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Title page

Presenting Features and Early Management of Childhood Intermittent Exotropia in the UK: Inception Cohort Study

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On behalf of the Improving Outcomes in Intermittent Exotropia Study Group

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ABSTRACT

Objective

To investigate factors associated with early management of intermittent exotropia [X(T)] in Hospital Eye departments in the UK.

Design

Prospective cohort study.

Setting

UK Hospital Children's Eye and Orthoptic Departments

Participants

An inception cohort of 460 children aged under 12 years with previously untreated X(T) (mean age 3.6 years, 55.9% girls) recruited from 26 UK Hospital Children's Eye Clinics and Orthoptic Departments.

Main Outcome Measures

Participants received a standard ophthalmic examination at recruitment and orthoptic assessment at 3-monthly intervals thereafter. The influence of severity of exotropia (control measured by Newcastle Control Score (NCS) and angle of strabismus, visual acuity, stereoacuity) and age on the type of management was investigated.

Results

Within the first 12 months following recruitment, 297 (64.6%) children received no treatment, either for impaired visual acuity or for strabismus. 96 (21%) children had treatment for impaired visual acuity. 89 (19.4%) received treatment for strabismus (22 of whom also received treatment for defective visual acuity); in 54 (11.7%) treatment was non surgical and in 35 (7.6%) eye muscle surgery was performed.

Children with poor (score 7-9) control of strabismus at recruitment were more likely to have surgery than children with good (score 1-3) control ($p < 0.001$). Children who had no treatment were younger (mean 3.38 years) than those who were treated (mean 4.07 years) ($p < 0.001$).

Stereoacuity and size of the angle of strabismus did not influence the type of management received.

Conclusions

X(T) can be a presenting sign of reduced visual acuity. Most children with well controlled X(T) receive no treatment within 12 months following presentation.

Introduction

Strabismus, a condition in which the eyes are misaligned, is common in childhood, having an estimated prevalence of 1-3%¹. Treatment of strabismus and amblyopia account for 90% of the work of children's eye departments in the UK².

Divergent strabismus accounts for approximately 25% of cases of strabismus in the Western world, it accounts for 72% of cases in Asia³. In childhood, the commonest form of divergent strabismus is Intermittent Exotropia [X(T)]⁴. In X(T), normal ocular alignment, and normal binocular sensory function, is maintained, other than in states of tiredness, inattention or distance fixation, when the eyes adopt a divergent alignment, with accompanying loss of stereoacuity⁵. The fact that children with X(T) do not complain of double vision is said to be because of suppression of the image of one eye by the developing visual system⁶. It has been suggested that children with X(T) who close one eye in bright light do so because of the increased amount of illumination incident on deviated, rather than aligned, eyes⁷. Unlike other forms of strabismus, for example constant exotropia, there are no reports of an increased prevalence of neurodevelopmental abnormality in children with X(T)^{4,8}. One report has suggested that children with exotropia may be at higher risk of later psychiatric illness⁹.

Treatment for X(T) may be requested by parents concerned about the appearance of the deviation, or may be recommended by health professionals concerned about the impact of periods of ocular misalignment on visual development and binocularity¹⁰.

A variety of surgical and non surgical treatments are available.

Surgical treatment of X(T) consists of adjustment of extraocular muscle position or length with the aim of improving ocular alignment¹¹. Initial overcorrection of the misalignment is thought to give the best chance of cure¹². Surgery may, however, be complicated by either undercorrection¹³ or persistent overcorrection of the misalignment, the latter converting an intermittent divergent deviation into a constant convergent misalignment (esotropia)¹⁴. This can, in turn, lead to amblyopia and loss of stereopsis in susceptible patients⁵.

Non surgical treatments of X(T) have been less thoroughly evaluated than has surgery. Correction of refractive error, intermittent occlusion of one eye¹⁵, glasses with over minus lenses to stimulate accommodation^{16,17}, and eye exercises¹⁸ have all been employed, either alone, or in combination with surgery¹⁹.

