

Untreated essential infantile esotropia: factors affecting the development of amblyopia

Abstract

Purpose A concomitant esotropia, presenting within the first 6 months of life, associated with a high incidence of dissociated vertical deviation, manifest latent nystagmus and asymmetric optokinetic nystagmus is termed essential infantile esotropia. Most studies concern patients diagnosed in infancy and treated throughout childhood. This paper addresses the factors that may influence the development of amblyopia in patients who remain untreated until visual adulthood.

Methods During a 3 year period 113 patients aged 8 years or more with a history of esotropia occurring within the first 6 months of life were examined for the study. All patients underwent full ocular motility assessment and cycloplegic refraction, and only those with one or more signs of essential infantile esotropia were included.

Results Of the 113 patients, 16 (14.3%) had a difference of 2 or more lines in the visual acuity of the two eyes and were diagnosed as having amblyopia. Anisometropia was present in 10 of the 16 (62.5%). The correlation between anisometropia and amblyopia was statistically significant ($p = 0.0001$).

Conclusions Amblyopia following early surgical intervention in essential infantile esotropia is well documented, but the risk is outweighed by the chance of obtaining some form of binocular vision. However, where access to ongoing therapy is not available, patients with essential infantile esotropia, free alternation and no anisometropia have a significant chance of retaining good visual acuity in both eyes if surgery is delayed until visual adulthood.

Key words Alternation, Amblyopia, Anisometropia, Infantile esotropia, Untreated

A concomitant esotropia presenting within the first 6 months of life, which is associated with monocular optokinetic (OKN) asymmetry and a high incidence of manifest latent nystagmus

(MLN), has been described as the infantile (congenital) esotropia syndrome.¹ The association of early-onset esotropia with dissociated vertical deviation (DVD) and MLN is well recognised.²⁻⁶ Ciancia² first described the association of infantile esotropia, horizontal jerking nystagmus and a compensatory face-turn to adduct the fixing eye. The term essential infantile esotropia is used when esotropia occurs in conjunction with one or more signs of asymmetric OKN, DVD or MLN.⁷

Most studies of early-onset esotropia have concerned patients diagnosed in infancy and treated within the development period. Therefore the natural history of the condition has been obscured by the effect of the therapy, which is designed to eliminate amblyopia and surgically re-align the visual axes in order to facilitate the development of binocular vision.

The presence of amblyopia in infants and young children with infantile esotropia is well documented.⁸⁻¹⁰ In 1984 Hoyt and co-workers¹¹ reported that in a group of 31 patients with early-onset esotropia only 4 were found to have amblyopia before operation, but 19 developed amblyopia within a year of surgery. Similarly, Harcourt and co-workers⁵ found that in a group of 35 patients who had alternating esotropia without fixation preference before operation, only 5 had continued to alternate after surgery. They noted that in the post-operative cases without amblyopia there was a considerable residual angle of convergent strabismus, and suggested that the decrease in the angle following surgery obviates the necessity for cross-fixation so fixation preference occurs. Therefore it should not be assumed that if spontaneous alternation was present prior to surgery, it would necessarily persist post-operatively.

Recent studies have suggested that there is a low incidence of amblyopia in patients from developing countries who remain untreated until they reach visual adulthood.¹²⁻¹⁶ This study addresses the factors that may have

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influenced the development of amblyopia in a group of visual adults with untreated essential infantile esotropia.

Materials and methods

All patients aged 8 years or more who attended Grootte Schuur Hospital, Cape Town or St John's Eye Hospital, Johannesburg between November 1986 and October 1989 with a history of concomitant esotropia present before the age of 6 months, with no neurological deficit, and who had had no previous ophthalmic examination were documented for the study. Patients fulfilling these criteria, who attended the mobile eye unit for examination during a tour of the Bureau for the Prevention of Blindness in October 1989 were also included. All patients underwent a full ophthalmological examination with special emphasis on the ocular motility assessment, cycloplegic refraction and fundus examination. Whenever possible, patients were evaluated by two orthoptists or an orthoptist and ophthalmologist, and periodic random sampling was undertaken to ensure continuity of test standards.

