NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of canaloplasty for primary open-angle glaucoma

Primary open angle glaucoma is a condition associated with a long-term increase of pressure within the eye. It may gradually lead to permanent loss of sight because of damage to the nerve that connects the eye to the brain (optic nerve), which is essential for sight. Canaloplasty involves widening the main drainage canal in the eye to help prevent the build up of fluid. The drainage canal is situated within the angle between the iris (the coloured part of the eye) and cornea (the transparent outer coating of the eye). A tiny tube is inserted into the canal and a thick fluid (viscoelastic) is injected to open it up. The tube is then removed and a stitch is placed within the canal to keep it open. The aim is to restore the eye's natural drainage system and reduce pressure within the eye.

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 2007.

Procedure name

- Canaloplasty for primary open-angle glaucoma

Specialty societies

The following society was approached to nominate Specialist Advisers.

- Royal College of Ophthalmologists

Description

Indications

Primary open-angle glaucoma

Glaucoma describes a group of conditions in which there is progressive damage to the optic nerve at the back of the eye. A certain level of pressure is needed within the eye for it to keep its shape. This pressure is maintained by the flow of a fluid (aqueous humour) within the eye. Within the drainage angle of the eye, the aqueous humour passes through the trabecular meshwork and into a collector channel known as Schlemm's canal (which is situated around the iris). It then drains away back into the blood stream. A balance between the fluid entering and leaving the eye determines the pressure in the eye (the intraocular pressure).

Most cases of glaucoma occur because the flow of fluid out of the eye becomes restricted and the pressure within the eye rises above the normal range (ie over 21 mmHg). This pressure causes damage to the optic nerve. In some cases, damage occurs even though the pressure is within normal limits (normal pressure or normal tension glaucoma). It is thought that this may be due to a poor blood supply or a weakness in the optic nerve structure. Most cases are primary but glaucoma can result from other eye or systemic disease (secondary glaucoma). There are two main types of glaucoma, ‘open-angle’ where there is no physical obstruction of the drainage angle of the eye and ‘closed-angle’ where there is a sudden complete blockage of the trabecular meshwork. The majority of people with glaucoma have primary open-angle glaucoma.

The early stages of primary open-angle glaucoma are usually asymptomatic; there is no pain and visual loss is in the mid-peripheral field of vision. As the condition progresses, the field of vision gradually becomes more impaired. If it remains untreated, central vision may also be lost. Both eyes are usually affected by the condition.

Current treatment and alternatives

Treatment for glaucoma is designed to reduce the level of intraocular pressure. The first stage of treatment is usually eye drops, either to reduce the amount of aqueous humour that is produced or increase the flow of aqueous humour out of the eye.

Laser therapy includes laser trabeculoplasty (discrete laser ablation to areas of the trabecular meshwork of the drainage angle) and laser cyclophotocoagulation (destroying part of the ciliary body that produces aqueous humour).

If eye drops or laser treatment are unsuccessful, surgery may be necessary. The most common surgical technique for primary open-angle glaucoma is trabeculectomy (also known as filtration surgery). This involves making a flap

over a small hole in the outer wall of the eye (sclera), forming a new passage for aqueous humour to leave the eye.

Non-penetrating surgical techniques have also been developed that avoid permanent, full-thickness penetration into the anterior chamber of the eye. In viscocanalostomy, a block of sclera is removed to leave a thin membrane through which the aqueous humour percolates and a thick fluid (viscoelastic) is injected into Schlemm's canal to dilate a portion of it. Deep sclerectomy is similar to viscocanalostomy but it usually involves insertion of an implant under the scleral flap.

Glaucoma drainage devices (also known as tube shunts) are sometimes used to treat glaucoma that does not respond to trabeculectomy. The drainage tube is inserted into the anterior chamber of the eye through an incision in the sclera. This allows fluid to drain out of the eye into a special reservoir under the conjunctiva, and it is then absorbed back into the bloodstream.