A Cochrane review has highlighted the lack of consensus and evidence concerning the management of X(T)²⁰. This study reports on the presenting features and early management of the cohort of a larger pragmatic, observational study - the Improving Outcomes in Intermittent Exotropia [IOX(T)] Study - established to improve the effectiveness and efficiency of the management of this common condition, by describing the current management practices and outcomes of treatment of X(T) in the UK and making recommendations for improvement.

Methods

The IOXT study group comprises 26 UK children's eye clinics and orthoptic departments (Appendix 1). The study was approved by the UK North West Multi Centre Research Ethics Committee. Each collaborating centre obtained local approval from their relevant NHS Trust R&D (Research and Development) Department. The study was conducted in accordance with the tenets of the Declaration of Helsinki.

Case Definition

Between May 2005 and December 2006, participating departments approached parents or carers of previously untreated children under the age of 12 years, diagnosed with X(T) within the previous 12 months, for consent to be recruited to the study.

Children with convergence insufficiency (near angle of exotropia greater than distance angle), constant exotropia or significant coexisting ocular pathology, such as cataract, were excluded from the study.

Clinical data collection

A standard assessment protocol, developed and tested during a pilot study²¹, was used in each collaborating centre. Participants were assigned a unique centre code and 3-digit participant study number, which was used for communication with the coordinating centre. Participating centres managed patients according to existing local protocols and guidelines, and collected study data at enrolment and at 3-monthly intervals for the first year following enrolment. In cases where a participant had surgery data were collected at the first postoperative visit (within one month of surgery) and at 6 months following surgery. A standardised clinical history was taken from all subjects that included details of pregnancy, birth, general and ocular health, and family history. Parents/carers were asked to estimate the age of onset of X(T).

Control of the strabismus was measured using the revised Newcastle Control Score²¹⁻²³ which combines an estimate of observed frequency of the strabismus by parents/carers (home control) with an assessment of the ability of the child with X(T) to realign the eyes following a cover test to induce misalignment (clinic control). Possible scores on the NCS range from 0 to 9, with higher scores indicative of a more severe squint. The angle of strabismus was measured using the alternate prism cover test (APCT) and the simultaneous prism cover test (SPCT). Near and distance stereoacuity were measured with the Frisby and Frisby Davis Distance Stereotest (FD2tm) respectively, using standard clinical protocols (<http://www.frisbystereotest.co.uk/index.htm>). Stereo data are reported only on children aged 4 years or older because younger children were unable to consistently understand and complete testing, particularly for distance stereoacuity (Table 1).

Other clinical measures of binocular function were recorded where the child was old enough to cooperate with testing. Management decisions were recorded and it was noted whether the treatment given was primarily for correction of impaired visual acuity or for X(T). Children who had treatment for both impaired visual acuity and for X(T) were classified as having treatment for X(T) for the purposes of analysis. Where

glasses were given as a non surgical treatment for X(T) only, measurements of control, stereopsis and angle were made without them. Health related quality of life data were collected using PedsQL v4tm and will be reported separately.

Data Analysis

Data were entered onto into an SPSS database (SPSS for Windows Version 11). Non-parametric (Kruskal-Wallis, Mann-Whitney and Chi-Square) tests were used to examine differences between groups. Age differences between groups were tested using t-test for independent samples.

For each reported variable, except stereoacuity measurements, all 460 patients are included in the base case analyses. We did not use any form of imputation methods for missing baseline data, nor for patients lost to follow-up.

Results

1. Demographics of the Cohort

The carers of 482 children were approached for consent to participate in the study. Fifteen eligible children cancelled or failed to attend the baseline assessment at least twice; 7 carers refused consent (reasons included travel difficulties, children in local authority care).

460 eligible children were recruited. 257 (55.9%) were female. Mean [SD] age at recruitment was 3.6 [1.9] years (range 0 – 11 years). The mean [SD] estimated age at onset of strabismus was 1.95 [1.5] years (range 0 – 96 months).

