NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of tenotomy of horizontal eye muscles for nystagmus (with reattachment at their original insertions)

Nystagmus is the involuntary movement of the eyes (most commonly from side to side) and is usually associated with impaired vision. Tenotomy involves cutting the horizontal muscles of the eye (which move the eye from side to side) and reattaching them at the same place. The aim of the procedure is to improve vision.

Introduction

This overview has been prepared to assist members of the Interventional Procedures Advisory Committee (IPAC) in making recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in November 2008.

Procedure name

- Tenotomy of horizontal eye muscles for nystagmus.

Specialty society

- Royal College of Ophthalmologists.

Description

Indications and current treatment

Nystagmus is an involuntary oscillatory movement of the eyes, usually from side to side, but sometimes the eyes move up and down or in a circular motion. Most people with nystagmus have reduced vision.

Many people with nystagmus have a position of gaze where the nystagmus is reduced and vision is improved. They may therefore turn their head to one side to make the best use of their vision. Patients with nystagmus may also have a condition called strabismus (also known as squint or heterotropia).

There are several types of nystagmus but there is no consistent classification system to describe them. Nystagmus that is present at birth or that develops in the first 6 months is usually called congenital or infantile nystagmus. This may be caused by a defect in the eye or in the visual pathway from the eye to the brain. Congenital/infantile nystagmus occurs in a wide range of childhood eye disorders such as cataract, glaucoma, some disorders of the retina, and albinism. It may also be found in children who have multiple disabilities or conditions such as Down's syndrome. Many children with nystagmus have no brain, health or other eye problems. In these children the condition is called 'congenital idiopathic nystagmus' or 'idiopathic infantile nystagmus'.

Acquired nystagmus, which develops later in life, may be a symptom of a variety of other conditions including stroke, multiple sclerosis or head injury.

There is currently no curative treatment for nystagmus. Treatments that have been tried include drugs such as anti-epileptics and muscle relaxants, injections of botulinum toxin, and biofeedback techniques (making people aware of the eye movement using visual and audio signals and encouraging them to control it). Lenses may be worn to improve visual acuity but these do not correct the nystagmus.

What the procedure involves

Tenotomy for nystagmus is carried out with the patient under general anaesthesia, and involves the two horizontal rectus muscles (lateral and medial) of each eye. A limbal incision is made in the conjunctiva and the muscle is detached from the sclera. The muscle is then reattached at its original place of insertion.

The aims of the procedure are to reduce the frequency and amplitude of nystagmus (how often and how far the eyes oscillate) and to improve visual acuity.

The exact mechanism by which this procedure may improve nystagmus is unknown. It is a modification of the established Anderson-Kestenbaum surgical procedure, which was designed to straighten the head posture of patients with nystagmus, who were turning their head in order to maximise their visual acuity. Secondary beneficial effects of this procedure were noted (broadening and dampening of nystagmus) and an animal model was used to demonstrate that these effects could be achieved by tenotomy of the eye muscles and reattachment at their original insertions without resection or recession.

Efficacy

This overview is based on approximately 22 patients from 4 case series.

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Eye movement

All four case series assessed eye movement using infrared reflection or a technique involving magnetic induction and scleral search coils (devices embedded into a contact lens or a rubber ring that adheres to the eye and generates electrical currents with eye movement). A combination of various eye movement recordings was used to calculate an 'expanded nystagmus acuity function', an objective measure of the quality of nystagmus waveform that can be used to predict potential visual acuity.

In a case series of 10 adults who had tenotomy, 9 patients had increased nystagmus acuity function scores and 1 patient had a decreased score (mean score change from baseline 43%) at 1 year [1].

In a case series of 5 children, only 2 were assessed for eye movement. Nystagmus acuity function scores improved by 8% in one child at 1 year and 36% in the other child at 6 months [2].

A case series of 9 children and adults reported that 8 had increased nystagmus acuity function scores (mean 60%) at 1 year and 1 had no change. All 9 patients had reduced nystagmus amplitude (mean 33%) and increased foveation period (when the eye is still and is pointed at the object of regard) (mean 104%) [3]. Another study reported the changes in target acquisition time in 5 of these 9 patients (measured by infrared reflection or high-speed digital video). All 5 patients had reduced time to target acquisition 1 year after the procedure [4].