What the procedure involves

Canaloplasty is a non-penetrating surgical technique that is similar to viscocanalostomy. It may be performed under local or general anaesthetic. A superficial flap and a deeper flap are made in the sclera and Schlemm's canal is exposed. A microcatheter with an illuminated tip is introduced into the entrance of the canal and advanced through the entire circumference of the canal. As the catheter tip is advanced, viscoelastic is injected into the canal to dilate it. After catheterisation of the entire canal length is complete, a suture is tied to the distal tip and the microcatheter is withdrawn, pulling the suture into the canal. The suture is cut from the microcatheter and tied in a loop encircling the inner wall of the canal. The suture is tightened to distend the trabecular meshwork inwards and keep the canal open. The deep scleral flap is excised and the superficial flap is tightly sutured. The aim of the procedure is to restore the natural drainage of fluid from the eye. A special ultrasound imaging system is used to help identify the canal and visualise the instruments in the canal before, during and after the surgery.

Efficacy

In one case series of 94 patients, successful circumferential catheterisation of the Schlemm's canal was achieved in 88% (83/94) of patients and a suture was successfully placed in the canal in 79% (74/94) of patients[1]. The mean baseline intraocular pressure was reduced from 24.7 mmHg at baseline to 15.3 mmHg at 12-month follow-up ($p < 0.05$). The mean number of intraocular pressure-lowering medications was reduced from 1.9 at baseline to 0.6 at 12-month follow-up. Furthermore, 61% (35/57) and 65% (31/48) of patients with successful suture placement who were not receiving intraocular pressure (IOP)-lowering medication at baseline had an IOP of 21 mmHg or lower after 3 months and 6 months, respectively. For patients who may or may not have continued receiving IOP-lowering medication, the corresponding rates were 88% (50/57) at 3 months and 96% (46/48) at 12 months. Four patients had poor intraocular pressure control after canaloplasty and required subsequent trabeculectomy.

Safety

The case series of 94 patients reported ocular-related complications including hyphema (the presence of blood in the anterior chamber) (3%), elevated intraocular pressure (3%), detachment of the Descemet's membrane (1%), hypotony (abnormally low intraocular pressure) (1%), choroidal effusion (1%) and exposed closure suture (1%)[1].

Some patients experienced a transient visual acuity decline after canaloplasty. At 1-month follow-up, 25% (18/71) of patients had lost two or more lines of best corrected visual acuity (BCVA) but this proportion was reduced to 7% (5/68) of patients at 3 months. At 12-month follow-up, 9% (4/47) of patients had lost two or more lines of best corrected visual acuity. The study authors noted that the decline in visual acuity in these patients was related to disease processes and not associated with the canaloplasty procedure.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to canaloplasty for primary open-angle glaucoma. Searches were conducted via the following databases, covering the period from their commencement to 23/10/2007: 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 these 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, laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising methodology.
Patient	Patients with primary open-angle glaucoma
Intervention/test	Canaloplasty
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.

List of studies included in the overview

This overview is based on one case series of 94 patients[1].

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.

Existing reviews related to this procedure

The Royal College of Ophthalmologists published guidelines on the management of open-angle glaucoma and ocular hypertension in 2004[2]. The guidelines state that the current operation of choice is trabeculectomy but that patients should be informed about the increased risk of cataract and long-term risk of blebitis and endophthalmitis associated with this procedure. With regard to non-penetrating glaucoma surgery, such as viscocanalostomy and deep sclerectomy, it stated that 'at the present time there is insufficient evidence from prospective studies that these operations have a lower incidence of long-term complications while maintaining good IOP [intraocular pressure] control to advocate their use in routine glaucoma practice.' These guidelines are due to be updated by June 2008.

A Cochrane review on medical versus surgical interventions for open-angle glaucoma was published in 2004[3]. The report included four trials (three on trabeculectomy and one on Scheie's procedure) with a total of 888 patients. The review concluded that 'for mild open angle glaucoma, the risk of progressive visual field damage is minimal and not significantly different at 5 years follow-up when primary contemporary medical treatment is compared to trabeculectomy. In early glaucoma primary trabeculectomy is associated with more local eye symptoms, a higher incidence of cataract and reduced visual acuity at up to 5-year follow-up. The comparative effectiveness of such treatments in more advanced glaucoma is not known.' No trials comparing medical therapy with non-penetrating glaucoma surgery were found.

