Glaucoma: acute and chronic primary angle-closure

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ABSTRACT

INTRODUCTION: Glaucoma is characterised by progressive optic neuropathy and peripheral visual field loss. The main risk factor for glaucoma is elevated intraocular pressure. This overview is focused on primary acute angle-closure and primary chronic angle-closure glaucoma. The number of people diagnosed with primary angle-closure glaucoma is predicted to rise over the next few years due to an increasingly ageing population and increased awareness of the condition. METHODS AND OUTCOMES: We conducted a systematic overview, aiming to answer the following clinical questions: What are the effects of treatments for primary acute angle-closure glaucoma? What are the effects of treatments for primary chronic angle-closure glaucoma? We searched: Medline, Embase, The Cochrane Library, and other important databases up to February 2014 (BMJ Clinical Evidence overviews are updated periodically; please check our website for the most up-to-date version of this overview). RESULTS: At this update, searching of electronic databases retrieved 683 studies. After deduplication and removal of conference abstracts, 490 records were screened for inclusion in the overview. Appraisal of titles and abstracts led to the exclusion of 467 studies and the further review of 23 full publications. Of the 23 full articles evaluated, three systematic reviews and one RCT were added at this update. We performed a GRADE evaluation for two PICO combinations. CONCLUSIONS: In this systematic overview, we categorised the efficacy for six interventions based on information about the effectiveness and safety of laser treatment (iridotomy or iridoplasty), medical treatments (any route), and surgical treatments (any) to treat people with either primary acute or primary chronic angle-closure glaucoma.

QUESTIONS

INTERVENTIONS

PRIMARY ACUTE ANGLE-CLOSURE GLAUCOMA

Likely to be beneficial

Unknown effectiveness

PRIMARY CHRONIC ANGLE-CLOSURE GLAUCOMA

Unknown effectiveness

Footnote

*No placebo-controlled RCTs found, but there is a strong consensus that treatments are effective

Key points

- Glaucoma is characterised by progressive optic neuropathy and peripheral visual field loss. It affects 1% to 2% of white people aged over 40 years and accounts for 8% of new blind registrations in the UK.

  The main risk factor for glaucoma is raised intraocular pressure (IOP).

  There are two main anatomical types of glaucoma, open angle and closed angle, where the trabecular meshwork (through which fluid drains from the anterior chamber of the eye) is open or closed, respectively. Previous versions of this overview included open-angle glaucoma and normal-tension glaucoma. However, this overview focuses on primary closed-angle glaucoma only. We searched for evidence from RCTs and systematic reviews of RCTs only.

  The presentation of primary angle-closure glaucoma can be acute, with sudden painful vision loss. This acute type is considered an ophthalmic emergency, although it has a good prognosis if treated promptly. Although termed 'glaucoma', not all patients will have damage to their optic nerve or glaucomatous field loss.

  Chronic primary angle-closure glaucoma usually presents painlessly but has a high incidence of permanent bilateral visual loss. Small eyes, which are usually long sighted, give a predisposition to angle closure, and Asian populations have a higher prevalence.

  Overall, we found few RCTs on the interventions considered in this overview. There is a need for further high-quality RCTs in this field to inform clinical practice.

- There is a consensus that medical and surgical treatments are beneficial in people with primary acute angle-closure glaucoma, although we don't know this for sure based on RCT evidence because it is unethical to withhold pressure-lowering treatment.

- Concerning laser treatment for primary acute angle-closure glaucoma:

  We don't know whether laser iridotomy is more effective than surgical iridectomy at preventing deterioration of visual acuity at 3 years in people with uniocular acute angle-closure glaucoma.

  The consensus about how laser iridoplasty compares with medical or surgical treatments in people with primary acute angle-closure glaucoma is currently uncertain, and more high-quality evidence is needed. We only found one small RCT, and it didn't report on adverse effects.

- We found no RCTs on the effects of medical treatment versus no treatment for people with primary chronic angle-closure glaucoma, or on the effects of surgical treatment versus no treatment.
- One small RCT found no significant difference in visual outcomes at 1 year between laser peripheral iridoplasty plus laser peripheral iridotomy versus laser peripheral iridotomy alone in people with primary chronic angle-closure glaucoma, but there is a need for further RCTs to draw robust conclusions.