Of 142 patients examined, 113 fulfilled the inclusion criteria. Their ages ranged from 8 to 38 years.

Visual acuity was tested monocularly using a Snellen chart at 6 m, and these results were masked from the examiners carrying out the ocular motility assessment. Any anomaly of head posture was noted, particularly if it related to an attempt to cross-fixate or to fixate in adduction. A cover test was performed at 6 m, in the nine cardinal positions of gaze, and at 33 cm in the primary position.

Particular attention was paid to fixation preference, and the presence of DVD, MLN and 'A' and 'V' patterns. Patients were said to have no fixation preference if there was spontaneous alternation in the primary position, or if they were able to fix and hold fixation with either eye through several blinks, and continued to maintain fixation through other visual tasks. Ocular movements were assessed and over- and underactions of the muscles quantified on a scale of 1 to 4.

The presence of microneystagmus was tested monocularly using an ophthalmoscope.

The deviation was measured by prism and cover test at 6 m, in the cardinal positions of gaze, and in the primary position at 33 cm. The diagnosis of an 'A' pattern was made if there was a difference of 10 prism dioptres (PD) or more between the prism cover test deviation on up- and downgaze, and a 'V' pattern if there was a difference of 15 PD or more between elevation and depression.

OKN was tested monocularly with a hand-held drum rotated at 20 cycles per minute at a distance of 30 cm from the patient.

Amblyopia was defined as a difference of 2 or more lines in the visual acuity between the two eyes. Normal visual acuity was taken as 6/6 and patients achieving 6/6 or better with their non-preferred eye were not considered to be amblyopic, even if there was a difference between the acuities of the two eyes.

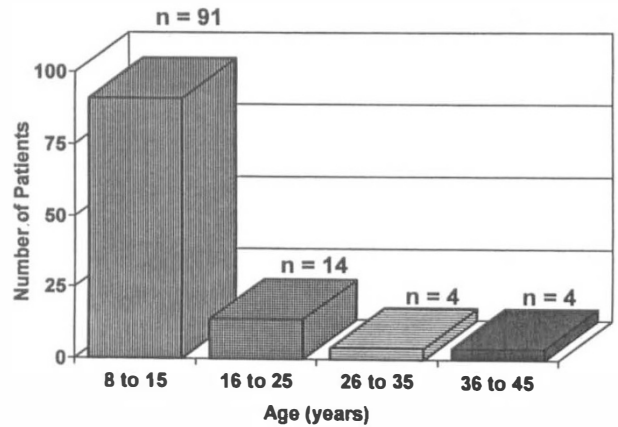


Fig. 1. Age at presentation.

Anisometropia was regarded as being present if there was a difference of more than 1 dioptre between the spherical equivalents of the two eyes.

Results

The age range at time of presentation was from 8 to 38 years (Fig. 1).

Asymmetric OKN was present in 97 patients (86%), MLN in 90 (80%) and DVD in 68 (60%). In 4 patients DVD not detected before surgery was noted post-operatively. The number of patients with each feature and combinations of these features is shown in Fig. 2.

Odds ratios indicated that those with DVD were 1.55 times more likely to have MLN than those without DVD, those with DVD were 2.14 times more likely to have OKN asymmetry than those without DVD, and those with MLN were 2.83 times more likely to have OKN asymmetry than those without MLN. However, the associations between the presence of DVD and MLN ($\chi^2 = 0.89$, d.f. = 1, $p = 0.3468$), between the presence of DVD and OKN asymmetry ($\chi^2 = 1.6$, d.f. = 1, $p = 0.2063$), and between the presence of MLN and OKN asymmetry ($\chi^2 = 3.38$ d.f. = 1, $p = 0.066$), were not statistically significant.

