Health-related quality of life in children with untreated intermittent exotropia and their parents

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*A full list of participating sites is provided as eSupplment 1, available at jaapos.org.

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Abstract

Purpose

To determine whether health-related quality of life (HRQOL) scores improved or worsened over 3 years of observation in childhood intermittent exotropia without treatment.

Methods

A total of 111 children aged 3-11 years with intermittent exotropia were assigned to observation in a previously reported randomized trial comparing patching with observation. The intermittent exotropia questionnaire (IXTQ) was administered at baseline, 6 months, and 36 months. Rasch-calibrated IXTQ domain scores (Child, Proxy, Parent-psychosocial, Parent-function, and Parent-surgery) were compared between time points. The Child IXTQ was administered only to children ≥5 years of age (n = 78).

Results

Overall, Child IXTQ and Proxy IXTQ scores showed no significant change over 36 months (mean improvement from baseline to 36 months of 3.2 points [95% CI, −1.9 to 8.2] and −2.4 points [95% CI: −7.9 to 3.1], resp.). By contrast, Parent-psychosocial, Parent-function, and Parent-surgery domain scores all improved over 36 months (mean improvements of 12.8 points [95% CI, 5.9-19.6] and 14.2 points [95% CI, 8.0-20.3] and 18.5 points [95% CI, 9.7-27.3], resp.).

Conclusions

HRQOL of children with intermittent exotropia remains stable with observation over 3 years (by both child and proxy report), whereas parental HRQOL improves.

Intermittent exotropia is one of the most common types of childhood strabismus, affecting approximately 0.6% of all children.[1] The Intermittent Exotropia Questionnaire (IXTQ)[2] was designed specifically to evaluate health-related quality of life (HRQOL) in children with intermittent exotropia and their parents. The IXTQ has three components: Child, Proxy (parent perception of the effect on their child), and Parent. The Parent IXTQ assesses the effect on the parent and family in three domains: Parent-psychosocial (parental concerns regarding the effect on the child's social interactions), Parent-function (parental concerns regarding the child's function), and Parent-surgery (parental concerns regarding the prospect of potential surgery for their child).[2] Example items in the Parent domains are "I worry about how my child's eyes will affect him/her socially" (Psychosocial), "I worry that my child doesn't see well" (Function), and "I worry about the possibility of surgery" (Surgery). The complete questionnaires and scoring algorithm are available at https://public.jaeb.org/pedig/view/Reference. The purpose of the present study was to determine whether health-related quality of life (HRQOL) scores improved or worsened over 3 years of observation in childhood intermittent exotropia without treatment.

Subjects and Methods

In a previously reported randomized controlled trial (www.clinicaltrials.gov: NCT 01032330; full protocol available at https://public.jaeb.org/pedig/stdy/154)[3] children with intermittent exotropia were assigned to either part-time patching (required for 5 months and at investigator discretion after 6 months) or observation and then subsequently followed for 3 years. The original study[3] from which these data were derived was supported through a cooperative agreement with the National Eye Institute of the National Institutes of Health and conducted according to the tenets of the Declaration of Helsinki by PEDIG at academic- and community-based sites. Health Insurance Portability and Accountability Act–compliant informed consent

forms and study protocols were approved by institutional review boards. A parent or guardian (henceforth, "parent") provided written informed consent, and children gave written assent when required by the local institutional review board, typically age 7 years and above.

Clinical outcomes for the observation cohort after 3 years of follow-up have been reported previously.[4] For the current report, analyses were limited to children 5 to <11 years of age (old enough for questionnaires to be completed) and parents of children aged 3 to <11 years of age who completed questionnaires at baseline. Participants included for analysis at each time point and reasons for exclusion are shown in eSupplement 2 (available at jaapos.org).