Clinical context

GENERAL BACKGROUND

Glaucoma is the most common cause of irreversible blindness. There are two main anatomical types of glaucoma, open angle and closed angle. The number of people diagnosed with primary angle-closure glaucoma is predicted to rise over the next few years. This is due to an increasingly ageing population worldwide and increased awareness of the condition. The population growth in Asia, where angle-closure glaucoma is as common as open-angle glaucoma, has a particular influence on diagnosis rates. It has been estimated that by the year 2020, more than 20 million people will be affected by angle-closure glaucoma, of which 5 million people will be blind.

FOCUS OF THE REVIEW

This overview examines the high-quality RCT evidence available on primary acute angle-closure glaucoma and primary chronic angle-closure glaucoma. We examined the effects of medical treatments, surgical treatments, and laser treatments (iridotomy and iridoplasty). We compared medical and surgical treatments with no treatment and medical, surgical, and laser treatments with each other.

COMMENTS ON EVIDENCE

We found few RCTs comparing different treatments with no treatment or with each other. The trials we did find were small and of limited quality. There is a need for further high-quality RCTs in this field. Further trials are under way, and their results awaited (e.g., the EAGLE trial, which will compare cataract surgery to the standard treatment, including laser iridotomy for people with newly diagnosed primary angle-closure glaucoma). One issue making evaluation of the evidence more difficult has been the lack of consistency over terminology for these conditions. Glaucoma is an optic neuropathy. In a patient with open angles, elevated pressure would be termed 'ocular hypertension', and only those with evidence of structural or functional changes to the nerve and field, respectively, would be described as having glaucoma. However, common text book definitions for acute angle closure glaucoma have included those with high pressure and scarring of the drainage channel but with no optic nerve or field changes. The use of the term 'glaucoma' to include those populations, with and without glaucomatous optic neuropathy or only those with optic neuropathy makes studies difficult to interpret and compare.

SEARCH AND APPRAISAL SUMMARY

The update literature search for this overview was carried out from the date of the last search, May 2010, to February 2014. A back search from 1966 was performed for the new options added to the scope at this update. For more information on the electronic databases searched and criteria applied during assessment of studies for potential relevance to the overview, please see the Methods section. Searching of electronic databases retrieved 683 studies. After deduplication and removal of conference abstracts, 490 records were screened for inclusion in the review. Appraisal of titles and abstracts led to the exclusion of 467 studies and the further review of 23 full publications. Of the 23 full articles evaluated, three systematic reviews and one RCT were added at this update.

DEFINITION

Glaucoma is a group of diseases characterised by progressive optic neuropathy. It is the most common cause of irreversible blindness. [1] There are two main anatomical types of glaucoma: open angle and closed angle. The trabecular meshwork (through which fluid drains from the anterior chamber of the eye) is open in people with open-angle glaucoma and closed in people with closed-angle glaucoma. **Primary open-angle glaucoma** occurs in people with an open anterior chamber drainage angle and no secondary identifiable cause. This overview focuses on primary closed-angle glaucoma only. **Primary chronic angle closure** is due to obstruction of the outflow of the anterior chamber, and may be accompanied by a rise in intraocular pressure (IOP). The obstruction of outflow is due to contact of the iris with the trabecular meshwork and this is usually identified by the examination technique of goniscopy. Iridotrabecular contact and obstruction of more than half of the trabecular meshwork drainage channel is defined as a closed angle. Advanced