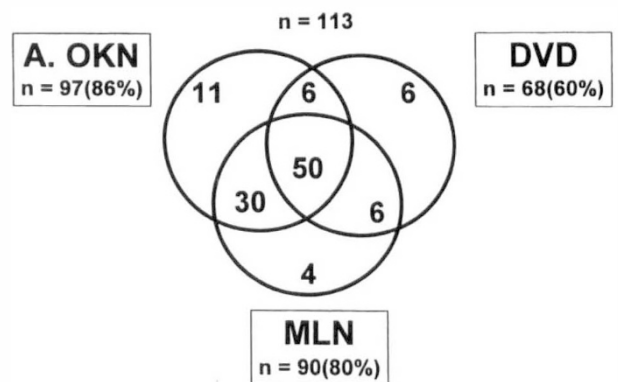


Fig. 2. The number of patients with asymmetric optokinetic nystagmus (A. OKN), manifest latent nystagmus (MLN), dissociated vertical deviation (DVD), and combinations of these features.

Table 1. Angle of deviation in alternators and non-alternators

Angle of deviation (PD)	Alternators	Non-alternators
50+	35	25
36-50	12	14
20-35	6	13
<20	3	5
Total	56	57

PD, Prism dioptres.

Fifty-seven patients (50.4%) had definite fixation preference and no alternation, and 56 (49.6%) were judged to have free alternation and no preference for fixation.

Of the 113 patients 36 (32%) had a difference of one line or more in the visual acuity of the two eyes. Twenty of the 36 (17.7%) had a difference of only one line and 16 (14.3%) showed a difference of 2 or more lines and were diagnosed as having clinically significant amblyopia. Anisometropia was present in 10 of the 16 (62.5%).

The associations between presence of alternation and absence of amblyopia ($f = 0.41$, $\chi^2 = 18.7$, d.f. = 1, $p = 0.0004$) and between anisometropia and amblyopia ($f = 0.38$, $\chi^2 = 16.2$, d.f. = 1, $p = 0.0001$) were statistically significant. Odds ratio showed that those with amblyopia were 8.3 times more likely to have anisometropia than those without amblyopia.

The mean angle of deviation was 49 prism dioptres with a range from 4 to 90 and a standard deviation of 18.5. The size of the deviation in patients with persistence of alternation was greater than in those with unocular fixation preference. Thirty-five of the 56 patients (62.5%) with continuance of alternation had an angle of deviation >50 PD, compared with 25 of the 57 (43%) with fixation preference (Table 1). The mean angle of the alternators was 53 PD, whereas that of the non-alternators was 45 PD. An unpaired *t*-test revealed this to be a moderate difference (effect size = 0.4, $t = 2.371$, d.f. = 111, $p = 0.0195$).

Twenty-five patients (22.2%) had no horizontal incomitance in the vertical meridian, 72 had an 'A' pattern (63.7%) and 16 (14.1%) were diagnosed as having a 'V' pattern. The association between the presence of an 'A' and 'V' pattern and the presence of clinical amblyopia ($\chi^2 = 2.5$, d.f. = 1, $p = 0.1153$) was not statistically significant.

No patient was found to utilise an abnormal head posture in order to cross-fixate in adduction.

Table 2 presents cross-tabulations of patients on the following variables: presence of amblyopia and persistence of alternation, anisometropia and presence of an 'A' or 'V' pattern.

Table 2. Cross-tabulation of variables

	Alternation		Anisometropia		'A' or 'V' pattern	
	Yes	No	Yes	No	Yes	No
Amblyopia	0	16	10	6	10	6
No amblyopia	56	41	16	81	78	19

Discussion

Early-onset non-accommodative esotropia with one or more of the features of essential infantile esotropia is well documented.^{1-7,9} The finding of monocular OKN asymmetry in an esotropic patient implies an 85% chance that the onset of esotropia occurred in the first 6 months of life.¹⁷ Asymmetric OKN occurred in 97 of our 113 patients (85.8%).