Visual acuity

In the case series of 5 children and 10 adults, an improvement in best-corrected visual acuity of at least five letters on the Early Treatment Diabetic Retinopathy Study chart (corresponding to a one-line improvement on the Snellen chart) was reported in 4 and 5 patients, respectively (assessed at 6 weeks and 12 months, respectively). The remaining patients in each study had no change in visual acuity [2, 1].

The case series of 9 patients reported that 3 patients had an improvement in visual acuity of at least one line, 3 had an improvement of a few letters and 3 had no change (method of assessment and follow-up was not described) [3].

Safety

In two case series of 5 and 10 patients no adverse events occurred [2, 1]. The case series of 9 patients did not report any information about safety [3].

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to tenotomy of horizontal eye muscles for nystagmus. Searches were conducted of the following databases, covering the period from their commencement to 14/05/08 and updated to 28/01/09: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy).

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with nystagmus.
Intervention/test	Tenotomy of horizontal eye muscles with reattachment at their original insertions.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

There is currently no NICE guidance related to this procedure.

Table 2 Summary of key efficacy and safety findings on tenotomy of horizontal eye muscles for nystagmus (with reattachment at their original insertions)

Abbreviation used: ETDRS, Early Treatment Diabetic Retinopathy Study

Study details	Key efficacy findings	Key safety findings	Comments
Hertle W (2003) [1] Study type: **prospective case series** Country: USA Study period: not stated Study population: adults with varied sensory defects and oculographic subtypes of congenital nystagmus (n = 5), and congenital asymmetric periodic alternating nystagmus (n = 5) n = **10** Age: 37 years (mean), 20–55 years (range) Sex: 70% male Inclusion criteria: • clinical and oculographic diagnosis of congenital nystagmus • best-corrected binocular visual acuity 20/400 to 20/50 Exclusion criteria: • prior extraocular muscle surgery • other treatment options (specifically patients with an eccentric null position or convergence dampening of nystagmus) • other indications for extraocular muscle surgery (e.g. abnormal head posture or strabismus requiring surgical correction) Technique: tenotomy of four horizontal rectus muscles and immediate reattachment at the original insertion site. Follow-up: **1 year**	**Eye movement** Assessed 1 year after the procedure by search-coil eye movement recordings. Scored using the 'expanded nystagmus acuity function': • 9/10 patients had persistent significant postoperative increases in expanded nystagmus acuity function score of their fixing eye • 1 patient had a decrease in expanded nystagmus acuity function score (from 0.436 to 0.374) • mean postoperative increase in expanded nystagmus acuity function score was 43% (range –14% to 108%). **Visual acuity** Assessed 1 year after the procedure using the ETDRS chart: • 50% of patients had an improvement in best-corrected visual acuity of at least five letters, corresponding to at least one line on the Snellen chart • 50% of patients had no change in visual acuity. **Vision-specific mental health** Assessed 1 year after the procedure using the National Eye Institute visual function questionnaire: • 90% of patients showed an increase in overall visual function questionnaire score; 1 patient had a decrease in score after the procedure (baseline score 78; 1-year score 68).	No adverse events occurred.	The 'expanded nystagmus acuity function' is an objective measure taking into account the quality of nystagmus waveform. It predicts best-corrected visual acuity under benign conditions, and assesses oscillation. A higher expanded nystagmus acuity function score indicates improvements in at least one of the following aspects of eye movement: decreased nystagmus amplitude, increased length of foveation periods, decreased positions and velocity variations. The foveation period is when the eye is still and is pointed at the object of regard.

