CLINICAL SCIENCE

Long term visual outcome in amblyopia treatment

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Aim: To evaluate long term visual outcome of treatment for amblyopia.
Methods: In a previous study, 44 children with unilateral amblyopia caused by strabismus or anisometropia were enrolled in a prospective study investigating the results of treatment. All children were regularly examined up to at least 8 years of age and outcome was evaluated. All subjects were invited to a re-examination and in total 26 subjects attended. Two of these were excluded because of insufficient records. The final sample consists of 24 subjects. Mean follow up time was 10.4 (SD 1.9) years.
Results: For the amblyopic eyes, 17% deteriorated in visual acuity, 50% were stable, and 33% gained in visual acuity. For the non-amblyopic eyes, 8% lost one line in visual acuity, 38% were stable, and 54% gained in visual acuity. No eye in any subject shifted more than 0.2 logMAR units. The increase in visual acuity for the non-amblyopic eyes was significant, while the increase for the amblyopic eyes was not. All straight eyed anisometropic amblyopes showed a distinct decrease in magnitude of anisometropia.
Conclusions: Visual acuity was essentially stable in the amblyopic eyes 10 years after cessation of treatment in the studied population.

Since the report "Preschool vision screening" by Snowdon and Stewart-Brown[1] was published in 1997 there has been an intense debate concerning almost every aspect of amblyopia and its treatment. Snowdon and Stewart-Brown pointed out several serious problems in research on amblyopia and related conditions (refractive error and non-cosmetically obvious squint), and concluded that there is no real evidence for the benefit of preschool vision screening.

Quite a number of studies have been initiated in order to find answers to these uncertainties. One of the major problems addressed in the report is the lack of evidence that treatment for amblyopia is effective. Since we do not know the natural history of amblyopia and since no placebo studies have been undertaken, there is scarce scientific evidence for the benefit of amblyopia treatment.

Even if not scientifically proved, occlusion of the better eye is the most prevalent therapy for amblyopia. Most clinicians are convinced that occlusion therapy really is effective. Unfortunately, the extent to which the assumed improvements of this therapy are maintained is insufficiently explored, a fact to which Snowdon and Stewart-Brown[1] also call attention. Only a small number of previous studies exist on the durability of the results of amblyopia treatment. Knowledge about the development of visual acuity several years after cessation of treatment is consequently limited.

The aim of this study was to evaluate long term visual outcome of treatment for amblyopia in a well controlled group. Or as LaRoche[2] aptly puts it in his survey on the literature on amblyopia in 2001: "Are the short-term results of amblyopia treatment making a tangible long-term difference to adult populations?"

MATERIALS AND METHODS

Between 1983 and 1987, 44 children (22 girls and 22 boys) diagnosed as amblyopic at the paediatric ophthalmology unit of Östra Hospital, Göteborg, Sweden were enrolled in a prospective study of the results of treatment. Inclusion criteria consisted of previously untreated unilateral amblyopia due to strabismus (n = 27) or anisometropia (n = 17), persisting after 8 weeks of spectacle wear if optical correction was needed. Amblyopia was defined as an interocular difference in visual acuity of at least two lines. Subjects with large angle strabismus, microstrabismus, or strabismus in combination with anisometropia were all classified as strabismic. Anisometropia was defined as the difference of 1 dioptre or more in any symmetrical meridian All children were regularly examined up to at least 8 years of age and outcome was evaluated.[3] At age approximately 8 years, visual acuity was assessed in all subjects according to a protocol. The children were born between 1976 and 1984.

In 2000 and 2001, all subjects were invited to a re-examination at the eye clinic at Sahlgrenska University Hospital/Mölndal, Sweden. Participation was voluntary and informed consent was obtained from all subjects participating. The study was approved by the local committee of medical ethics.

In total, 26 subjects (14 male and 12 female) accepted re-examination. Two of these were excluded because of insufficient information about visual acuity at termination of treatment in childhood. The final sample thus consisted of 24 subjects (13 male and 11 female); 11 of these were anisometropic amblyopes and 13 were strabismic amblyopes. One of the anisometropic amblyopes was classified as non-compliant in the previous report. Mean follow up time was 10.4 (SD 1.9) years. Mean age at follow up was 19.2 (1.6) years.