Most clinical studies of infantile esotropia concern patients who have been observed throughout their childhood, and where surgical correction of the strabismus has been undertaken in infancy.^{7,8,10,19-25} The incidence of amblyopia is variously reported as being between 30% and 75%. Some authors specify the incidence of amblyopia prior to surgery, those who required occlusion therapy, and the number who remained amblyopic despite treatment, and indicate that in infantile esotropia occlusion for post-operative amblyopia is a therapeutic necessity.^{11,20-25} Hiles and co-workers¹⁰ state that 75% of patients with infantile esotropia will require occlusion post-operatively, whilst Leffler and co-workers²⁶ found no increased risk of amblyopia developing post-operatively but do not mention whether their patients required occlusion following surgery. Harcourt and co-workers⁵ and Hoyt and co-workers¹¹ report that amblyopia is more likely to occur after surgery. This premise has been supported by studies of adult untreated groups.^{12,14-16}

In this series of visual adult patients with untreated essential infantile esotropia, the diagnosis of amblyopia was made on the basis of Snellen acuity. This was compared with the patient's performance on fixation preference as assessed during normal viewing in the primary position and on the cover/uncover test, since this would be the most commonly used test for assessing the visual performance of pre-verbal infants.²⁷

Accurate observation of the point at which alternation occurs in cross-fixating infants will reveal that a significant number of apparently cross-fixating children will in fact have amblyopia. Dickey and co-workers²⁸ confirmed mild to moderate amblyopia with Teller card acuities in patients where alternation of fixation did not occur at the midline. However, this does not apply to our untreated visual adult group, as there were no patients who adopted a face-turn to facilitate fixation in adduction. In our series there was a statistically significant correlation between alternation and absence of amblyopia ($p = 0.0001$).

Fixation preference testing is a reliable method of diagnosing amblyopia in patients with 3 lines or more of difference in the visual acuity.²⁹ However, fixation preference testing alone is likely to overestimate the incidence of amblyopia, and patients with less than 2 lines of difference between the visual acuity of the two eyes may demonstrate fixation preference in the absence of amblyopia.³⁰ Fixation preference testing appears to be more accurate than forced choice preferential looking

techniques, which underestimate amblyopia in the strabismic infant,^{31,32} and visually evoked potential studies, which tend to be too sensitive.¹¹

In this study 85.7% of the untreated visual adults with essential infantile esotropia did not demonstrate amblyopia. Therefore, the factors influencing the development of amblyopia in the 14.3% who did develop a visual defect in one eye warrant careful consideration, particularly as these findings must affect the management of patients who do not have access to ongoing treatment throughout childhood.

An explanation for the low incidence of amblyopia (14.3%) in this group of untreated essential infantile esotropes may be the persistence of a large deviation (mean 49 PD) in the absence of any other reason for developing a fixation preference.^{13,33}

This study suggests that there is a reduced tendency to develop fixation preference when there is a gross deviation, as 62.5% of the patients who continued to demonstrate alternation had a deviation of >50 PD, compared with only 43% of the non-alternators. Similarly only 16.5% of the alternators had deviations of <35 PD, whilst 31.5% of the patients with fixation preference had a deviation of <35 PD. In a retrospective study Page and co-workers²³ found no difference in the incidence of amblyopia between patients with a final post-operative deviation of more than 5° and those with a smaller deviation. However, none of the reported cases had final deviations in excess of 14°. In our series, patients with a larger deviation demonstrated an increased frequency of alternation that was statistically significant ($p = 0.0195$). The incidence of amblyopia (14.3%) in this group correlates closely with the incidence of 15% in a similar group of untreated infantile esotropes.¹⁶