Conflict of interest: not stated			

Abbreviation used: ETDRS, Early Treatment Diabetic Retinopathy Study

Study details	Key efficacy findings	Key safety findings	Comments
Hertle RW (2004) [2] Study type: **prospective case series** Country: USA Study period: not stated Study population: children with infantile nystagmus syndrome n = **5** Age: 10 years (mean), 5–16 years (range) Sex: 80% male Inclusion criteria: not stated Exclusion criteria: not stated Technique: tenotomy of four horizontal rectus muscles and immediate reattachment at the original insertion site. Follow-up: **1 year** Conflict of interest: not stated	**Eye movement** Assessed by search-coil eye movement recordings. Scored using the 'expanded nystagmus acuity function. This outcome could not be assessed for 3 patients (for various technical reasons): • expanded nystagmus acuity function score improved from 0.656 to 0.708 (8% increase) in one patient (at 1-year follow-up) and from 0.532 to 0.722 (36% increase) in another patient (at 6-month follow-up). **Visual acuity** Assessed 6 weeks after the procedure using the ETDRS chart: **Patient** / **Baseline** / **Postoperative** 1 / 20/60 / 20/40 2 / 20/60 / 20/60 3 / 20/50 / 20/40 4 / 20/40 / 20/25 5 / 20/50 / 20/25 • 4 patients had an improvement in visual acuity of at least five letters • 1 patient had no change.	No adverse events occurred.	

Study details	Key efficacy findings	Key safety findings	Comments
Wang Z (2006) [3] Study type: **prospective case series** Country: USA Study period: not stated Study population: patients with infantile nystagmus syndrome. No patients had undergone previous eye muscle surgery n = **9** Age: 20 years (mean), 6–49 years (range) Sex: 56% male Inclusion criteria: • patients who could not benefit from other known surgical or non-surgical therapies for nystagmus Exclusion criteria: • patients with fusion maldevelopment nystagmus or asymmetric periodic alternating nystagmus Technique: tenotomy of four horizontal rectus muscles and immediate reattachment at the original insertion site Follow-up: **3–12 months** (mean not stated) Conflict of interest: not stated	**Eye movement** Assessed 3–12 months after the procedure by infrared reflection (n = 8) or high-speed digital video (n = 1). Scored using the 'expanded nystagmus acuity function'. Eight of nine patients had an immediate increase in expanded nystagmus acuity function score after the procedure, which was retained at 1-year follow-up (mean 60%): • large improvement: 5/9 (range 39.9–162.4%) • moderate improvement: 3/9 (range 13.9–32.6%) • no change: 1/9. All patients had reductions in nystagmus amplitudes ranging from 15% to 37% (mean 33%). All patients had foveation period increases ranging from 11% to 200% (mean 104%). **Primary position visual acuity** Obtained by the referring physician and recorded in the patient's clinical notes (method of assessment and duration of follow-up not stated). Six of nine patients had improvement in primary position visual acuity: • improvement of at least one line: 3/9 • improvement of a few letters: 3/9 • no change: 3/9.	No safety outcomes were reported.	

Study details	Key efficacy findings	Key safety findings	Comments
Wang ZI (2008) [4] Study type: **prospective case series** Country: USA Study period: not stated Study population: patients with infantile nystagmus syndrome n = **5** Age: 27 years (mean), 9–49 years (range) Sex: 60% male Inclusion criteria: not stated Exclusion criteria: not stated Technique: tenotomy of four horizontal rectus muscles and immediate reattachment at the original insertion site Follow-up: **1 year** Conflict of interest: not stated	**Target acquisition time** Assessed by infrared reflection and high-speed digital video: • time to target acquisition was reduced in all 5 patients • average time to target acquisition was 280 ms (range 200–500 ms).		Same patients as in Wang et al. 2006 (above)[3]. The study objective was to compare post-tenotomy target acquisition changes predicted from a model with data from patients. There were few clinically relevant outcomes reported.

Validity and generalisability of the studies

- Many of the studies had duplicate reporting of patients
- There was variation in the age of patients (mean age ranged from 10 to 32 years).

Specialist Advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and does not represent the view of the society.

Irene Gottlob, John Lee, Isabelle Russell-Eggit, Robert H Taylor (Royal College of Ophthalmologists).