One of the anisometropic amblyopes had a very severe anisometropia and had gained 14 D of myopia since treatment was terminated (from −6D to −20D). Unfortunately, this subject discontinued follow up examinations at the eye clinic, thus we do not know the nature of the condition. However, such severe myopia very likely has an organic cause, and therefore this individual is excluded from calculations on alteration of anisometropia.

Examination

Visual acuity (VA) was assessed monocularly with the Hedin letter test[4] at 4 metres. The chart used was the very same as in the examinations at 8 years of age. For a majority of the subjects, visual acuity was even assessed by the same nurse as during childhood. The examiner did not know the results from previous testing at the time of the test. If visual acuity was less

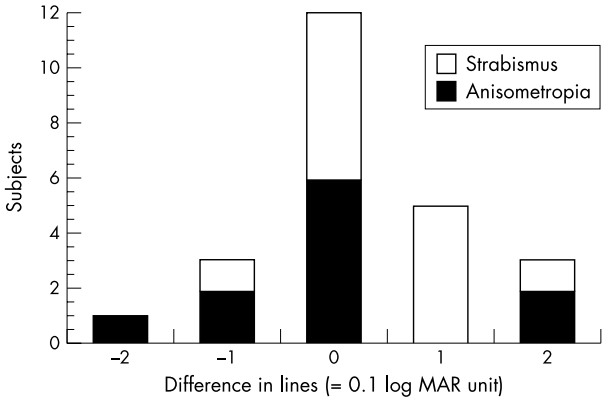

Figure 1 Changes in visual acuity since cessation of treatment for the amblyopic eyes. One line = 0.1 logMAR unit.

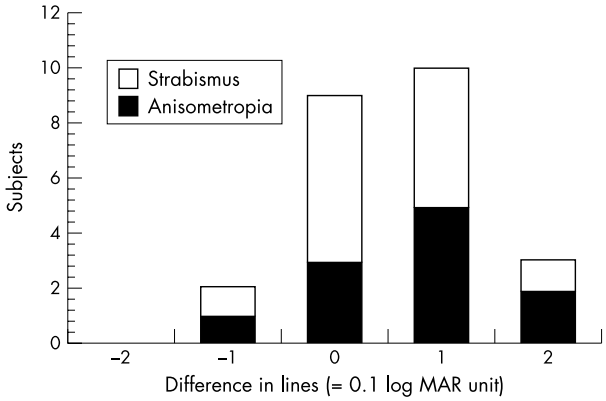

Figure 2 Changes in visual acuity since cessation of treatment for the non-amblyopic eyes. One line = 0.1 logMAR unit.

than 0.25, chart distance was reduced to 2 metres. Passing criterion was 75%. The visual acuity values were recalculated to logMAR units. "One line" refer to 0.1 logMAR unit.

Near visual acuity was examined with the Haase C-test, 2.6 seconds of arc, at 40 cm. A maximum of three errors was accepted per line.

Binocularity and stereopsis were tested with Bagolini glasses, the TNO stereo test, and the Lang II stereo card.

Alignment and motility were examined with the cover test and prism test at near and far. Finally, retinoscopy was performed in tropicamide cycloplegia.

A brief anamnesis of possible treatments after the last control at the paediatric ophthalmology clinic was also taken.

Statistics

The Wilcoxon signed rank test was used for statistical evaluation.

RESULTS

No subject had undergone any surgical or other ophthalmological treatment (except change of prescription glasses) since termination of treatment.

All numbers refer to best correctable visual acuity. Results for near visual acuity will be presented elsewhere.

Amblyopic eye

Four eyes (17%) deteriorated in visual acuity, 12 (50%) were stable, and eight (33%) gained one or two lines of visual acuity (Fig 1). Only one subject lost more than one line of visual acuity. In previous parts of the study this subject was classified as non-compliant. There was no significant increase in visual acuity among the anisometropic subjects (p=0.88), while the increase among strabismic subjects was close to significant (p=0.083).

Non-amblyopic eye

Two eyes (8%) lost one line of visual acuity, nine (38%) were stable, and 13 (54%) gained in visual acuity (Fig 2).

Mean visual acuity was calculated using logMAR scores, according to recommendations.[5] Both the amblyopic and the non-amblyopic eye gained in visual acuity (Fig 3). The increases for the non-amblyopic eyes are statistically significant (p=0.0022), while those for the amblyopic eyes are not (p=0.18).

