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Laser peripheral iridoplasty for angle-closure

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ABSTRACT

Background
Angle-closure glaucoma is a leading cause of irreversible blindness in the world. Treatment is aimed at opening the anterior chamber angle and lowering the IOP with medical and/or surgical treatment (e.g. trabeculectomy, lens extraction). Laser iridotomy works by eliminating pupillary block and widens the anterior chamber angle in the majority of patients. When laser iridotomy fails to open the anterior chamber angle, laser iridoplasty may be recommended as one of the options in current standard treatment for angle-closure. Laser peripheral iridoplasty works by shrinking and pulling the peripheral iris tissue away from the trabecular meshwork. Laser peripheral iridoplasty can be used for crisis of acute angle-closure and also in non-acute situations.

Objectives
To assess the effectiveness of laser peripheral iridoplasty in the treatment of narrow angles (i.e. primary angle-closure suspect), primary angle-closure (PAC) or primary angle-closure glaucoma (PACG) in non-acute situations when compared with any other intervention. In this review, angle-closure will refer to patients with narrow angles, PAC and PACG.

Search methods
We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (which contains the Cochrane Eyes and Vision Group Trials Register) (The Cochrane Library), MEDLINE, EMBASE and LILACS (Latin American and Caribbean Literature on Health Sciences). The databases were last searched on 11 February 2008.

Selection criteria
Only randomised controlled trials (RCTs) were eligible for inclusion in this review. Patients with narrow angles, PAC or PACG were eligible. Studies that included only patients with acute presentations, using laser peripheral iridoplasty to break acute crisis were excluded.

Data collection and analysis
No analysis was carried out due to lack of trials.

Main results
There were no RCTs assessing laser peripheral iridoplasty in the non-acute setting of angle-closure.
Authors’ conclusions

There is currently no strong evidence for laser peripheral iridoplasty's use in treating angle-closure.

**PLAIN LANGUAGE SUMMARY**

**Laser peripheral iridoplasty for angle-closure glaucoma**

Angle-closure glaucoma is a leading cause of irreversible blindness in the world. Treatment is aimed at opening the drainage system and lowering the pressure in the eye with medical and/or surgical treatment. Laser peripheral iridoplasty is used in patients with angle-closure when other treatments fail to open the anterior drainage system. It works by shrinking and pulling the peripheral iris tissue away from the trabecular meshwork. Due to the lack of randomised controlled trials, this review found no strong evidence for the use of laser peripheral iridoplasty in the treatment of angle-closure.

**BACKGROUND**

Angle-closure glaucoma is a leading cause of irreversible blindness in the world. Treatment is aimed at opening the anterior chamber angle and lowering the intraocular pressure (IOP) with medical and/or surgical treatment (e.g. trabeculectomy, lens extraction). Laser iridotomy works by eliminating pupillary block and widens the anterior chamber angle in the majority of patients. When laser iridotomy fails to open the anterior chamber angle, laser iridoplasty may be recommended as one of the options in current standard treatment for angle-closure. Laser peripheral iridoplasty works by shrinking and pulling the peripheral iris tissue away from the trabecular meshwork. Laser peripheral iridoplasty can be used for crisis of acute angle-closure and also in non-acute situations.

**Description of the condition**

Glaucoma has been defined as a progressive optic neuropathy with characteristic appearances of the optic discs and specific pattern of visual field defects. Based on the appearance of the anterior chamber angle it can be classified into open-angle or closed-angle glaucoma. In the latter, an elevated IOP occurs as a consequence of an obstruction of the outflow pathway located in the anterior chamber angle (i.e. trabecular meshwork) by the peripheral iris. Closure of the anterior chamber angle can be appositional (reversible) or synechial (permanent, due to adherent uveal tissue). Among patients with appositional closure of the anterior chamber angle, many have normal IOP without any signs of glaucoma. They are usually described as having "narrow angles" or "primary angle closure suspects". If the IOP is elevated and/or there are parts of the angle with synechial closure (but without signs of glaucomatous damage), the preferred term is 'primary angle-closure' (PAC).