The IXTQ was completed by participants and one of their parents at baseline (enrollment), 6 months (window, 5-7 months), and 36 months (window, 34-38 months). Participants ≥5 years of age completed the 12-item Child IXTQ, administered by study personnel for 5- to 7-year-old children and self-administered for children 8 years and older, with help from study personnel if needed. Children 5-7 years of age completed the Child IXTQ using a 3-point Likert scale ("Not at all," "Sometimes," "A lot"), while a 5-point scale was used for children ≥8 years old ("Never," "Almost Never," "Sometimes," "Often," "Almost Always"). All parents were asked to self-complete the 12-item Proxy IXTQ (parental assessment of their child's HRQOL) and the 17-item Parent IXTQ questionnaire. Both Proxy and Parent questionnaires used the 5-point response scale.

IXTQ responses to each question were converted to Rasch-based logit scores using IXTQ Rasch lookup tables (https://public.jaeb.org/pedig/view/reference, accessed 9/1/2020)[5] and averaged to obtain a participant-level score for each domain (Child, Proxy, Parent-psychosocial, Parent-function, and Parent-surgery). The raw Rasch scores (logit values) were analyzed to obtain p-values but, to aid in interpretation, participant-level scores were converted to a 0 (worst)

to 100 (best) scale for reporting group means and confidence intervals. HRQOL scores were compared between baseline and 6 months, and between baseline and 36 months, using Wilcoxon signed rank tests due to a non-normal distribution. Rasch scores from the respective age-appropriate version of the Child IXTQ (5 to <8-year-old version and ≥8-year-old version) were used for analysis. Rasch scores from the ≥8-year-old version of the questionnaire were scaled to match the range of the younger questionnaire.

All *P* values and 95% confidence intervals were adjusted for multiplicity using the Stepdown Bonferroni method,[6] with analyses grouped to control the type 1 error rate at the 5% level. No imputation was performed for missing data. Analyses were conducted using SAS version 9.4 (SAS Institute Inc, Cary, NC).

Results

From baseline to 6 months and from baseline to 36 months, the Child IXTQ and Proxy IXTQ scores showed no significant change (Table 1 and Figure 1). In contrast, the Parent-function and Parent-psychosocial domain scores improved over the same time periods with observation, whereas Parent-surgery domain scores improved from baseline to 36 months.

Discussion

Comparing our results with previous studies, Clarke and colleagues[7] reported longitudinal Child, Proxy, and Parent IXTQ data (baseline and 9 months follow-up) in a pilot randomized trial comparing active monitoring (observation, n = 20 with follow-up) with surgery (n = 25). With observation, they found no significant change in score on any IXTQ domain.[7] Our current results are consistent for the Child and Proxy domains (at our time points of 6 and 36 months), but we found improvement in Parent IXTQ scores at both 6 and 36 months. It is possible that differences in results might be attributable to Clarke's smaller sample size, our longer follow-up,

or difference in comparison group in each of the studies (observation vs surgery in the study of Clarke and colleagues, whereas observation vs patching in the present study).

The stability of Child or Proxy IXTQ scores and improvement of Parent IXTQ scores is possibly related to the low frequency of clinical deterioration of intermittent exotropia in these children who were observed over this 36-month period.[4] In this population, there was a mean improvement (over 36 months) in distance and near stereoacuity, distance control, and magnitude of distance exodeviation.[4] Moreover, when we applied a definition of "resolution or near resolution" (exodeviation $<10^{\Delta}$ at distance and near, no reduction in stereoacuity, and no other nonsurgical treatment for intermittent exotropia)[8] we found 6 (7%) of the current observed cohort met these criteria at 36 months. Another reason why the Child or Proxy IXTQ scores remained stable and the Parent IXTQ scores improved over this 36-month period, is that parents may have become less anxious about the condition with time, and there may have been an effect of counselling by the treating provider and study coordinators, who may have provided positive feedback to the family during the 36-month period of observation.