2. Baseline Clinical Measures

a. Control of Strabismus

Total Newcastle Control Scores were obtained for 459/460 children at recruitment. The median total score was 4 (range 1 – 9). Median home control was 1 (range 0 – 3); median clinic control was 2 (range 0 – 6).

b. Visual acuity

A baseline measurement of LogMAR visual acuity in each eye was achieved in 368 (80%) recruits. Mean (SD) visual acuity in the better eye was 0.121 (0.112) LogMAR (Figure 1), and in the worse eye was 0.158 (0.130) LogMAR (Figure 2). 96 of these children (26%) had a visual acuity poorer than 0.2 LogMAR in their worse eye. The worst recorded acuity was 0.900 (in one child only). The children for whom acuity data were missing were significantly younger (mean 2.35 years compared to 3.95 years, t-test $p < 0.001$).

c. Fusional Vergence

Data on base out fusional vergence was obtained on 453/460 children. 235 children could overcome a 20 dioptre base out prism at near fixation; 75, a 15; and 63, a 10 dioptre base out prism.

d. Near Stereoacuity

Children under 4 years (248/460 (54%)) were unable to consistently perform stereo testing using the FNS (Table 1). Of the 212 children aged 4 years or older, 198 (93%) had near stereoacuity assessed. In 3/198 stereopsis appeared to be absent. Median near stereoacuity in the remaining 195 children was 85 seconds of arc.

e. Distance Stereoacuity

Of 212 children aged 4 years or older, 127 (60%) had measurements of distance stereoacuity at recruitment (Table 1). In 33 of these, distance stereoacuity was absent. Median distance stereoacuity in the remaining 94 was 30 seconds of arc.

f. Angle of Strabismus

416 (90%) children had baseline measurement of the angle of strabismus (APCT) fixing in the distance and 419 (91%) fixing at near. Median distance angle was 25 prism dioptres. Median near angle was 14 prism dioptres. The children for whom angle data were missing were significantly younger: mean 1.74 years compared to 3.82 years for distance, t-test $p < 0.001$; mean 1.87 years compared to 3.79 years for near, t-test $p < 0.001$.

3. Management of X(T) within the first year

297 (64.6%) children, including 11 who failed follow up after recruitment, had no treatment, either for impaired visual acuity or for strabismus in the 12 months following recruitment.

74 (16.1%) children received treatment for impaired visual acuity only, either with glasses alone (48), occlusion (patching) (17) or both (9). Mean (SD) visual acuity in the worse eye of these children at recruitment was 0.250 (0.156), and was worse than 0.300 in only 16 of these children.

Of 89 (19.4%) children receiving treatment for strabismus, 54 (11.7%) had non surgical treatments (22 of whom also had treatment for impaired visual acuity) and 35 (7.6%) had surgery (9 of whom who also had prior non surgical treatment after recruitment – 1 glasses for squint, 4 occlusion for squint, 1 convergence exercises for squint, 2 glasses for vision and 1 occlusion for vision).

Of the 54 children having non surgical treatment for strabismus, the types of treatment given were: alternating sensory occlusion (10); exercises (5 - one of whom also had prisms), and glasses (39). Of the 39 children treated with glasses, 21 were prescribed “over minus” lenses to stimulate accommodation and convergence (median prescription -1.75, range -4 to -0.5) and 18 had correction of minor refractive error in an attempt to improve control of X(T). 35 children had eye muscle surgery for X(T) within the first 12 months, consisting in 16 cases of resection of the medial rectus and recession of the lateral rectus of one eye; and in 19 cases of recession of both lateral rectus muscles. Children who had no treatment were younger (mean [SD] age 3.38 [1.69] years) than those who were treated (for visual acuity and strabismus treatment combined, mean 4.07 [2.15] years ($p < 0.001$); for strabismus treatment (surgical and non) only, mean 3.97 [2.19] years ($p < 0.01$)). Children with poor control of strabismus (total NCS 7-9) at recruitment were more likely to have surgery than children with good control (total NCS 1-3) ($p < 0.001$, Table 2). Breaking the total NCS down into its home control and clinic control components, the median scores were higher in the surgery group than in the other treatment groups for each of these components and in terms of Total NCS (Table 3). Neither median baseline, nor the presence or absence of near or distance stereoacuity, differed significantly between observation and treatment groups. Similarly, neither distance nor near angle of strabismus at recruitment (median total (APCT) measurements) differed significantly between treatment and observation groups.