The term ‘primary angle-closure glaucoma’ (PACG) is reserved for those patients with angle-closure and evidence of glaucomatous optic disc damage and/or visual field loss. In this review, angle-closure will refer to patients with narrow angles, PAC and PACG. Primary angle-closure glaucoma is a leading cause of irreversible blindness in the world. Sixty-seven million people worldwide are affected by glaucoma. Open-angle glaucoma is more common than PACG but the latter is more likely to result in bilateral blindness (Quigley 1996; Resnikoff 2004). Primary angle-closure glaucoma is more common in Asians and women. Foster et al estimated that the number of persons with narrow angles in China, based on previous studies in Mongolia (Foster 1996) and Singapore (Foster 2000) is 28.2 million, while 9.1 million would have angle-closure. Furthermore, of the 1.7 million persons bilaterally blind from glaucoma in China, 91% are caused by PACG. Foster et al concluded that PACG might be the leading cause of glaucoma blindness in the world today (Foster 2001).

Patients with angle-closure may present with acute symptoms of highly elevated IOP but the majority of patients have a chronic course with no symptoms in the early stages of the disease. Interventions for acute presentation of angle-closure are being evaluated in another Cochrane review and will not be considered in this review.

**Description of the intervention**

Argon laser is applied using a contact lens (e.g. Abraham contact lens) to the iris periphery, approximately six shots per quadrant. The argon laser is typically set at 500-micron spot size, with a duration of 0.5 seconds, and an initial starting laser energy of 50 to 200 mW. This laser energy level is gradually increased if iris stromal shrinkage is not observed initially. It has been suggested...
that heat shrinkage of collagen may be responsible for the short-term response to laser peripheral iridoplasty, and that contraction of the fibroblastic membrane may be responsible for its long-term effects (Sassani 1993). Laser peripheral iridoplasty can be used as a primary treatment or after laser peripheral iridotomy for acute angle-closure attacks.

How the intervention might work

Treatment of angle-closure is aimed at (1) opening the anterior chamber angle, most commonly by laser iridotomy, and (2) lowering the IOP with medical and/or surgical treatment (e.g. trabeculectomy, lens extraction). Laser iridotomy works by eliminating pupillary block and widens the anterior chamber angle in the majority of patients, although in some of them the anterior chamber angle remains closed. The latter situation may be due to plateau iris syndrome or a prominent and thick peripheral iris. When laser iridotomy fails to open the anterior chamber angle, laser peripheral iridoplasty may be recommended as one of the options in current standard treatment for angle-closure. Laser peripheral iridoplasty tries to pull away and ‘remove’ iris tissue away from the trabecular meshwork by shrinking the peripheral iris tissue.

Why it is important to do this review

Laser peripheral iridoplasty is part of the standard treatment for angle-closure and is indicated in patients who do not respond to laser iridotomy. The use of laser peripheral iridoplasty appears to be increasingly reported in the literature and among experts in specialist meetings (Agarwal 1991; Lai 1999; Lam 1992; Weinreb 2006). So far, there has been no systematic review to assess the effectiveness of laser peripheral iridoplasty in the treatment of eyes with angle-closure in non-acute situations.

OBJECTIVES

The objective of this review was to assess the effectiveness of laser peripheral iridoplasty in the treatment of eyes with angle-closure in non-acute situations when compared with any other intervention including observation, medical treatment, laser peripheral iridotomy or surgical interventions such as trabeculectomy or cataract extraction.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials were eligible for inclusion in this review. Trials included should have analysis based on one eye per patient.

Types of participants

Patients with narrow angles, PAC or PACG were eligible. It was anticipated that some trials would include patients with a previous history of acute presentations while others would evaluate participants with non-acute conditions only. Studies that included only patients with acute presentations, using laser peripheral iridoplasty to break the acute phase were excluded. We included studies which had participants with a past history of an acute presentation but had not had laser peripheral iridoplasty during the attack. There were no restrictions with respect to previous treatments (i.e. peripheral iridotomy), age, gender, ethnicity or the number of participants.

Types of interventions

We only included trials that compared laser peripheral iridoplasty with or without medical treatment versus a control group without laser peripheral iridoplasty and with similar management (observation or medical treatment).