imaging techniques of the anterior segment can also identify the closure. Primary angle closure is staged and defined as glaucoma when there is evidence of glaucomatous optic neuropathy (please see 'Inconsistency in terminology' for further discussion). Chronic primary angle closure usually presents painlessly. Treatment of pressure is with IOP-lowering medication. However, the underlying mechanism of primary angle closure is treated with pilocarpine to constrict the pupil and laser or surgical peripheral iridotomy to relieve pupil block. More recently, elective lens extraction is being evaluated in an ongoing RCT because this may increase the capacity of the anterior chamber and open the drainage angle. This has been proposed for both acute and chronic angle closure. **Primary acute angle closure** is a sudden rapid rise in IOP due to obstruction of the outflow of the anterior chamber. The presentation is acute, usually with pain, and may be associated with sudden vision loss. This is considered an ophthalmic emergency. Secondary angle closure (not covered in this overview) requires treating the pressure, underlying cause, and usually dilation of the pupil. **Inconsistency in terminology** Clinicians commonly use the term 'glaucoma' in the context of angle closure, even without evidence of nerve or field damage, especially in acute cases. Although the term 'glaucoma' should be used where there is evidence of optic neuropathy, older papers and text books have used the term 'acute angle closure glaucoma' to describe the mechanism of angle closure in the presence of elevated pressure with occlusion of the outflow mechanism, either by pupil block causing the peripheral iris to move forward and/or peripheral adhesion of the iris to the drainage channel caused by intracocular inflammation, as in secondary angle closure. But, in the absence of glaucomatous optic neuropathy, this is now termed 'primary or secondary angle closure'. The new definition proposes to distinguish between the mechanism (i.e., closed or open angle), by which IOP becomes elevated and the resultant damage that is caused by primary angle closure glaucoma. [2] **Population for this overview** We have used the terminology as reported in the trials and, where possible, have retrieved detail on presence or absence of evidence of optic neuropathy and added this information to our reporting. For the question, What are the effects of treatments for primary acute angle-closure glaucoma?, the population included people with acute primary angle-closure glaucoma (resulting from a rapid and severe rise in intraocular pressure caused by physical obstruction of the anterior chamber drainage angle), including people with any comorbid conditions, but excluding people with secondary primary angle-closure glaucoma. For the question, What are the effects of treatments for primary chronic angle-closure glaucoma?, the population included people with chronic primary angle-closure glaucoma (resulting from slow rise in intraocular pressure caused by physical obstruction of the anterior chamber drainage angle), including people with any comorbid conditions, but excluding people with secondary chronic angle-closure glaucoma.

INCIDENCE/ PREVALENCE

Glaucoma (all types) occurs in 1% to 2% of white people aged over 40 years, rising to 5% at 70 years. Primary open-angle glaucoma accounts for two-thirds of those affected, and normal-tension glaucoma for about one quarter. [3] [4] Glaucoma-related blindness is responsible for 8% of new blind registrations in the UK. [5] Primary angle-closure glaucoma occurs at about one tenth of the frequency of open-angle glaucoma in white Europeans, with a prevalence of 0.4% in people who are over 40 years and of European ancestry. [6] It is more common in Chinese people. [7] The number of people diagnosed with primary angle-closure glaucoma is predicted to rise over the next few years. This is due to an increasingly ageing population worldwide, and an increased awareness of the condition. The population growth in Asia particularly has an influence on diagnosis rates. It has been estimated that by the year 2020, over 20 million people will be affected by angle-closure glaucoma, of which 5 million people will be blind. [8]

AETIOLOGY/ RISK FACTORS

Angle closure is a result of the iris being in contact with the trabecular meshwork. Risk factors for angle closure include Asian ethnicity, family history, female sex, being long-sighted, large lens, cataracts, and older age. One systematic review (search date 1999, 6 observational studies, 594,662 people with mydriasis) found no evidence supporting the theory that routine pupillary dilatation with short-acting mydriatics was a risk factor for acute angle-closure glaucoma. [9]

PROGNOSIS

Primary acute angle closure is considered an ophthalmic emergency, although it has a good prognosis if treated promptly. Chronic primary angle closure has a high incidence of permanent bilateral visual loss.

AIMS OF INTERVENTION

To prevent progression of visual field loss and to minimise adverse effects of treatment.

OUTCOMES

Disease progression onset or progression of glaucoma; visual acuity; visual fields. Optic disc cupping and IOP are surrogate outcomes, which we do not report in this review. However, some RCTs reported combined outcomes including these measures. In these cases, we report these surrogate outcomes as part of the combined outcome reported. **Adverse effects**.

METHODS

Search strategy *BMJ Clinical Evidence* search and appraisal date February 2014. Databases used to identify studies for this systematic overview include: Medline 1966 to February 2014, Embase