Strabismic subjects

In no subject had the clinical strabismic state changed significantly since termination of amblyopia treatment.

Anisometropic subjects

There were 11 straight eyed anisometropic amblyopes, and four out of the 13 strabismic amblyopes had additional

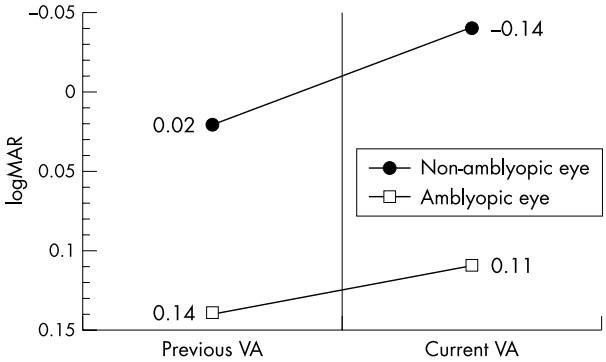

Figure 3 Mean visual acuity at end of treatment and at current follow up. 0.14 logMAR = 0.72 decimal, 0.11 = 0.78, 0.02 = 0.95, –0.04 = 1.10

anisometropia at the time of inclusion. One of the straight eyed anisometropes was excluded from further calculations because of severe myopia. The remaining 10 straight eyed anisometropic amblyopes all showed a distinct decrease in magnitude of anisometropia, while the decrease for the four strabismic anisometropic amblyopes not was as substantial (Table 1).

DISCUSSION

For the amblyopic eyes, 17% deteriorated in visual acuity, 50% were stable and 33% gained in visual acuity. No subject lost more than two lines of visual acuity and only one subject lost two lines. Previous authors report different results (Table 2). Our findings are in concordance with those of Ching *et al*,[6] Scott *et al*,[7] and Leiba *et al*,[8] who also found that visual acuity is generally stable after cessation of treatment. Others report the opposite, stating that the majority of amblyopic eyes deteriorate in visual acuity after cessation of treatment,[9–11] and some maintain that only about half deteriorate.[12–14] It should be noted that previous authors either report results in Snellen lines (as opposed to logMAR lines), or have not stated the definition of "one line."

Previous studies on natural history of untreated amblyopia have shown that the VA of the amblyopic eye deteriorates during childhood[15] as well as during adolescence.[16] The stability of visual acuity found in our sample is interesting and encouraging. It is notable that the one subject who lost more than one line was non-compliant during treatment. Theoretically, successful treatment could lead to a "normalisation" of the use and thus development of the amblyopic eye. Most of the previous studies also deal with successfully treated amblyopes.

Depth of amblyopia has been suggested to influence outcome of treatment,[17] with mild amblyopia being more

Table 1 Decrease in anisometropia (spherical equivalent) in anisometropic subjects

	Anisometropia (D)	Mean age
A Staight eyed anisometropic amblyopes (n=10)		
Treatment onset	2.16 (1.27)	4 years 0.5 months
Conclusion	1.38 (1.32)	8 years
Long term follow up	0.75 (0.87)	19 years 8 months
B Strabismic anisomteropic amblyopes (n=4)		
Treatment onset	0.97 (0.16)	4 years
Conclusion	0.94 (0.79)	8 years 6 months
Long term follow up	0.50 (0.41)	18 years 9 months

A = straight eyed anisometropic amblyopes (n=10). B = strabismic anisometropic amblyopes (n=4).

Table 2 Previous works on development of visual acuity in treated amblyopic eyes

						Deterioration	
Author	Follow up time	Age at follow up	Sample size	Improvement	Stable	1–2 lines	>2 lines
Gregersen *et al* (1965)[9]	"10 years"	16.9 years	53	–	24%	53%	23%
Leydhecker *et al* (1967)[10]	"8–10 years"	–	22	–	5%	95%	–
Malik *et al* (1975)[13]	21.4 months	13.4 years	50	–	46%	24%	30%
Schröpfer *et al* (1975)[11]	"7–10 years"	–	100	–	12%	88%	–
Sparrow *et al* (1977)[14]	5.4 (1.8) years	–	30	–	66%	28%	7%
Ching *et al* (1986)[6]	"5 years"	14 years	23	–	78%	22%	–
Scott *et al* (1988)[7]	–	15.9 years	89	0%	75%	17%	8%
Levartovsky *et al* (1995)[12]	6.4 (1.8) years	13.8 (2.4) years	94	–	47%	53%	–
Leiba *et al* (2001)[8]	21.5 (2.1) years	29.0 (2.1) years	54	17%	50%	33%	–
Present study	10.4 (1.9) years	19.2 (1.6) years	24	33%	50%	17%	0%