Types of outcome measures

Primary outcomes

Conversion rates using life-table analysis (Kaplan Meier and Cox hazard model) will be estimated. Conversion rates of a) or b) between one to five years follow up, based on survival data, will then be reported.

a) From narrow angle (IOP < 21), to PAC (IOP ≥ 21), and/or
b) From PAC to PACG (with glaucomatous disc damage and/or glaucomatous visual field damage; see below for definition).

Glucomatous optic disc damage would include the presence of thinning or ‘notching’ of the neuroretinal rim, vertical enlargement of cup, or asymmetry greater than 0.2 in the cup-disc ratio without differences in disc size or refractive error between eyes. Glaucomatous visual field (VF) damage will be defined for Humphrey perimeter as a reproducible defect in at least two consecutive and reliable VFs of (1) (a) two or more contiguous points with \( P < 0.01 \) loss or greater, or (b) three or more contiguous points with \( P < 0.05 \) loss or greater, or (c) a 10-dB difference across the nasal horizontal midline at two or more adjacent points in the total deviation plot; (2) a Glaucoma Hemifield Test (GHT) outside normal limits in the same sector. For other perimeters, equivalent criteria would be used.
Secondary outcomes
Post-treatment the data below will be collected at all reported times. From this data, the variable at one and five years post-treatment will be used for data analysis.
(1) Intraocular pressure as measured by Goldmann’s (mmHg).
(2) Number of anti-glaucoma medications.
(3) Opening of the anterior chamber angle, determined clinically by a masked clinician or with imaging technology.
(4) Any additional laser or surgical interventions for glaucoma.
(5) Best-corrected visual acuity.
(6) In patients with angle-closure glaucoma, any deterioration of visual field loss. Any event analysis or trend analysis used by the authors to measure visual field loss will be accepted.
(7) Quality of life measures will be tabulated if reported.

Methods to be used in future updates to the review
As studies are identified in the future, they will be included in the review using the following methods.

Data extraction and management
Two authors will extract data independently using a paper form developed by Cochrane Eyes and Vision Group. One author will enter data into RevMan followed by the second author who will enter the data using a double-data entry facility to verify the data entered.

Assessment of risk of bias in included studies
As no RCTs were found that met our inclusion criteria, we briefly described the case series reporting the effectiveness of laser peripheral iridoplasty (see below and Table 1).
Should any trials become available two authors will independently assess the included studies for sources of systematic bias according to the guidelines in Chapter 8 of the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2008). The studies will be evaluated for the following criteria: allocation concealment (selection bias), masking of outcome assessors (detection bias), and rates of follow up and intention-to-treat analysis (attrition bias).
(a) Allocation concealment will be reported as ‘adequate’, ‘inadequate’ or ‘unclear’. Any reasonable method of allocation concealment will be considered to be ‘adequate’. If the adequacy of allocation concealment is unclear from the trial report we will contact the primary investigators for clarification. If they do not respond within six weeks we will classify the study based on available information and update it as more information becomes available.
(b) Masking of outcome assessors will be noted. Masking of investigators and participants might not be possible with the interventions being examined and will not be assessed.
(c) Rates of follow up, reason for loss to follow up will be examined.
(d) Masking of outcome assessors will be noted.
We will resolve disagreements through discussion and reach a consensus. We will contact the authors of the studies for additional information on issues that are categorised as ‘unclear’ from information available in the report. If there is a failure to communicate with the primary investigators, or if they do not respond within a reasonable period of time, we will assess the methodological quality based on the available information.

Selection of studies
Two authors independently assessed the titles and abstracts of all reports identified by the electronic and manual searches. Each report was labelled A (definitely exclude), B (unsure), or C (definitely include). Full text articles of abstracts labelled as ‘unsure’ were reassessed according to the inclusion criteria for this review. Studies labelled ‘definitely exclude’ were excluded from the review. Studies labelled as ‘definitely include’ were assessed for methodological quality. We resolved any differences between the two authors by discussion. No studies were identified that met our inclusion criteria.