1980 to February 2014, The Cochrane Database of Systematic Reviews 2014, issue 1 (1966 to date of issue), the Database of Abstracts of Reviews of Effects (DARE), and the Health Technology Assessment (HTA) database. **Inclusion criteria** Study design criteria for inclusion in this systematic overview were systematic reviews and RCTs published in English, at least single-blinded, and containing 20 or more individuals (with a minimum of 10 in each arm), of whom more than 80% were followed up. There was no minimum length of follow-up. We excluded split eye studies (that is, a study in which one eye of a person is allocated to one treatment, and the other eye gets another treatment). We excluded all studies described as 'open', 'open label', or not blinded unless blinding was impossible. We excluded any studies in people with secondary angle-closure glaucoma, where included populations were not clear or were mixed, and RCTs that did not report on our outcomes of interest. *BMJ Clinical Evidence* does not necessarily report every study found (e.g., every systematic review). Rather, we report the most recent, relevant, and comprehensive studies identified through an agreed process involving our evidence team, editorial team, and expert contributors. **Evidence evaluation** A systematic literature search was conducted by our evidence team, who then assessed titles and abstracts, and finally selected articles for full text appraisal against inclusion and exclusion criteria agreed *a priori* with our expert contributor. In consultation with the expert contributor, studies were selected for inclusion and all data relevant to this overview extracted into the benefits and harms section of the overview. In addition, information that did not meet our pre-defined criteria for inclusion in the benefits and harms section may have been reported in the 'Further information on studies' or 'Comment' sections (see below). **Adverse effects** All serious adverse effects, or those adverse effects reported as statistically significant, were included in the harms section of the overview. Pre-specified adverse effects identified as being clinically important were also reported, even if the results were not statistically significant. Although *BMJ Clinical Evidence* presents data on selected adverse effects reported in included studies, it is not meant to be, and cannot be, a comprehensive list of all adverse effects, contraindications, or interactions of included drugs or interventions. A reliable national or local drug database must be consulted for this information. **Comment and Clinical guide sections** In the Comment section of each intervention, our expert contributors may have provided additional comment and analysis of the evidence, which may include additional studies (over and above those identified via our systematic search) by way of background data or supporting information. As *BMJ Clinical Evidence* does not systematically search for studies reported in the Comment section, we cannot guarantee the completeness of the studies listed there or the robustness of methods. Our expert contributors add clinical context and interpretation to the Clinical guide sections where appropriate. **Structural changes this update** At this update, we have removed the following previously reported questions: What are the effects of treatments for established primary open-angle glaucoma, ocular hypertension, or both? What are the effects of lowering intraocular pressure in people with normal-tension glaucoma? We have added the following new question: What are the effects of treatment for primary chronic angle-closure glaucoma? **Data and quality** To aid readability of the numerical data in our overviews, we round many percentages to the nearest whole number. Readers should be aware of this when relating percentages to summary statistics such as relative risks (RRs) and odds ratios (ORs). *BMJ Clinical Evidence* does not report all methodological details of included studies. Rather, it reports by exception any methodological issue or more general issue that may affect the weight a reader may put on an individual study, or the generalisability of the result. These issues may be reflected in the overall GRADE analysis. We have performed a GRADE evaluation of the quality of evidence for interventions included in this review (see table, p 13). The categorisation of the quality of the evidence (high, moderate, low, or very low) reflects the quality of evidence available for our chosen outcomes in our defined populations of interest. These categorisations are not necessarily a reflection of the overall methodological quality of any individual study, because the Clinical Evidence population and outcome of choice may represent only a small subset of the total outcomes reported, and population included, in any individual trial. For further details of how we perform the GRADE evaluation and the scoring system we use, please see our website (www.clinicalevidence.com).

QUESTION What are the effects of treatment for primary acute angle-closure glaucoma?

OPTION MEDICAL TREATMENT (ANY ROUTE) IN PRIMARY ACUTE ANGLE-CLOSURE GLAUCOMA

- For GRADE evaluation of interventions for Glaucoma: acute and chronic primary angle-closure, see table, p 13 .
- There is consensus that medical treatments are beneficial in people with primary acute angle-closure glaucoma, although we found no direct evidence from RCTs. This is unsurprising because it would be considered unethical to withhold pressure-lowering treatment. There are case reports of blindness from untreated raised intraocular pressure (IOP).

- We also found no direct evidence from RCTs comparing medical treatments with surgical or laser therapy (iridotomy or iridoplasy).

Benefits and harms

Medical treatment (any route) versus placebo or no treatment:

We found one systematic review (search date 2002), which identified no RCTs assessing our outcomes of interest. [10] We found no subsequent RCTs.

Medical treatment (any route) versus surgical treatment (any type) or laser (iridotomy or iridoplasty) treatment:

We found one systematic review (search date 2002), which identified no RCTs. [10] We found no subsequent RCTs.

High-dose pilocarpine versus low-dose pilocarpine:

We found one systematic review (search date 2002), which identified no RCTs. [10] We found no subsequent RCTs.

Comment:

Pressure-lowering treatment is given to patients with potential vision if the IOP is more than 30 mmHg, irrespective of the presence of glaucomatous optic neuropathy. This is because there is a higher risk of conversion to glaucoma at higher pressure, the nerve is more vulnerable to progression if there is already glaucomatous change, and there is an association with high pressure and retinal venous occlusion.