There have been other possible explanations for the lack of amblyopia in untreated visual adults. Good and co-workers¹⁶ have suggested that the presence of persistent cross-fixation acts as part-time occlusion therapy, as the abducting eye receives intermittent stimulation when it is used for fixation on side gaze, because the vision of the preferred adducting eye is obscured by the nose. On the other hand Dickey and co-workers⁸ found that approximately half of a group of cross-fixating infants with early-onset esotropia had amblyopia. However, 57 (50.4%) of the patients in our series had a definite fixation preference without cross-fixation, and yet only 16 had significant amblyopia. The age at which fixation preference occurs, the factors that affect its development and its relationship to amblyopia are not well defined.⁷ Fixation preference may develop before clinically detectable amblyopia.^{31,32}

The association between anisometropia and amblyopia was first described by Lagleyze,³⁴ who in his analysis of a group of squinting patients found amblyopia in 79.5% of those with pronounced anisometropia. In our study of untreated essential infantile esotropia, anisometropia appears to have influenced the choice of eye used for fixation, or forced an eye preference. Ten of 16 patients (62.5%) with amblyopia had 1 dioptre or more of anisometropia. In 3

patients an astigmatic error was present, which did not manifest as a significant difference in the spherical equivalent of the 2 eyes. The relationship between the presence of anisometropia of more than 1 dioptre in any meridian and the incidence of amblyopia was statistically significant ($p = 0.0001$), and supports the finding of other reports.^{16,35} In our cases the degree of anisometropia did not affect the depth of the amblyopia. While two other studies reported similar findings,^{36,37} a recently proposed index of anisometropia suggested that these factors may be correlated.³⁸

The close correlation between anisometropia and amblyopia in our group emphasises that the examination of the infant or child must include an accurate cycloplegic refraction to determine those patients with essential infantile esotropia who are at risk for amblyopia. However, factors other than anisometropia must influence the development of amblyopia in some cases, as 6 of the patients with amblyopia in our study did not have anisometropia.

A close correlation between amblyopia and asymmetric inferior oblique overaction has been reported.³⁹ In their group of patients with infantile esotropia the authors do not differentiate between cases where the upshoot in adduction may be attributable in part to DVD, and those where there is inferior oblique overactivity and a 'V' pattern. No patient in our series had unilateral inferior oblique overaction and there was a low prevalence of bilateral inferior oblique overaction, with a 'V' pattern in only 14.8% of cases. An 'A' pattern was present in 63.7% of cases.⁴⁰ The correlation between the presence of an 'A' or 'V' pattern and clinical amblyopia was not statistically significant ($p = 0.1153$).

The fact that there is a decreased tendency to amblyopia in patients with untreated essential infantile esotropia is of particular relevance in considering the management of patients where continuity of treatment is in doubt. Not all patients with early-onset esotropia have essential infantile esotropia and if untreated may be at greater risk of developing amblyopia.^{13,23} Whilst bifoveal fusion as the outcome of surgical re-alignment has been infrequently reported,⁴¹⁻⁴⁵ there is evidence that appropriate surgery before the age of 2 years results in an increased incidence of some form of binocularity and is the treatment of choice.^{7,18,20,21,46,47} However, visual adults with untreated infantile esotropia have a poor chance of developing binocular vision after late surgical re-alignment, although some are reported to achieve fusion.^{9,48,49}

The European multi-centre study of early and late surgery for infantile esotropia may in time answer some of these questions.^{50,51}

Conclusions

This study shows that there is a significant correlation between the presence of anisometropia and amblyopia, and between the persistence of alternation and a large angle esotropia. This would suggest that in the absence of anisometropia, it is the presence of a large convergent

deviation that stimulates the continuation of alternation and prevents the development of amblyopia. The implication for the treatment of essential infantile esotropia in developing countries is important. Patients identified in infancy with a large esotropia, free alternation in the primary position, no anisometropia, and at least one sign suggesting the diagnosis of essential infantile esotropia, have a significant chance of retaining good visual acuity in both eyes if surgery is delayed until after the patient attains visual adulthood. Whether late surgical alignment can produce functional binocularity in this group of patients is not known.

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