A recent review summarised 10 randomised studies comparing trabeculectomy with viscocanalostomy and deep scelerectomy[4]. The review concluded that non-penetrating glaucoma drainage surgery (NPGDS) had a lower immediate and long-term complication rate compared with trabeculectomy, particularly with regard to cataract formation. According to most of the randomised controlled trials, however, NPGDS was considerably less effective in lowering the intraocular pressure in an intermediate time period such as 3-7 years. It stated that 'with the need for target IOPs [intraocular pressures] in the low teens for advanced glaucoma damage, NPGDS may not be adequate to halt progression.' The author noted that there is a need for further research on NPGDS to improve the learning curve and efficacy of the procedures.

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B details the recommendations made in each piece of guidance listed below.

Interventional procedures:

None

Technology appraisals:

None

Clinical guidelines:

A clinical guideline on glaucoma is currently in development and due to be published in April 2009. The scope includes the effectiveness of penetrating and non-penetrating surgical drainage procedures with and without pharmacological augmentation or drainage devices.

Public health:

None

Table 2 Summary of key efficacy and safety findings on canaloplasty for primary open angle glaucoma

Abbreviations used: IOP, intraocular pressure; POAG, primary open angle glaucoma; SD, standard deviation

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Lewis RA (2007)[1]

Case series (multicentre, prospective)

United States, Germany

Study period: not stated

n = 94 patients

Population: adult patients with open-angle glaucoma

56% (53/94) women

Mean age = 69 years (range 38–89)

Diagnosis:
POAG = 89% (88/94)
Exfoliation glaucoma = 7% (7/94)
POAG mixed with another type of glaucoma = 3% (3/94)
Pigmentary dispersion glaucoma = 1% (1/94)

Mean baseline intraocular pressure (IOP) = 24.7 mmHg (range 16–36)

30% (28/94) patients were on three or more IOP-lowering medications at baseline.</td>
<td>Successful circumferential catheterisation of the canal = 88% (83/94)
Successful placement of tension sutures = 79% (74/94)

Reasons for not inserting a suture: 15 cases had device/anatomical issues (for example, microcatheter tip meeting resistance during catheterisation); in one patient the Schlemm’s canal could not be located; one patient had respiratory failure on the operating table and the procedure was not completed; the paper reported that the remaining three cases did not have detailed information on why the suture was not placed.

IOP results for all patients (group 1)
<table>
<tr><th></th><th>Number of patients</th><th>Mean IOP ± SD (mmHg)</th><th>Range (mmHg)</th></tr>
<tr><td>Baseline</td><td>94</td><td>24.7 ± 4.8</td><td>16–36</td></tr>
<tr><td>3 months</td><td>73</td><td>16.5 ± 4.9</td><td>5–30</td></tr>
<tr><td>6 months</td><td>76</td><td>15.7 ± 4.2</td><td>8–30</td></tr>
<tr><td>12 months</td><td>59</td><td>15.3 ± 3.9</td><td>8–24</td></tr>
</table>
IOP results for patients with suture placement (group 2)
<table>
<tr><th></th><th>Number of patients</th><th>Mean IOP ± SD (mmHg)</th><th>Range (mmHg)</th></tr>
<tr><td>Baseline</td><td>74</td><td>23.9 ± 4.3</td><td>16–36</td></tr>
<tr><td>3 months</td><td>57</td><td>16.1 ± 4.7</td><td>5–30</td></tr>
<tr><td>6 months</td><td>59</td><td>15.6 ± 4.0</td><td>8–29</td></tr>
<tr><td>12 months</td><td>48</td><td>15.3 ± 3.8</td><td>8–24</td></tr>
</table>
</td>
<td>Bleb formation
At one or more follow-up examinations, 11 patients (12%) had a subconjunctival bleb. Six blebs resolved at 3 months and one at 12 months; four patients still had blebs at the last examination.

Ocular related complications
Hyphema = 3.2% (3/94)
Elevated IOP = 3.2% (3/94)
Descemet’s membrane detachment = 1.1% (1/94)
Hypotony = 1.1% (1/94)
Choroidal effusion = 1.1% (1/94)
Exposed closure suture with eyelid oedema and erythema epiphora = 1.1% (1/94)
Six of these complications were categorised as ‘mild’, four were ‘moderate’ and one was ‘severe’.