Clinical guide

RCTs comparing medical treatments with placebo are considered unethical. There is consensus that medical treatment with pressure-lowering drugs (especially those that can be given parenterally, such as IV acetazolamide) are effective in primary acute angle-closure glaucoma. We found no evidence from RCTs to support or challenge this view.

OPTION SURGICAL TREATMENT (ANY TYPE) IN PRIMARY ACUTE ANGLE-CLOSURE GLAUCOMA

- For GRADE evaluation of interventions for Glaucoma: acute and chronic primary angle-closure, see table, p 13 .
- We found no direct information from RCTs about whether surgical treatments (any type) are better than no active treatment.
- There is consensus that surgical treatments are beneficial in people with primary acute angle-closure glaucoma, although we don't know this for sure because it is unethical to withhold pressure-lowering treatment.
- We don't know how surgical peripheral iridectomy compares with Nd:YAG laser iridotomy, in terms of their effectiveness at preventing deterioration in visual acuity at 3 years in people with uniocular acute angle-closure glaucoma. We only found one small RCT.

Benefits and harms

Surgical treatment (any type) versus no treatment:

We found one systematic review (search date 2002), which identified no RCTs (see Comment). [10]

Surgical treatment (any type) versus laser treatment (iridotomy or iridoplasty):

We found one systematic review (search date 2002), including one RCT that met *BMJ Clinical Evidence* inclusion criteria comparing surgical peripheral iridectomy with Nd:YAG laser iridotomy. [10]

Disease progression

Surgical peripheral iridectomy compared with Nd:YAG laser iridotomy We don't know whether surgical iridectomy is more effective than laser iridotomy at preventing deterioration of visual acuity at 3 years in people with uniocular acute angle-closure glaucoma (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Vision					
[11] RCT	48 people with uniocular acute angle-closure glaucoma In review [10]	**Visual acuity , after 3 years** 0.30 logMAR units with peripheral iridectomy 0.57 logMAR units with Nd:YAG laser iridotomy	Reported as not significant P value not reported	⟷	Not significant

Adverse effects

No data from the following reference on this outcome. [10]

Surgical treatment (any type) versus medical treatment (any route):

We found one systematic review (search date 2002), which identified no RCTs. [10] We found no subsequent RCTs.

Comment:

Surgical peripheral iridectomy: further information on harms

Surgical iridectomy involves an open operation on the eye, with risk of serious complications including intraocular infection or haemorrhage. We found no published evidence quantifying these risks.

Clinical guide

Surgical peripheral iridectomy is a long-established treatment for angle-closure glaucoma whether acute, subacute, or chronic; the principle being the relief of relative pupil block with accumulation of aqueous humour behind the iris shallowing the anterior chamber and occluding the drainage angle. Consensus suggests that surgical treatments are effective in the treatment of acute angle-closure glaucoma. Management of acute angle-closure glaucoma is aimed at restoring flow of aqueous humour to the anterior chamber angle and adjacent trabecular meshwork. Surgical iridectomy is sometimes the only means of relieving pupil block in irises that are resistant to a laser iridotomy, and these are usually dark brown irises. Laser iridotomy is more accessible and requires less expertise. We don't know if prophylactic surgical iridectomy or laser iridotomy are effective at preventing angle closure in the fellow eye.

OPTION LASER TREATMENT (IRIDOTOMY OR IRIDOPLASTY) IN PRIMARY ACUTE ANGLE-CLOSURE GLAUCOMA

- For GRADE evaluation of interventions for Glaucoma: acute and chronic primary angle-closure, see table, p 13 .
- We searched for RCTs comparing laser treatments (iridotomy, iridoplasty) with medical or surgical treatments.
- We found no direct information from RCTs about whether laser treatments are better than medical treatment.
- We don't know how Nd:YAG laser iridotomy compares with surgical peripheral iridectomy in terms of effectiveness at preventing deterioration in visual acuity at 3 years in people with uniocular acute angle-closure glaucoma, as we found insufficient evidence from one small RCT to draw firm conclusions.
- The consensus about how laser iridoplasty compares with medical or surgical treatments in people with primary acute angle-closure glaucoma is currently uncertain, and more high-quality evidence is needed.

Benefits and harms

Laser treatment (iridotomy or iridoplasty) versus medical treatment (any route):

We found one systematic review (search date 2002), which identified no RCTs meeting *BMJ Clinical Evidence* inclusion criteria. [10] We found no subsequent RCTs in people with primary acute angle-closure glaucoma that reported on our outcomes of interest as primary outcomes (see Comment).