Discussion

In the first year of the study 96 children (21%) had impaired visual acuity requiring treatment (74 of whom were given this treatment for vision problems only). Impaired visual acuity in children with intermittent exotropia has been reported before²⁴, but is not often emphasised as a feature of the condition. The degree of impairment was generally mild and although in some cases it was associated with a refractive error, in 17/74 cases (23%) it appeared to be due to strabismic amblyopia alone.

It was not possible to approach all patients with intermittent exotropia seen in the 26 collaborating departments during the recruitment period. However the range of the baseline control reported (1 to 9 NCS) suggests that those recruited reflect the spectrum of the severity of the condition in the UK.

It proved possible to measure control, using the NCS, in almost all children, whatever their age. Although objective measurements of control can be subject to variation depending on time of day and states of attention²⁵, the NCS incorporates a parental rating of frequency of strabismus which may make it more useful in serial assessment of the severity of the condition. Children with higher scores on the NCS were more likely to have surgery.

The utility of stereo acuity data as a clinical measure by which improvement or deterioration could subsequently be assessed will be limited by the inability of younger children with X(T) to respond to testing and by the natural maturation process of stereo acuity development.

The majority of the cohort (64.6%) received no treatment during the first twelve months of the study which may reflect the uncertainty regarding how to manage this condition. Whilst these children were recalled at 3-monthly intervals for data collection it is likely that, due to their relatively young age, they would all have remained under the care of the hospital eye service for this time routinely. This raises the question of whether current follow up protocols could be revised, reducing the burden of appointments on children's eye departments and on patients themselves. We plan to describe natural history data over a two year period which may help to inform a pragmatic follow up schedule. Similarly we intend to report early (12-month) and longer-term (2-year) clinical outcomes of surgical and non surgical treatments, as well as any impact on quality of life.

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Competing interests

Helen Davis has a financial interest in the Frisby Davis Distance Stereotest (FD2). None of the other authors have any competing financial interest.

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Table 1: Comprehension of near and distance stereoacuity tests at recruitment by age category

Age at recruitment	Comprehended near Frisby at recruitment	Comprehended FD2 at recruitment
< 3 years (n=142)	62/142 (44%)	5/105 (5%) <i>(plus test not available in 37 cases)</i>
Negative (absent)	3/62 (5%)	4/5 (80%)
3 years (n=106)	78/105 (75%) <i>(plus poor concentration in one case; missing in one case)</i>	24/77 (31%) <i>(Plus poor concentration in 2 cases; missing in one case; test not available in 26)</i>
Negative (absent)	2/78 (3%)	11/24 (46%)
4 years (n=76)	67/74 (90%) <i>(plus 'other test used' in one case; poor concentration in one)</i>	41/63 (65%) <i>(plus poor concentration in 2 cases; missing in one; not available in 10)</i>
Negative (absent)	1/67 (1.5%)	11/41 (27%)
>5 years (n=136)	131/133 (99%) <i>(plus 'other test used in 3)</i>	86/96 (90%) <i>(plus poor concentration in 3; not available in 37)</i>
Negative (absent)	2/131 (1.5%)	22/86 (26%)

Table 2: Relationship between squint severity (control) at recruitment and treatment within first 12 months*

	Control (Total NCS) at recruitment:		
Treatment within first 12 months	NCS 1-3	NCS 4-6	NCS 7-9
No intervention (n=285)	n=159 (56%)	n=119 (42%)	n=7 (2%)
Surgery (n=35)	n=5 (14%)	n=20 (57%)	n=10 (29%)
Non-surgical treatment for squint (n=54)	n=19 (35%)	n=30 (56%)	n=5 (9%)
Treatment for vision only (n=74)	n=42 (57%)	n=28 (38%)	n=4 (5%)

Chi-square test, $p < 0.001$

*excludes the 11 children who failed to attend after recruitment and one child for whom total NCS at recruitment was not available

Table 3: Relationship between home control and clinic control components of NCS at recruitment and treatment within first 12 months*