Search methods for identification of studies
Electronic searches
We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (which contains the Cochrane Eyes and Vision Group Trials Register) (The Cochrane Library, Issue 1, 2008), MEDLINE (January 1966 to February 2008), EMBASE (January 1980 to February 2008) and LILACS (Latin American and Caribbean Literature on Health Sciences) (1982 to February 2008). There were no date or language restrictions in the electronic search for trials. The databases were last searched on 11 February 2008.
See: Appendices for search strategies for each database.

Data collection and analysis

Searching other resources
We searched the reference lists of retrieved articles for details of further relevant studies. We did not handsearch journals or conference proceedings specifically for this review.

Revision of included studies

Selection of studies
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(b) Masking of outcome assessors will be noted. Masking of investigators and participants might not be possible with the interventions being examined and will not be assessed.
(c) Rates of follow up, reason for loss to follow up will be examined.
(d) Masking of outcome assessors will be noted.
We will resolve disagreements through discussion and reach a consensus. We will contact the authors of the studies for additional information on issues that are categorised as ‘unclear’ from information available in the report. If there is a failure to communicate with the primary investigators, or if they do not respond within a reasonable period of time, we will assess the methodological quality based on the available information.

Measures of treatment effect
Data analysis will be done according to the guidelines set out in Chapter 9 of the Cochrane Handbook for Systematic Reviews of Interventions (Deeks 2008). Outcomes will be summarised as a relative risk, or mean difference.
**Unit of analysis issues**
We will only include studies with analysis on an one eye per patient basis.

**Dealing with missing data**
We expect studies to be analysed on an intention-to-treat basis. There will be concern regarding the validity of the study if there is no information on the characteristics of the missing data or whether this may introduce any bias. Where data are missing or unclear, the authors will be contacted for clarification and further information.

**Assessment of heterogeneity**
Should any trials become available we will attempt to quantify the proportion of variability within included randomised studies that is explained by heterogeneity using the $I^2$ statistic (Higgins 2002). If the $I^2$ statistic is greater than 50% we will consider it as substantial heterogeneity and will not combine the study results in a meta-analysis. Instead we will present the studies in a tabulated or narrative summary.

**Assessment of reporting biases**
Selection, detection, performance and attrition biases will be assessed as above. Funnel plots will be used to detect the presence of any publication bias.

**Data synthesis**
Data analysis will be performed according to the guidelines set out in Chapter 9 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Deeks 2008). Dichotomous outcomes will be summarised as risk ratios and continuous outcomes will be summarised as a mean difference. Standardised mean difference will be calculated when outcomes are measured on different scales. If there is no substantial heterogeneity as per the $I^2$ statistic we will combine the results of the included studies in a meta-analysis using a random-effects model. We will use a fixed-effect model if there are fewer than three studies. This is to avoid reporting potentially poor effect estimates due to random-effects models in situations with very few trials. Meta-analysis will be performed on the primary outcomes and difference in mean Goldmann IOP and its standard error.

**Sensitivity analysis**
We will examine the impact of excluding studies with lower methodological quality, unpublished data and industry funded data in sensitivity analyses.

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**Results of the search**
The searches were designed to include a filter to identify RCTs. However, when the filter was applied the search retrieved very few references. We decided to run the searches without the filters to retrieve any type of study discussing the use of laser peripheral iridoplasty for the treatment of angle-closure glaucoma. The electronic searches retrieved 3 references from *The Cochrane Library*, 79 references from MEDLINE, 68 references from EMBASE and 5 references from LILACS. After deduplication the search identified a total of 96 references. The Trials Search Co-ordinator scanned the results and removed any references that were not relevant to the scope of the review. The authors then excluded twenty-seven references which assessed laser peripheral iridoplasty in acute angle-closure glaucoma. Only two studies reported its use in the non-acute setting but neither were RCTs nor case controlled studies. Hence, no trials were available for further analysis.

**Included studies**
No trials were eligible for analysis. We found two case series which assessed laser peripheral iridoplasty in angle-closure. One described the long-term success rate of laser peripheral iridoplasty in plateau iris syndrome in 23 eyes of 14 patients (Ritch 2004). The other reports the functional success rate of laser peripheral iridoplasty use after inferior 180° goniosynechialysis for PACG with 360° peripheral anterior synechiae in five patients (Lai 2000). These case series will be mentioned in the discussion section and characteristics of these studies can be found in Table 1.