Loss of two or more lines best corrected visual acuity:
26% (19/73) at 1 week
25% (18/71) at 1 month
7% (5/68) at 3 months
8% (5/64) at 6 months
9% (4/47) at 12 months</td>
<td>14 clinical sites and 16 surgeons were involved in the study.

4% (4/94) patients were terminated early from the study: one respiratory failure during surgery; two deaths during postoperative period; one loss to follow-up.

12 month results are only presented for 63% (59/94) of patients.

Results for patients with successful suture placement were analysed separately (group 2).

The use of IOP-lowering medications was not discontinued before study enrolment.

Some of the study investigators acknowledged that the learning curve caused procedural failure in some patients.

The text of the paper states that there were 11 ocular related complications but only 10 were listed in a table.</td>
</tr>
</table>

Abbreviations used: IOP, intraocular pressure; POAG, primary open angle glaucoma; SD, standard deviation

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Indications: inclusion criteria were age 18 years or older; ability to understand and provide informed consent; glaucoma diagnosis of POAG, pigmentary glaucoma, exfoliation glaucoma or POAG mixed with another mechanism; IOP of 16 mm Hg or higher taken within 60 days of surgery (baseline) and a maximum historical IOP 21 mm Hg or higher. Patients with more than two laser trabeculoplasty procedures or a history of angle closure were excluded. Only one eye per patient was eligible.

Technique: ultrasound biomicroscopy images were obtained for some patients preoperatively, intraoperatively and postoperatively (depending on availability). 27 patients had cataract extraction with intraocular lens implantation at the same time as canaloplasty.

Follow-up: 12 months

Conflict of interest: the study was supported by a medical device company (iScience Interventional) and three authors are consultants to the same company.</td>
<td>One-way analysis of variance (ANOVA) confirmed that there was a statistically significant difference in IOP between baseline and follow-up visits in both groups of patients ($p < 0.05$ for each follow-up visit).

Success rate (with or without medication) in group 1
<table>
<tr><th>IOP (mm Hg)</th><th>3 months (n = 73)</th><th>6 months (n = 76)</th><th>12 months (n = 59)</th></tr>
<tr><td>≤ 21</td><td>84%</td><td>93%</td><td>95%</td></tr>
<tr><td>≤ 18</td><td>68%</td><td>76%</td><td>78%</td></tr>
<tr><td>≤ 15</td><td>42%</td><td>51%</td><td>47%</td></tr>
</table>
Success rate (with or without medication) in group 2
<table>
<tr><th>IOP (mm Hg)</th><th>3 months (n = 57)</th><th>6 months (n = 59)</th><th>12 months (n = 48)</th></tr>
<tr><td>≤ 21</td><td>88%</td><td>93%</td><td>96%</td></tr>
<tr><td>≤ 18</td><td>70%</td><td>78%</td><td>79%</td></tr>
<tr><td>≤ 15</td><td>42%</td><td>53%</td><td>50%</td></tr>
</table>
The mean number of IOP-lowering medications dropped from 1.9 (range 0–5) at baseline to 0.6 (range 0–3) at 12 months.
Four patients had poor IOP control and required subsequent conversion trabeculectomy (paper does not state whether these patients had successful placement of tension suture)</td>
<td>One of the four patients with significant visual acuity loss at 12 months was in the combined surgery group; one patient was diagnosed with epiretinal membrane approximately 6 months after surgery; one patient had extreme dry eye, resulting in corneal epithelial degradation.

12 nonocular adverse events occurred and were determined to be not related to the canaloplasty procedure (back fracture, death due to natural causes, dizziness, dry mouth, indigestion, nasal congestion, respiratory failure, and tinnitus).</td>
<td>Although the paper presents results separately for patients not on medication, the denominators used are the same as the whole group. The results have not been presented here as the figures cannot be reconciled.</td>
</tr>
</table>

Validity and generalisability of the studies

- The single study was not randomised and did not have a control group.
- The study had a relatively short follow-up period of 12 months.

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.

