than in the intensive group (3/40). The difference for amblyopia A was not significant (odds ratio 1.56, 95% confidence interval 0.62 to 3.92), but for amblyopia B the difference was more marked (4.11, 1.04 to 16.29).

Visual acuity in the worse seeing eye after patching treatment—Visual acuity in the worse seeing (amblyopic) eye was significantly better for treated children in the intensive group than for similar children in the control group: mean acuity 0.15 (95% confidence interval 0.085 to 0.215) compared with 0.26 (0.173 to 0.347). The corresponding acuities for children who had not had patching treatment were -0.02 (-0.024 to -0.016) and -0.01 (-0.016 to -0.004) in the two groups.

Age at first referral to hospital eye service—A higher proportion of children who received patching treatment were first seen in the hospital eye service before the age of 3 years in the intensive group (19/40) than in the control group (5/40) ($\chi^2=10.06$, $df=1$, $P=0.002$).

Adjustment for confounding variables—Birth weight, duration of breast feeding, maternal education, having a first degree relative with strabismus or amblyopia, sex, and use of a car were also associated with the outcome data (see bmj.com). Only maternal education remained significantly associated with the outcome in a multivariate analysis. Maternal education may be a proxy for socioeconomic status, which is associated with the likelihood of adherence to treatment for amblyopia in young children.⁹ Adjustment for maternal education within the multivariate model made little difference to the results: the adjusted mean acuities in the worse seeing eyes of children treated with patching were again 0.15 (0.083 to 0.217) in the intensive group and 0.26 (0.170 to 0.350) in the control group ($P<0.001$).

Discussion

The mechanisms underlying the improved results in the intensive group cannot be ascertained from this study. Potential explanations include greater effectiveness of treatment due to age dependent plasticity, referral at an earlier stage in the course of the visual defect, greater adherence to treatment, and perceptual learning due to repeated testing. More of the children who were given patches in the intensive group than in the control group had been seen in the hospital eye service when aged less than 37 months, but these referrals were made at a variety of ages (see bmj.com). The earlier report from the present study suggested that screening using only photorefractometry at the ages of 8, 12, 18, 25, or 31 months alone could have increased the yield of children with amblyopia compared with

What is already known on this topic

Observational studies have produced conflicting results about whether early treatment for amblyopia gives better results than later treatment

A recent systematic review highlighted the lack of high quality data available and recommended the cessation of preschool vision screening programmes

This has led to fierce debate and to confusion about the provision of vision screening services

What this study adds

Children treated for amblyopia are four times more likely to remain amblyopic if they were screened at 37 months only than if they were screened repeatedly between 8 and 37 months

Children screened early can see an average of one line more with their amblyopic eye after treatment than children screened at 37 months

Early treatment is more effective than later treatment for amblyopia, supporting the principle of preschool vision screening

the actual yield from the intensive programme, which used acuity and cover testing.¹⁰ The specificity of such an approach would have been poor initially but would have increased to over 95% when the children were aged 31 months and older; these data may help in the design of potentially feasible programmes.

A prospective UK cohort study found no difference in the prevalence of amblyopia between children who had been offered primary orthoptic screening at 3 years and children offered only surveillance by a health visitor.¹¹ The difference between the results of that study and those presented here may be due to differences in methods. Our study included screening offered before the age of 3 years, the groups were randomised, the outcome data were detailed and prospectively collected, and additional data were available to control for confounding variables.

The limitations of this study stem from the fact that it was opportunistic and designed to fit in with the ALSPAC study. The groups were unevenly sized for pragmatic reasons. Only approximately half the children were followed up, which may have biased the results, so caution must be exercised when interpreting these data. However, the effect of the intervention was undiminished when the results were adjusted for the only potential confounder detected after investigating several known and suspected factors. The bias towards more frequent breast feeding and fewer low birth-weight babies in those who attended the final assessment would be expected to improve the visual status in these children,^{12 13} whereas the greater likelihood of a family history of strabismus or eye problems would be expected to have a deleterious effect on their visual status,^{14 15} compared with the children who did not attend for follow up. The overall effect of these biases is uncertain, but there is no reason to assume that they would invalidate the study findings.

An important question is whether feasible programmes could deliver the same benefits as the intensive programme without repeated testing, which would be extremely expensive. Future research needs to investigate whether cost effective strategies can be designed that produce similar results. The data presented here support the hypothesis that treatment given for amblyopia is more effective if it starts as early as possible and may contribute to the debate on the management of amblyopia.

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Spiritual beliefs may affect outcome of bereavement: prospective study

Kiri Walsh, Michael King, Louise Jones, Adrian Tookman, Robert Blizard

Abstract

Objective To explore the relation between spiritual beliefs and resolution of bereavement.

Design Prospective cohort study of people about to be bereaved with follow up continuing for 14 months after the death.

Setting A Marie Curie centre for specialist palliative care in London.

Participants 135 relatives and close friends of patients admitted to the centre with terminal illness.

Main outcome measure Core bereavement items, a standardised measure of grief, measured 1, 9, and 14 months after the patients' death.

Results People reporting no spiritual belief had not resolved their grief by 14 months after the death. Participants with strong spiritual beliefs resolved their grief progressively over the same period. People with low levels of belief showed little change in the first nine months but thereafter resolved their grief. These differences approached significance in a repeated measures analysis of variance ($F=2.42$, $P=0.058$). Strength of spiritual belief remained an important predictor after the explanatory power of relevant confounding variables was controlled for. At 14 months the difference between the group with no

beliefs and the combined low and high belief groups was 7.30 (95% confidence interval 0.86 to 13.73) points on the core bereavement items scale. Adjusting for confounders in the final model reduced this difference to 4.64 (1.04 to 10.32) points.

Conclusion People who profess stronger spiritual beliefs seem to resolve their grief more rapidly and completely after the death of a close person than do people with no spiritual beliefs.

Introduction

Religious faith addresses the existential questions of life and death. Death of a close relative or companion is an extremely distressing experience, and grieving can take a long time. But little research on whether spiritual or religious beliefs alter the process of grief has been carried out. Studies of families coping with the death of a child^{1,2} and research into the adaptation of older people to widowhood³ suggest that religious belief affects the outcome of bereavement. Research is often retrospective, however, and causal connections are difficult to establish.¹ Furthermore, research has been hampered by a lack of standardised measures.

The development of valid and reliable measures of spiritual beliefs⁴ and of the process of bereavement⁵



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Department of Psychiatry and Behavioural Science, Royal Free Campus, Royal Free and University College Medical School, London NW3 2PF

Kiri Walsh
research fellow
Michael King
professor

Robert Blizard
medical statistician

Edenhall Marie Curie Centre, London NW3 5NS

Louise Jones
research physician in specialist palliative care

Adrian Tookman
consultant physician in specialist palliative care

Correspondence to: M King
m.king@rfc.ucl.ac.uk

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