– = not stated

stable. In our sample, 17 (71%) subjects had VA = 0.3 at the beginning of treatment.

Levartovsky *et al*[17] found that strabismic amblyopia is more prone to deterioration than anisometropic amblyopia, but in our study we found the opposite.

Age at cessation of treatment might be of importance for future stability of the result. Our subjects were all followed to at least 8 years of age, and maintenance therapy was initiated if deterioration was more than or equal to 0.2 logMAR. None of the anisometropic subjects out of the original sample required maintenance therapy, while six strabismic amblyopes did require it (unpublished data). Three of these subjects are included in the present follow up, and all were stable or had gained in visual acuity in the amblyopic eyes. Levartovsky[17] found that deterioration was more pronounced in subjects who had not been monitored to age 9 years of age. Keech *et al*[18] studied the upper age limit for development of amblyopia and found that no subject developed amblyopia after age 6 years. One could consequently suggest that the risk for deterioration in an amblyopic eye is less likely after 6 years of age. In the paper "When is it safe to stop patching?" Oster *et al*[19] suggest that patching can be discontinued after the third birthday, but they also found that patients who did not need maintenance therapy were older at end of treatment (mean 40 months). Ching *et al*[6] found that 52% of successfully treated children needed maintenance therapy. Age at cessation of treatment was about 3.5 years in that study.

For the non-amblyopic eye, there was a mean gain in visual acuity of 0.06 logMAR. This change was statistically significant. To our knowledge, no previous study has reported results for development of visual acuity of the fellow non-amblyopic eyes. The development of visual acuity has been suggested to peak in the mid-twenties,[20] and the non-amblyopic eyes seem to follow this normal development, which is interesting since the non-amblyopic fellow eye has previously been shown to have subnormal visual performance.[21]

The reported test-retest variability in measurements of visual acuity varies between authors. Test-retest variability has been reported to be as low as 0.10 (0.09) (decimal notation)[20] and as high as plus or minus 0.24 logMAR.[22] Other authors report numbers in between.[23–25] The magnitude of the measurement error is probably due largely to changes of visual chart and examiner. In the present study both the visual chart and the examiner (for most subjects) was the very same at cessation of treatment and at current examination.

The straight eyed anisometropic amblyopes in our study showed a pronounced decrease in anisometropia with increasing age, as previously shown by several authors. Abrahamsson *et al*[26] and Almeder *et al*[27] both found that in a majority of subjects, anisometropia disappears over time. Considering anisometropic subjects with concurrent strabismus, the decrease of anisometropia was less marked. This is in concordance with Lepard[28] and Abrahamsson *et al*,[29] who both report that in strabismic amblyopes, the fixating, non-amblyopic eye emmetropises, while the deviating eye fails to emmetropise and thus remains more hyperopic.

The fact that 45% (20/44) out of the original sample are not included in the analysis needs to be addressed. Out of these 20, 18 did not attend the re-test and two were excluded due to loss of protocols for visual acuity at age 8 years. The reason for non-attendance is unclear, but it is likely that several of the subjects were unable to participate owing to temporary residence elsewhere for higher education or national service. The depth of amblyopia do not differ at treatment onset from those subjects participating. In nine of the cases the exit protocol is missing, but for the remaining 11 the visual acuity at age 8 years is similar to that of the subjects attending.

In conclusion, our results suggest that visual acuity is stable in the amblyopic eye 10 years after cessation of treatment. Together with other results showing that visual acuity is stable more than 20 years after cessation of treatment,[8] this is good news. It must be judged as very unlikely that deterioration would be initiated after such a long period of time. It seems like successful amblyopia therapy results in a lasting improvement in visual acuity, and that the short term results of amblyopia treatment really are making a tangible long term difference to adult populations.

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