- One Specialist Adviser had performed this procedure at least once and three had not performed it at all (although one sees patients who would potentially benefit and another intends to start performing the procedure within the year).
- Two Specialist Advisers thought it was a novel procedure (one stated that the actual technical procedure is based upon an established procedure but the concept is novel and there are new potential hazards if it is applied to young children as advocated by its exponents).
- Two Specialist Advisers thought it was a minor variation of an established technique (similar to strabismus surgery but for a new indication).
- Three Advisers stated that there is no direct comparator.
- Specialist Advisers listed the following theoretical adverse events: loss of vision, retinal damage, need for revision surgery, damage to the eye, redness, swelling, diplopia, infection, perforation of globe, slipped muscles, worse eye alignment, induced strabismus and loss of vision.
- One Specialist Adviser stated that development of a conjunctival cyst had been reported in the literature.
- Three Specialist Advisers stated that there are no uncertainties about the safety of the procedure.
- Specialist Advisers listed the following efficacy outcomes: best corrected binocular visual acuity under varying gaze angles, null point width, stereoacuity, ocular movement recordings, nystagmus, visual function in day-to-day life, quality of life, cosmesis and head posture.
- One Specialist Adviser thought that the main uncertainty with the procedure was the difficulty in measuring improvement and standardising viewing angles. Another stated that the procedure produces a small improvement in a measurable feature of ocular movement (foveation time) but there is no consistent improvement in visual acuity assessed by Snellen charts. One Specialist Adviser thought that there is uncertainty relating to the long-term benefit of the procedure.

- Three Specialist Advisers thought that clinicians should have experience in performing strabismus/eye muscle surgery.
- Three Specialist Advisers thought that the procedure would potentially have a minor impact on the NHS and one thought it would have a moderate impact.
- A few studies reported on vertical eye muscle surgery for vertical nystagmus. These were not included in the overview.

Issues for consideration by IPAC

- Consider alternative titles:
  - Tenotomy of horizontal eye muscles for nystagmus (with re-attachment at original insertion)
  - Four muscle surgery
  - Horizontal rectus tenotomy without recession.
- No adverse events were reported.
- There are very small patient numbers in the evidence base.

References

1 Hertle RW, Dell'Osso LF, FitzGibbon EJ et al. (2003) Horizontal rectus tenotomy in patients with congenital nystagmus: results in 10 adults. Ophthalmology 110: 2097–105.

2 Hertle RW, Dell'Osso LF, FitzGibbon EJ et al. (2004) Horizontal rectus muscle tenotomy in children with infantile nystagmus syndrome: a pilot study. Journal of Aapos: American Association for Pediatric Ophthalmology and Strabismus 8: 539–48.

3 Wang Z, Dell'Osso LF, Jacobs JB et al. (2006) Effects of tenotomy on patients with infantile nystagmus syndrome: foveation improvement over a broadened visual field. Journal of Aapos: American Association for Pediatric Ophthalmology and Strabismus 10: 552–60.

4 Wang ZI and Dell'Osso LF. (2008) Tenotomy procedure alleviates the 'slow to see' phenomenon in infantile nystagmus syndrome: model prediction and patient data. Vision Research 48: 1409–19.

Appendix A: Additional papers on tenotomy of horizontal eye muscles for nystagmus (with reattachment at their original insertions)

The following table outlines the studies that are considered potentially relevant to the overview but were not included in the main data extraction table (table 2). It is not an exhaustive list of potentially relevant studies.

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Hertle RW and Yang D (2006) Clinical and electrophysiological effects of extraocular muscle surgery on patients with infantile nystagmus syndrome (INS). Seminars in Ophthalmology 21: 103–10.	n = 75 (only 15 patients with nystagmus alone, i.e. without additional strabismus or abnormal head posture) Follow-up: 18 months	The results are summarised as follows: null zone acuity increased 0.1 LogMar or greater in 75% with those patients ≤ 8 years significantly better. Subjective gaze dependent acuity and null zone width measured from eye movement recordings showed persistent, significant increases. This report adds to the evidence that surgery on the extraocular muscles in patients with INS has independent neurological and visual results, from simply repositioning the head, eye(s) or visual axis.	Patient group was mixed – some patients had recession of horizontal eye muscles and others had tenotomy with immediate reattachment. Results were not reported separately.
Hertle RW, Anninger W, Yang D et al. (2004) Effects of extraocular muscle surgery on 15 patients with oculo-cutaneous albinism (OCA) and infantile nystagmus syndrome (INS). American Journal of Ophthalmology 138: 978–87.	n = 15 (only 3 patients with nystagmus alone, i.e. without additional strabismus or abnormal head posture) Follow-up: 17 months	Various measures of eye movement showed persistent, significant increases in all patients. 14/15 patients had improvement in best optically corrected acuity of ≥ 0.1 LogMar. Patients with abnormal head posture improved significantly postoperatively ($p < 0.01$).	Patient group was mixed – some patients had recession of horizontal eye muscles and others had tenotomy with immediate reattachment. Results were not reported separately.
Miura K, Hertle RW, FitzGibbon EJ et al. (2003) Effects of tenotomy surgery on congenital nystagmus waveforms in adult patients. Part I: Wavelet spectral analysis. Vision Research 43: 2345–56.	n = 8 Follow-up: not stated	No common effect of tenotomy on nystagmus waveforms was found across the patients. This suggests that tenotomy has no, or very small, effect on the waveform structure of nystagmus.	This study focused on analysis of wavelet spectral. The outcomes reported were less clinically relevant than in papers included in table 2.
Miura K, Hertle RW, FitxGibbon EJ et al. (2003) Effects of tenotomy surgery on congenital nystagmus waveforms in adult patients. Part II: Dynamic systems	n = 8 Follow-up: not stated	There were no significant differences in the correlation dimensions that could be associated with tenotomy. This suggests that tenotomy has no effect on the underlying	This study focused on analysis of wavelet spectral. The outcomes reported were less clinically relevant

