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[Intervention Review]

Laser peripheral iridoplasty for chronic angle closure

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ABSTRACT

Background

In at least a third of primary angle closure cases, appositional angle closure persists after laser peripheral iridotomy, and further intervention may be considered. Laser peripheral iridoplasty (LPIp) can be used in treating chronic angle closure when angle closure persists after laser peripheral iridotomy. Previous reviews have found insufficient data to determine its clinical effectiveness, compared to other interventions. This is an update of a Cochrane Review first published in 2008 and updated in 2012. It examines all studies to date to establish whether LPIp shows any effectiveness over other available treatment options.

Objectives

To assess the effectiveness of laser peripheral iridoplasty in the treatment of people with chronic angle closure, when compared to laser peripheral iridotomy, medical therapy or no further treatment.

Search methods

We searched various electronic databases. The date of the search was 20 December 2020.

Selection criteria

We included only randomised controlled trials (RCTs) assessing the use of LPIp in cases of suspected primary angle closure (PACS), confirmed primary angle closure (PAC), or primary chronic angle-closure glaucoma (PACG). We applied no restrictions with respect to gender, age or ethnicity of participants. Trials evaluating LPIp for acute attacks of angle closure were not eligible.

Data collection and analysis

We used standard methodological procedures expected by Cochrane. Two authors independently assessed studies for risk of bias using Cochrane's 'risk of bias' tool. We collected adverse effects information from the trials.

Main results

We included four RCTs involving 252 participants (276 eyes). In total, three different methods of intervention were used and 15 outcomes reported, with different time points. We used narrative synthesis to describe the majority of the findings, as meta-analysis was only possible for a limited number of outcomes due to the variation in study design and outcomes assessed.

Study Characteristics

Participants were adults recruited from outpatient settings in the UK, Singapore, China and Korea with either PACS, PAC or PACG. All studies compared argon LPIp (as either a primary or secondary procedure) to an alternative intervention or no further treatment. Three studies were of parallel group design, and one within-person, randomised by eye. All studies showed elements of high risk of bias. Due to the nature of the intervention assessed, a lack of masking of both participants and assessors was noted in all trials.

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Findings

Laser peripheral iridoplasty with iridotomy versus iridotomy alone as a primary procedure
Two RCTs assessed the use of argon LPIp as a primary procedure with peripheral iridotomy, compared with peripheral iridotomy alone. However, neither study reported data for the primary outcome, disease progression. Argon LPIp showed no evidence of effect on: final mean intraocular pressure (IOP) at 3 months and 12 months (mean difference (MD) 0.39 mmHg, 95% confidence interval (CI) -1.07 to 1.85; I^2 = 38%; 2 studies, 174 participants; low-certainty evidence); further surgical or laser intervention at 12 months (risk ratio (RR) 1.21, 95% CI 0.66 to 2.21; 1 study, 126 participants; low-certainty evidence); or mean number of additional medications required at 12 months (MD 0.10, 95% CI -0.34 to 0.54; 1 study, 126 participants; low-certainty evidence). Complications were assessed at 3 to 12 months (2 studies, 206 participants; low-certainty evidence) and found to be mild and uncommon, with comparable levels between groups. The only severe complication encountered was one case of malignant glaucoma in one study's argon LPIp group. Quality of life measures were not assessed. In the other study, investigators found that argon LPIp showed no evidence of effect on final mean anterior segment optical coherence tomography (AS-OCT) measurements, including anterior chamber depth (MD 0.00 mm, 95% CI -0.10 to 0.10; 24 participants, 48 eyes; very low-certainty evidence).

Laser peripheral iridoplasty as a secondary procedure versus no treatment
One RCT assessed the use of argon LPIp as a secondary procedure compared with no further treatment in 22 participants over three months. Disease progression, additional medications required, complications, further surgical or laser intervention, and quality of life outcomes were not assessed. There was only very low-certainty evidence regarding final maximum IOP value (MD -1.81 mmHg, 95% CI -3.11 to -0.51; very low-certainty evidence), with no evidence of effect on final minimum IOP values (MD -0.31 mmHg, 95% CI -1.93 to 1.31; very low-certainty evidence). The evidence is very uncertain about the effect of argon LPIp on AS-OCT parameters. The trial did not report AS-OCT measurements for the control group.