Laser treatment (iridotomy or iridoplasty) versus surgical treatment (any type):

See option on Surgical treatment in primary acute angle-closure glaucoma, p 5 .

Laser iridotomy versus laser iridoplasty:

We found no RCTs.

Comment:

One RCT (64 people, 73 eyes with first presentation of acute primary angle-closure glaucoma, not considered suitable for immediate laser peripheral iridotomy) compared argon laser peripheral iridoplasty versus conventional systemic medical treatment (acetazolamide [iv followed by oral] plus potassium [oral]). All people also received topical pilocarpine plus topical timolol before randomisation. This RCT did not report on our outcomes of interest for this *BMJ Clinical Evidence* overview as primary outcomes. However, we have included a brief comment from this RCT on reducing intraocular pressure, despite it being a surrogate outcome, because of the importance of relieving an acute attack in acute angle-closure glaucoma. The RCT found that argon laser peripheral iridoplasty significantly reduced intraocular pressure compared with standard medical treatment at 15 minutes, 30 minutes, and 1 hour after treatment. However, it found no significant difference between groups after 2 hours. [12]

Nd:YAG laser iridotomy: further information on harms

Nd:YAG laser iridotomy is associated with haemorrhage from the iris, pressure spikes, dysphotopsia, and corneal oedema. [13] [14]

Nd:YAG and argon laser iridotomy can produce focal, non-progressive lens opacity. [15] In one non-RCT, iris haemorrhage was more common with the Nd:YAG laser, but pupil distortion, iritis, and late blockage were more common with the argon laser. [16] One non-RCT found that the mean number of laser burns required to penetrate the iris was 6 with the Nd:YAG laser and 73 with the argon laser. [16] An iridotomy positioned superiorly or in the tear lake of the lid margin appears to be associated with a higher incidence of dysphotopsia. [14]

Screening and prophylactic laser peripheral iridotomy

A single-blinded RCT assessed the effect of screening and prophylactic laser peripheral iridotomy on the incidence of primary angle-closure glaucoma. It compared no screening with screening in 4597 Mongolian participants aged 50 years or older. Screening consisted of using ultrasound to measure central anterior chamber depth (cACD). If the measurement was less than 2.53 mm, participants were examined using gonioscopy, and if confirmed to have angle closure, treated with prophylactic laser peripheral iridotomy. Follow-up at 6 years found that, of the 2047 (53.92%) participants who were traced and had full follow-up ophthalmic examination, 33 had primary angle-closure glaucoma; 19 of these were in the screened group and 14 in the no-screening group (OR 1.29, 95% CI 0.65 to 2.60, P = 0.47). [17]

QUESTION What are the effects of treatment for primary chronic angle-closure glaucoma?

OPTION MEDICAL TREATMENT (ANY ROUTE) IN PRIMARY CHRONIC ANGLE-CLOSURE GLAUCOMA New

- For GRADE evaluation of interventions for Glaucoma: acute and chronic primary angle-closure, see table, p 13 .

- We don't know whether whether medical treatments (any) are better than no active treatment in people with primary chronic closed-angle glaucoma. We only found one RCT with small numbers in people with 'narrow angle'.

Benefits and harms

Medical treatment (any route) versus placebo or no treatment:

We found one systematic review (search date 2002), [10] which found one RCT that did not meet our inclusion criteria because the participants did not have structural or functional evidence to diagnose glaucoma (they had normal visual fields and normal optic discs). However, we have added information on this RCT to the Comment section, p 7 for interest.

Medical treatment (any route) versus surgical treatment (any type):

We found two systematic reviews (search dates 2002; [10] and 2005 [18]), which found no RCTs. We found no subsequent RCTs.

Medical treatment (any route) versus laser (iridotomy or iridoplasty) treatment:

We found two systematic reviews (search dates 2002; [10] and 2012 [19]), which identified no RCTs. We found no subsequent RCTs.

High-dose pilocarpine versus low-dose pilocarpine:

We found one systematic review (search date 2002), which found no RCTs. [10] We found no subsequent RCTs.

Comment:

The systematic review [10] included one RCT comparing timolol with no treatment in 25 participants described as having 'narrow angles', intra-ocular pressure (IOP) of more than 21 mmHg, normal visual fields, and optic discs. It found no significant differences in mean IOP or visual field loss between the two groups at 66 months follow-up (no P value reported in the systematic review).