Our study has some limitations. Our cohort may have had somewhat less severe intermittent exotropia than an unselected cohort, because a simultaneous surgical study was being conducted by the same investigator group.[9] In the original RCT from which the current IXTQ data was derived, the mean magnitude of distance exodeviation in the Observation group was 23^{Δ} by prism and alternate cover test and the mean distance control was 2.4 points,[3] and therefore caution should be taken extrapolating the current IXTQ data to more severe cases of intermittent exotropia. Although there was possibly a component of regression to the mean, we did not enroll based on any IXTQ threshold. We did not have complete follow-up (80% at 3 years) and we excluded participants who received treatment over the course of the study (n =

15). We did not compare IXTQ scores in the observed cohort with those who were randomized to patching in the original RCT,[3] because those who underwent patching were instructed to stop patching one month before initial 6-month outcome examination and were released to patching treatment at investigator discretion after the 6-month examination.

In conclusion, HRQOL of children remains stable with observation of intermittent exotropia over 3 years (by both child and proxy report), whereas parental HRQOL improves.

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Legends

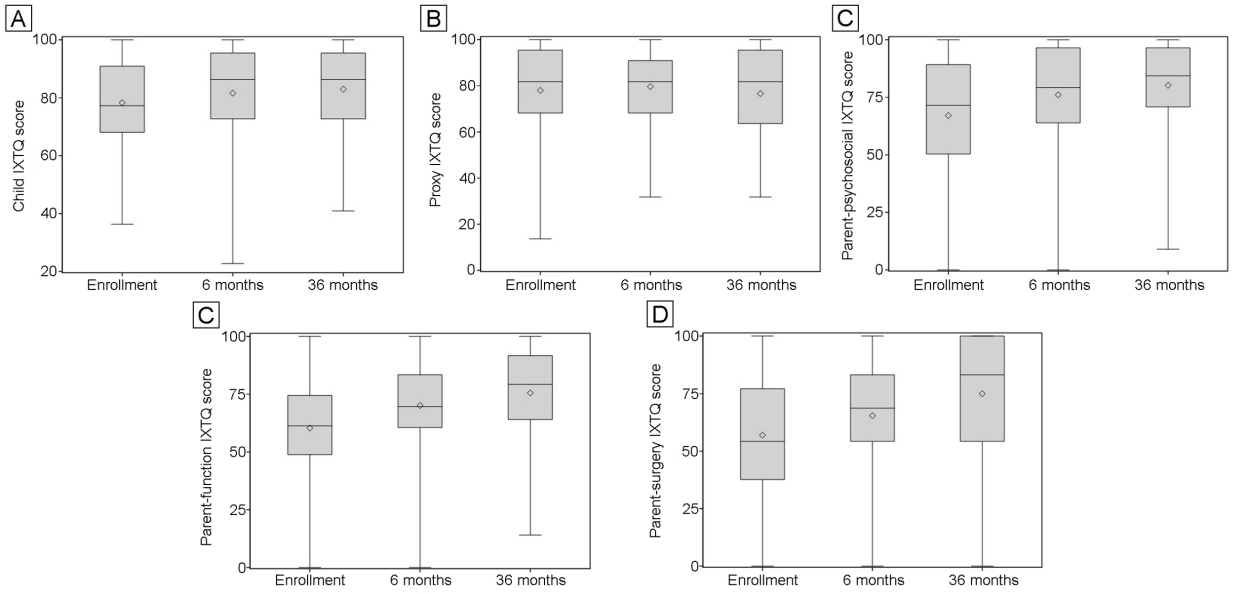
FIG 1. IXTQ scores at baseline, 6 months, and 36 months. A, Child IXTQ. B, Proxy IXTQ. C, Parent-psychosocial IXTQ. D, Parent-function IXTQ. E, Parent-surgery IXTQ. The center line of each box represents the median domain score, the boundary of each box represents 25th and 75th percentiles, and the whiskers represent the extreme values. The diamond within each box represents the mean value.