Mr N Anand, Mr P Wishart

- One Specialist Adviser described canaloplasty as a minor variation of an existing procedure which is unlikely to alter that procedure's safety and efficacy. Another described it as definitely novel and of uncertain safety and efficacy (but stated that canaloplasty is an additional step to viscocanalostomy).
- Appropriate comparators would be viscocanalostomy and deep sclerectomy.
- There are uncertainties about long-term efficacy in lowering eye pressure.
- Key efficacy outcomes include lowering of eye pressure (without causing hypotony), preservation of visual fields and ocular comfort.
- Theoretical adverse events include immediate and possibly sustained rise in eye pressure; anterior chamber perforation; tearing of Descemet's membrane with resultant corneal opacification, or retinal damage; formation of cataract; exposure of suture with endophthalmitis; bleb formation with endophthalmitis; hypotony (low pressure with collapse of the eye); suture may give rise to intraocular inflammation.
- Adverse events reported in the literature include hypotony, Descemet's membrane tear, choroidal effusion, and severe elevation in intraocular pressure to more than 30 mmHg.
- Canaloplasty is an additional step to an already established procedure - viscocanalostomy. Therefore, any audit will not be able to tell if the success of the procedure is due to the additional step or despite the additional step. To establish clear benefit would require a randomised

controlled trial of viscocanalostomy versus viscocanalostomy plus canaloplasty.

- Adverse events for audit include failure to control intraocular pressure, loss of visual acuity and intraocular inflammation. Visual field analysis would be required to determine if deleterious effect on fields occurred due to postoperative ocular hypertension.
- There is a learning curve and significant training is required.
- The potential impact on the NHS is minor in terms of numbers of patients eligible for treatment and use of resources.
-

Issues for consideration by IPAC

None other than those described above.

References

1. Lewis RA, Von Wolff K, Tetz M et al. (2007) Canaloplasty: circumferential viscodilation and tensioning of Schlemm's canal using a flexible microcatheter for the treatment of open-angle glaucoma in adults. Journal of Cataract and Refractive Surgery 33: 1217–26.
2. The Royal College of Ophthalmologists. (2004) Guidelines for the management of open angle glaucoma and ocular hypertension. Available from www.rcophth.ac.uk (accessed 16/11/2007).
3. Burr J, Azuara-Blanco A, Avenell A. (2004) Medical versus surgical interventions for open angle glaucoma. Cochrane Database of Systematic Reviews Issue 2. Art No.:CD004399. DOI: 10.1002/14651858.
4. Grehn F (2005) Comparison of trabeculectomy with non-penetrating drainage glaucoma surgery in open-angle glaucoma. In: Weinreb RN and Crowston JG, editors *Glaucoma Surgery. Open Angle Glaucoma.* The Netherlands: Kugler Publications, p 109–116.

Appendix A: Additional papers on canaloplasty for primary open-angle glaucoma not included in summary table 2

The following table outlines studies considered potentially relevant to the overview not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article title	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
No additional studies were identified			

Appendix B: Related published NICE guidance for canaloplasty for primary open-angle glaucoma

Guidance programme	Recommendation
Interventional procedures	None applicable
Technology appraisals	None applicable
Clinical guidelines	None applicable
Public health	None applicable

Appendix C: Literature search for canaloplasty for primary open-angle glaucoma

Database	Date searched	Version searched
Cochrane Library	22/10/2007	Issue 3, 2007
CRD databases (DARE & HTA)	21/10/2007	Issue 3, 2007
Embase	23/10/2007	1980 to 2007 Week 42
Medline	23/10/2007	1950 to October Week 2 2007
Premedline	23/10/2007	October 22, 2007
CINAHL	23/10/2007	1982 to August Week 3 2007
British Library Inside Conferences	23/10/2007	_
NRR	23/10/2007	2007 Issue 3
Controlled Trials Registry	23/10/2007	_

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

1	Canaloplast$.tw.
2	Viscocanalost$.tw.
3	Phaco-viscocanalost$.tw.
4	phacoviscocanalost$.tw.
5	or/1-4
6	Open Angle Glaucoma/
7	Glaucoma/
8	Glaucom$.tw.
9	(open$ adj3 angle$ adj3 glaucoma$).tw.
10	((ocular$ or Intraocul$) adj3 hypertens$).tw.
11	Ocular Hypertension/
12	Intraocular Pressure/
13	(Intraocul$ adj3 pressur$).tw.
14	or/6-13
15	5 and 14
16	Animals/
17	Humans/
18	16 not (16 and 17)
19	15 not 18