Clinical guide

Pilocarpine treats the underlying mechanism of pupil block. It relieves this by constricting the pupil, so relieving the apposition of the iris to the convex-shaped lens. Unfortunately it is poorly tolerated as it causes eye pain and a change in refraction. Conversely, in some patients it can worsen the angle closure configuration by shortening the anterior position of the lens through ciliary body rotation.

OPTION SURGICAL TREATMENT (ANY TYPE) IN PRIMARY CHRONIC ANGLE-CLOSURE GLAUCOMA

New

- For GRADE evaluation of interventions for Glaucoma: acute and chronic primary angle-closure, see table, p 13 .
- We found no direct information from RCTs about whether surgical treatments (any type) are better than no active treatment.

Benefits and harms

Surgical treatment (any type) versus no treatment:

We found two systematic reviews (search dates 2002; [10] and 2005 [18]), which found no RCTs.

Surgical treatment (any type) versus medical treatment (any route):

We found two systematic reviews (search dates 2002; [10] and 2005 [18]), which found no RCTs. We found no subsequent RCTs.

Surgical treatment (any type) versus laser (iridotomy or iridoplasty) treatment:

We found two systematic reviews (search dates 2005; [18] and 2012 [19]), which found no RCTs. We found no subsequent RCTs.

Comment: For further information on surgical peripheral iridectomy, please see Comment section in option on Surgical treatment (any type) in primary acute angle-closure glaucoma, p 5 .

OPTION LASER TREATMENT (IRIDOTOMY OR IRIDOPLASTY) IN PRIMARY CHRONIC ANGLE-CLOSURE GLAUCOMA New

- For GRADE evaluation of interventions for Glaucoma: acute and chronic primary angle-closure, see table, p 13 .
- We found no direct information from RCTs about whether laser treatments (iridotomy or iridoplasty) are better than surgery or medical treatments in people with primary chronic angle-closure glaucoma.
- We don't know whether laser peripheral iridoplasty plus laser peripheral iridotomy differs from laser peripheral iridotomy alone in preventing disease progression at 1 year, as we found insufficient evidence from one small RCT.

Benefits and harms

Laser treatment (iriotomy or iridoplasty) versus medical treatment (any route):

We found two systematic reviews (search dates 2002; [10] and 2012 [19]), which identified no RCTs. We found no subsequent RCTs.

Laser treatment (iriotomy or iridoplasty) versus surgical treatment (any type):

We found two systematic reviews (search dates 2005; [18] and 2012 [19]), which found no RCTs. We found no subsequent RCTs.

Laser peripheral iridoplasty plus laser peripheral iridotomy versus laser peripheral iridotomy alone:

We found one systematic review (search date 2012), [19] which identified one RCT [20] that included 158 people aged 40 years or older in Bejing, China.

Disease progression

Laser peripheral iridoplasty plus laser peripheral iridotomy compared with laser peripheral iridotomy alone We don't know whether laser peripheral iridoplasty plus laser peripheral iridotomy differs from laser peripheral iridotomy alone in effectiveness at preventing disease progression at 1 year in people with synechial primary angle closure or primary angle-closure glaucoma (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Disease progression					
[20] RCT	158 people (158 eyes) with synechial primary angle-closure or primary angle-closure glaucoma (absolute numbers of each not reported) In review [19]	**Median best corrected visual acuity (BCVA, quartile range) , 1 year** 0.20 logMAR units with laser peripheral iridoplasty plus laser peripheral iridotomy 0.20 logMAR units with laser peripheral iridotomy alone 126/158 (80%) people in this analysis	P = 0.431	⟷	Not significant
[20] RCT	158 people (158 eyes) with synechial primary angle-closure or primary angle-closure glaucoma (absolute numbers of each not reported) In review [19]	**Visual field mean deviation (categorised as <6 dB, 6dB–<12 dB, 12 dB or greater) , 1 year** with laser peripheral iridoplasty plus laser peripheral iridotomy with laser peripheral iridotomy alone Absolute results not reported 126/158 (80%) people in this analysis	P = 0.674	⟷	Not significant

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Corneal decompensation					
[20] RCT	158 people (158 eyes) with synechial primary angle-closure or primary angle-closure glaucoma (absolute numbers of each not reported) In review [19]	**Corneal endothelial cell count (per mm^2) , 1 year** 2610 with laser peripheral iridoplasty plus laser peripheral iridotomy 2704 with laser peripheral iridotomy alone 126 people in this analysis	Reported as not significant P value not reported	⟷	Not significant

Further information on studies

[19] The method of randomisation was described, while the review reported that the RCT [20] was at high risk of bias for blinding of participants and outcome assessment as the RCT was unblinded. The review noted that follow-up was 79.2% in the iridotomy group and 80.2% in the iridotomy plus iridoplasty group, while the reasons for loss to follow-up were not reported.