Table 1. IXTQ scores at baseline, 6 months, and 36 months for untreated Intermittent exotropia

Study parameter	Baseline	6 months	36 months
Child IXTQ, no.	78	70	62
Median (IQR)	77.3 (68.1, 90.9)	86.4 (72.7, 95.4)	86.3 (72.7, 95.4)
Mean ± SD	78.3 ± 16.6	81.6 ± 17.1	83.0 ± 15.6
Median change from baseline (IQR)[a]	—	2.3 (−4.6, 9.1)	0.0 (−9.1, 13.6)
P value for change from baseline[b,c]	—	0.92	1.0
Mean change from baseline (adjusted 95% CI)[a,b]	—	2.7 (−2.2, 7.7)	3.2 (−1.9, 8.2)
Proxy IXTQ, no.	111	101	86
Median (IQR)	81.8 (68.2, 95.5)	81.8 (68.2, 90.9)	81.8 (63.6, 95.5)
Mean ± SD	78.0 ± 20.2	79.7 ± 16.7	76.6 ± 19.8
Median change from baseline (IQR)[a]	—	0.0 (−9.1, 9.1)	0.0 (−9.1, 4.6)
P value for change from baseline[b,c]	—	1.0	1.0
Mean change from baseline (adjusted 95% CI)[a,b]	—	1.2 (−3.6, 6.0)	−2.4 (−7.9, 3.1)
Parent psychosocial IXTQ, no.	111	101	86
Median (IQR)	71.5 (50.4, 89.2)	79.2 (63.9, 96.5)	84.4 (70.8, 96.5)
Mean ± SD	67.1 ± 26.1	76.1 ± 23.2	80.2 ± 22.0
Median change from baseline (IQR)[a]	—	3.5 (−3.5, 21.5)	5.9 (0.0, 28.1)
P value for change from baseline[b,c]	—	0.004	<0.0001
Mean change from baseline (adjusted 95% CI)[a,b]	—	8.2 (1.5, 14.9)	12.8 (5.9, 19.6)
Parent function IXTQ	111	101	86
Median (IQR)	61.3 (48.9, 74.4)	69.6 (60.6, 83.4)	79.3 (64.0, 91.7)
Mean ± SD	60.4 ± 21.1	70.1 ± 19.9	75.6 ± 19.6
Median change from baseline (IQR)[a]	—	6.2 (−1.4, 20.0)	12.8 (2.8, 25.0)
P value for change from baseline[b,c]	—	<0.0001	<0.0001
Mean change from baseline (adjusted 95% CI)[a,b]	—	8.8 (3.6, 14.0)	14.2 (8.0, 20.3)
PARENT surgery IXTQ	111	101	86
Median (IQR)	54.2 (37.7, 77.1)	68.7 (54.2, 83.2)	83.2 (54.2, 100.0)
Mean ± SD	56.9 ± 26.4	65.4 ± 25.8	75.0 ± 23.6
Median change from baseline (IQR)[a]	—	0.0 (0.0, 21.1)	16.7 (0.0, 33.2)
P value for change from baseline[b,c]	—	0.06	<0.0001
Mean change from baseline (adjusted 95% CI)[a,b]	—	7.3 (0.1, 14.4)	18.5 (9.7, 27.3)

CI, confidence interval; *IQR*, interquartile range; *IXTQ*, Intermittent Exotropia Questionnaire; *SD*, standard deviation.

[a]Positive values for change indicate improvement.
[b]*P* value for change from baseline calculated on raw Rasch scores using the Wilcoxon signed-rank test; *P* values adjusted for multiple testing using the stepdown-Bonferroni method to control type I error rate at 5%.
[c]CIs adjusted for multiple testing using the stepdown-Bonferroni method to control type I error rate at 5%.


A
Child IXTQ score
100
80
60
40
20
Enrollment
6 months
36 months
B
Proxy IXTQ score
100
80
60
40
20
0
Enrollment
6 months
36 months
C
Parent-psychosocial IXTQ score
100
75
50
25
0
Enrollment
6 months
36 months
C
Parent-function IXTQ score
100
75
50
25
0
Enrollment
6 months
36 months
D
Parent-surgery IXTQ score
100
75
50
25
0
Enrollment
6 months
36 months