	Components of the Newcastle Control Score at recruitment:		
Treatment within first 12 months:	Median home control component <i>(possible range 0-3)</i>	Median clinical component <i>(possible Range 0-6)</i>	Median Total NCS <i>(possible range 0-9)</i>
No intervention	1	2	3
Surgery	2	3	5
Non-surgical treatment for squint	1	3	3.5
Treatment for vision only	1	2	3
Statistical difference between treatment group (Kruskal-Wallis test)	P<0.001	P<0.001	P<0.001

Appendix 1: IOXT study collaborating centres

Birmingham Children's Hospital, Eye Dept, Birmingham, UK
Bradford Royal Infirmary, Bradford, UK
Sussex Eye Hospital, Brighton, UK
Bristol Eye Hospital, Bristol, UK
Queen's Hospital, Orthoptics Dept, Burton upon Trent, UK
West Suffolk Hospital, Bury St Edmunds, UK
Ninewells Hospital, Dundee, UK
University Hospital of North Durham, Orthoptic Dept, Durham, UK
The Princess Alexandra Eye Pavilion, Edinburgh, UK
Royal Devon & Exeter Hospital, West of England Eye Unit, Exeter, UK
Hull & East Yorkshire Eye Hospital, Kingston upon Hull and Hull Royal Infirmary, Orthoptic Dept, Hull, UK
St James's University Hospital, Orthoptic Dept, Leeds, UK
Moorfields Eye Hospital, London, UK
North Middlesex University Hospital, Orthoptic Dept, London, UK
Manchester Royal Eye Hospital, Orthoptic Dept, Manchester, UK
Milton Keynes General Hospital, Milton Keynes, UK
Royal Victoria Infirmary, Eye Dept, Newcastle upon Tyne, UK
Royal Shrewsbury Hospital, Orthoptics Dept, Shrewsbury and Princess Royal Hospital, Telford, UK
Southampton General Hospital, Eye Unit, Southampton, UK
Sunderland Eye Infirmary, Sunderland, UK
Mayday University Hospital, Eye Unit, Thornton Heath, UK
Torbay District General Hospital, Orthoptics Dept, Torquay, UK
Christopher Home Eye Unit, Orthoptics Dept, Royal Albert Edward Infirmary, Wigan, UK
Singleton Hospital, Orthoptic Dept, Swansea, UK

University Hospital of Wales, Cardiff, UK

York Hospital, Ophthalmology Dept, York, UK

Figure 1

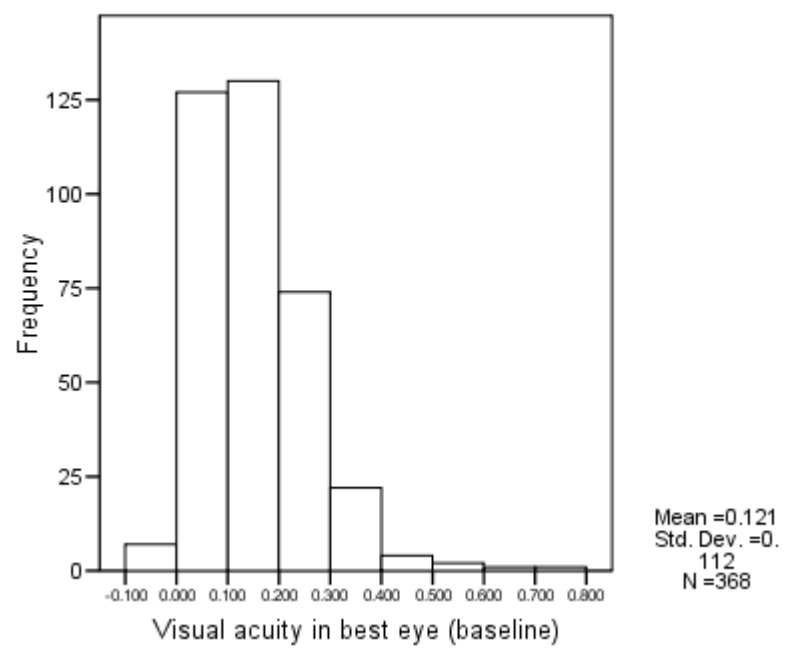


Figure 2