analysis. Vision Research 43: 2357–62.		mechanism of nystagmus beats.	than in papers included in table 2.
Wang Z, Dell'Osso LF, Zhang Z et al. (2006) Tenotomy does not affect saccadic velocities: support for the 'small-signal' gain hypothesis. Vision Research 46: 2259–67.	n = 10 Follow-up: not stated	Tenotomy successfully reduced nystagmus, enabling higher visual acuity without adversely affecting saccadic characteristics.	The outcomes reported were less clinically relevant than in papers included in table 2. More clinically relevant outcomes for the same patients are included in table 2 (Wang et al. 2006)[3].

Appendix B: Related NICE guidance for tenotomy of horizontal eye muscles for nystagmus (with reattachment at their original insertions)

There is currently no NICE guidance related to this procedure.

Appendix C: Literature search for tenotomy of horizontal eye muscles for nystagmus (with reattachment at their original insertions)

Database	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	13/5/2008	Issue 2, 2008
Database of Abstracts of Reviews of Effects – DARE (CRD website)	14/5/2008	N/A
HTA database (CRD website)	14/5/2008	N/A
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	13/5/2008	Issue 2, 2008
MEDLINE (Ovid)	13/5/2008	1950 to April Week 3 2008
MEDLINE In-Process (Ovid)	13/5/2008	April 29, 2008
EMBASE (Ovid)	13/5/2008	1980 to 2008 Week 17
CINAHL (Search 2.0, NLH)	13/5/2008	1982 to date (via Dialog)
BLIC (Dialog DataStar)	14/5/2008	1993 to date
National Research Register (NRR) Archive	12/5/2008	N/A
UK Clinical Research Network (UKCRN) Portfolio Database	12/5/2008	N/A
Current Controlled Trials metaRegister of Controlled Trials - mRCT	12/5/2008	N/A
Clinicaltrials.gov	12/5/2008	N/A

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1	Tendon/su
2	Tendon Transfer/
3	Tenotom$.tw.
4	Tendotom$.tw.
5	(Tendon$ adj3 (surg$ or cut$ or reattach$ or re-attach$ or transfer$)).tw.
6	Oculomotor Muscles/su
7	(Oculomotor$ adj3 muscle$ adj3 surg$).tw.
8	(Extraocular$ adj3 muscle$ adj3 surg$).tw.

9	(Eye$ adj3 muscle$ adj3 surg$).tw.
10	Ophthalmologic Surgical Procedures/
11	(Ophthalmolog$ adj3 Surg$ adj3 Procedure$).tw.
12	or/1-11
13	Nystagmus, Optokinetic/
14	Nystagmus, Physiologic/
15	Nystagmus, Congenital/
16	Nystagmus, Pathologic/
17	Nystagmu$.tw.
18	(Involuntar$ adj3 eye$ adj3 movement$).tw.
19	or/13-18
20	12 and 19
21	Animals/
22	Humans/
23	21 not (21 and 22)
24	20 not 23