**Risk of bias in included studies**
This section will be completed when RCTs are included in the review.

**Effects of interventions**
This section will be completed when RCTs are included in the review.

**Discussion**
Literature surrounding the use of laser peripheral iridoplasty in angle-closure is scarce. There are relatively more studies reporting
its efficacy in breaking attacks of angle-closure where it can be used in medically unbreakable attacks. However, in a recent consensus meeting among glaucoma experts (Weinreb 2006) laser iridoplasty was considered a standard treatment in patients with persistent appositional angle-closure after peripheral iridotomy.

We have found only two studies which have reported the effectiveness of laser peripheral iridoplasty in the non-acute setting. Ritch et al carried out a retrospective case series involving 23 eyes of 14 patients (Ritch 2004). They had a mean follow up of 78.9 months and found that in all patients the anterior chamber angle did open after treatment, and only three eyes needed repeat laser peripheral iridoplasty. They suggested that it is a safe and effective procedure with a satisfactory long term success rate.

Laser peripheral iridoplasty’s use has also been reported post inferior 180° goniosynechialysis for eyes with angle-closure. Lai et al recruited five patients with PACG and 360° peripheral anterior synechiae for inferior 180° goniosynechialysis (Lai 2000). Laser peripheral iridoplasty was then applied on day four after surgery and the functional success rate (defined as having an IOP of less than 20 mmHg at last follow up) was observed in four patients. The authors suggested that laser peripheral iridoplasty is a safe and effective adjunct to goniosynechialysis for treatment of angle-closure with total synechial angle-closure.

Although at present there is no strong evidence for the use of laser peripheral iridoplasty in angle-closure, these two positive case series and the consensus among experts suggest that it is worth conducting a randomised study to determine its effectiveness in angle-closure.

**Summary of main results**

There were no RCTs assessing laser peripheral iridoplasty in the non-acute setting of angle-closure.

**Overall completeness and applicability of evidence**

No strong evidence was found.

**Quality of the evidence**

There was no strong evidence for the use of laser peripheral iridoplasty’s use in treating angle-closure.

**AUTHORS’ CONCLUSIONS**

**Implications for practice**

Laser peripheral iridoplasty may be used for breaking attacks of acute angle-closure if unresponsive to medical therapy or successful iridotomy.

It has been proposed to be effective in non-acute situations in patients with angle-closure when laser iridotomy fails to open the anterior chamber angle.

However, there is currently no strong evidence for its role in the treatment of angle-closure.

**Implications for research**

Future trials will need to include patients with residual angle-closure after peripheral iridotomy. Laser iridoplasty should be compared with a control group without this intervention. A RCT would be the ideal study design. Comparison of argon laser iridoplasty with other interventions designed to open the anterior chamber angle (e.g. lens extraction) in a randomised trial would also be of interest. Description of the methods to examine the anterior chamber angle, before and after intervention, would be essential. If clinical examination is going to be used, standardisation of grading would be important. The use of imaging techniques (such as anterior segment optical coherence tomography (OCT) or ultrasound biomicroscopy) would complement qualitative evaluation of the anterior chamber angle and would be recommended. Mid and long-term effectiveness would be measured in terms of IOP, extension of anterior chamber angle-closure, visual field changes, visual acuity, and vision-related quality of life. Outcomes would need to be assessed by masked investigators. Standard ethical requirements would apply.

**ACKNOWLEDGEMENTS**

The Cochrane Eyes and Vision Group created and ran the electronic searches. We thank Catey Bunce, Scott Fraser and Tianjing Li for providing peer referee comments.
REFERENCES

Additional references

Agarwal 1991

Deeks 2008

Foster 1996

Foster 2000

Foster 2001

Glanville 2006

Higgins 2008

Lai 1999

Lai 2000

Lam 1992

Quigley 1996

Resnikoff 2004

Ritch 2004

Sassani 1993

Weinreb 2006

* Indicates the major publication for the study
DATA AND ANALYSES

This review has no analyses.