Comment: One prospective clinical trial compared long-term outcomes of neodymium:YAG (Nd:YAG) and argon laser iridotomies in 43 participants with bilateral chronic pupillary-block glaucoma. Each participant had one eye assigned to receive argon laser therapy and the other eye assigned to receive Ng:YAG laser therapy. At between 20 and 42 months follow-up, the trial reported no significant differences between the interventions. However, more participants who were treated with argon laser therapy required re-treatment. [21] A further clinical trial compared pre-treatment using a

532 nm continuous-wave Nd:YAG (frequency-doubled) green laser with no pre-treatment (standard treatment) in people with occludable anterior chamber angles and dark irides undergoing bilateral standard pulsed 1064 nm Nd:YAG laser iridotomy. It found higher rates of iris haemorrhage in people receiving standard treatment compared with the intervention with pre-treatment (43% in the standard treatment group; 13% in the pre-treatment group [P = 0.0126]). [22]

Clinical guide
Iridoplasty is considered to have a place in the management of primary angle closure with plateau iris configuration.

GLOSSARY

Drainage angle Area in the anterior chamber of the eye where the iris meets the sclera, and where fluid from the aqueous humour drains by the trabecular meshwork.

Laser iridotomy Involves making a hole in the base of the iris (without opening the eye) using either an argon or Nd:YAG laser.

Surgical iridectomy Opening the eye at the corneal limbus and removing a triangle of tissue from the base of the iris.

Argon laser iridoplasty A procedure that involves placing circumferential argon laser burns (approximately 16–20 burns) in the peripheral iris to induce a contraction and pulling away of the peripheral iris from the drainage angle with the aim of opening the angle.

Dysphotopsia Disturbed vision that includes a light phenomenon, such as a subjective halo or streak of light in the vision.

Low-quality evidence Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

SUBSTANTIVE CHANGES

Medical treatment (any route) in primary chronic angle-closure glaucoma New option. Three systematic reviews added. [10] [18] [19] Categorised as 'unknown effectiveness'.

Surgical treatment (any type) in primary chronic angle-closure glaucoma New option. Three systematic reviews added. [10] [18] [19] Categorised as 'unknown effectiveness'.

Laser treatment (iridotomy or iridoplasty) in primary chronic angle-closure glaucoma New option. Three systematic reviews [10] [19] [18] and one RCT [20] added. Categorised as 'unknown effectiveness'.

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Competing interests: RPLW has received honoraria for speaking and attending meetings from various pharmaceutical companies producing treatments for glaucoma including Alcon, Allergan, and Pfizer, and is an author of references cited in this overeview. EJ declares that she has no competing interests.
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Disclaimer

GRADE **Evaluation of interventions for Glaucoma: acute and chronic primary angle-closure.**

Important outcomes				Disease progression					
Studies (Participants)	**Outcome**	**Comparison**	**Type of evidence**	**Quality**	**Consistency**	**Directness**	**Effect size**	**GRADE**	**Comment**
What are the effects of treatment for primary acute angle-closure glaucoma?									
1 (48) [11]	Disease progression	Surgical treatment (any type) versus laser treatment (iridotomy or iridoplasty)	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
What are the effects of treatment for primary chronic angle-closure glaucoma?									
1 (126) [20]	Disease progression	Laser peripheral iridoplasty plus laser peripheral iridotomy versus laser peripheral iridotomy alone	4	–2	0	0	0	Low	Quality points deducted for sparse data and weak methods (blinding, outcome assessment, follow-up)

We initially allocate 4 points to evidence from RCTs, and 2 points to evidence from observational studies. To attain the final GRADE score for a given comparison, points are deducted or added from this initial score based on preset criteria relating to the categories of quality, directness, consistency, and effect size. Quality: based on issues affecting methodological rigour (e.g., incomplete reporting of results, quasi-randomisation, sparse data [<200 people in the analysis]). Consistency: based on similarity of results across studies. Directness: based on generalisability of population or outcomes. Effect size: based on magnitude of effect as measured by statistics such as relative risk, odds ratio, or hazard ratio.