ADDITIONAL TABLES

Table 1. Other studies assessing laser iridoplasty in non-acute ACG

<table>
<thead>
<tr>
<th>Study name</th>
<th>Methods</th>
<th>Participants</th>
<th>Intervention</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lai 2000</td>
<td>prospective case series</td>
<td>n=5 patients with chronic angle-closure</td>
<td>inferior 180 goniosynechialysis is followed by laser peripheral iridoplasty</td>
<td>intraocular pressure and number of medications</td>
</tr>
<tr>
<td>Ritch 2004</td>
<td>retrospective case series</td>
<td>n=14 patients with plateau iris syndrome treated with laser peripheral iridoplasty</td>
<td>argon laser peripheral iridoplasty</td>
<td>need of repeat laser peripheral iridoplasty or additional means of intervention</td>
</tr>
</tbody>
</table>

APPENDICES

Appendix 1. CENTRAL search strategy

#1 MeSH descriptor Glaucoma, Angle-Closure  
#2 glaucoma*  
#3 angle* near close*  
#4 narrow near angle*  
#5 (#1 OR #2 OR #3 OR #4)  
#6 iridoplast*  
#7 (#5 AND #6)

Appendix 2. MEDLINE search strategy

1. exp clinical trial/ [publication type]  
2. (randomized or randomised).ab,ti.  
3. placebo.ab,ti.  
4. dt.fs.  
5. randomly.ab,ti.  
6. trial.ab,ti.  
7. groups.ab,ti.  
8. or/1-7  
9. exp animals/  
10. exp humans/  
11. 9 not (9 and 10)  
12. 8 not 11
13. exp glaucoma angle closure/
14. glaucoma$.tw.
15. (angle$ adj3 close$).tw.
17. or/13-16
18. iridoplast$.tw.
19. 17 and 18

The search filter for trials at the beginning of the MEDLINE strategy is from the published paper by Glanville et al (Glanville 2006)

Appendix 3. EMBASE search strategy
1. exp randomized controlled trial/
2. exp randomization/
3. exp double blind procedure/
4. exp single blind procedure/
5. random$.tw.
6. or/1-5
7. (animal or animal experiment).sh.
8. human.sh.
9. 7 and 8
10. 7 not 9
11. 6 not 10
12. exp clinical trial/
14. ((singl$ or doubl$ or trebl$ or tripl$) adj3 (blind$ or mask$)).tw.
15. exp placebo/
16. placebo$.tw.
17. random$.tw.
18. exp experimental design/
19. exp crossover procedure/
20. exp control group/
21. exp latin square design/
22. or/12-21
23. 22 not 10
24. 23 not 11
25. exp comparative study/
26. exp evaluation/
27. exp prospective study/
28. (control$ or prospectiv$ or volunteer$).tw.
29. or/25-28
30. 29 not 10
31. 30 not (11 or 23)
32. 11 or 24 or 31
33. exp closed angle glaucoma/
34. glaucoma$.tw.
35. (angle$ adj3 close$).tw.
36. (narrow adj3 angle$).tw.
37. or/33-36
38. "iridoplasty"/
39. argon laser peripheral iridoplasty/
40. iridoplast$.tw.
41. or/38-40
Appendix 4. LILACS search strategy
iridoplast$
Data management for the review
- Entering data into RevMan: WSN, AAB
- Analysis of data: AAB, WSN

Interpretation of data
- Providing a methodological perspective: AAB, WSN
- Providing a clinical perspective: AAB
- Providing a policy perspective: AAB
- Providing a consumer perspective: AAB

Writing the review: AAB, WSN
Providing general advice on the review: AAB
Securing funding for the review: AAB
Performing previous work that was the foundation of the current study: AAB

DECLARATIONS OF INTEREST
None known.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW
The title was changed from chronic angle-closure glaucoma to angle-closure. Angle-closure refers to patients with narrow angles, angle-closure and angle-closure glaucoma.

INDEX TERMS
Medical Subject Headings (MeSH)
*Laser Therapy; Glaucoma, Angle-Closure [*surgery]; Iris [*surgery]

MeSH check words
Humans