Laser peripheral iridoplasty as a secondary procedure versus medication
One RCT assessed the use of argon LPIp as a secondary procedure compared with travoprost 0.004% in 80 participants over 12 months. The primary outcome of disease progression was reported for this method: argon LPIp showed no evidence of effect on mean final cup/disk ratio (MD -0.03, 95% CI -0.11 to 0.05; low-certainty evidence). Argon LPIp showed no evidence of effect for: mean change in IOP (MD -1.20 mmHg, 95% CI -2.87 to 0.47; low-certainty evidence) or mean number of additional medications (MD 0.42, 95% CI 0.23 to 0.61; low-certainty evidence). Further surgical intervention was required by one participant in the intervention group alone, with none in the control group (low-certainty evidence). No serious adverse events were reported, with mild complications consisting of two cases of 'post-laser IOP spike' in the argon LPIp group. Quality of life measures were not assessed. The evidence is very uncertain about the effect of argon LPIp on AS-OCT parameters. The trial did not report AS-OCT measurements for the control group.

Adverse events
Availability of data were limited for adverse effects. Similar rates were observed in control and intervention groups, where reported. Serious adverse events were rare.

Authors' conclusions

After reviewing the outcomes of four RCTs, argon LPIp as an intervention may be no more clinically effective than comparators in the management of people with chronic angle closure. Despite a potential positive impact on anterior chamber morphology, its use in clinical practice in treating people with chronic angle closure is not supported by the results of trials published to date. Given these results, further research into LPIp is unlikely to be worthwhile.

PLAIN LANGUAGE SUMMARY

What are the benefits and risks of laser peripheral iridoplasty (a surgical procedure) for chronic primary angle closure (an eye condition)?

Why is this question important?
'Primary angle closure' (PAC) is a condition in which the eye does not drain properly because the iris (the coloured part of the eye) blocks the drainage channel. A blockage can happen suddenly (acute PAC) or slowly (chronic PAC). A blockage causes a build-up of fluid and raises pressure inside the eye, which damages the optic nerve and can lead to partial or complete vision loss.

The main treatment for PAC is a surgical procedure called laser peripheral iridotomy. Peripheral iridotomy involves using a laser to create an opening in the iris so that fluid can drain out. For more than one in three people, however, peripheral iridotomy does not improve drainage. An alternative to peripheral iridotomy is laser peripheral iridoplasty (LPIp), in which a laser is used to reshape the iris so that it does not block drainage.

To find out how well LPIp works for people with chronic PAC, we reviewed the research evidence.

How did we identify and evaluate the evidence?

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First, we searched the medical literature for studies that compared the effects of LPIp to other treatments or no treatment. We then compared the results, and summarised the evidence from all the studies. Finally, we rated our confidence in the evidence, based on factors such as study methods and sizes, and the consistency of findings across studies.

What did we find?

We found four studies on a total of 252 people, mostly from Asia. The studies followed participants for between 3 and 12 months, and compared:

- LPIp plus peripheral iridotomy to peripheral iridotomy alone, as a primary treatment (that is, in people who had not received any other treatment for PAC before);

- LPIp to no treatment, as a secondary treatment (that is, in people who had previously been treated for PAC, but not with LPIp); and

- LPIp to eye drops (travoprost 0.004%), as a secondary treatment.

LPIp plus peripheral iridotomy compared to peripheral iridotomy alone, as a primary treatment

The evidence suggests that adding LPIp to peripheral iridotomy may make little or no difference to:

- eye pressure (2 studies, 174 people);

- the need for medicines after 12 months (1 study, 126 people);

- the need for further laser or surgical treatment (1 study, 126 people); and

- the shape of the front of the eye (1 study, 48 people).

Evidence provided by two studies suggests that:

- unwanted effects (such as bleeding inside the front of the eye) are uncommon; and

- adding LPIp to peripheral iridotomy may make little or no difference to the frequency of unwanted events.

We do not know if adding LPIp to peripheral iridotomy slows disease progression or improves quality of life because no study investigated this.

LPIp compared to no treatment, as a secondary treatment

We found one study on 22 people that compared the effects of LPIp to no treatment on:

- eye pressure; and

- the shape of the front of the eye.

This study was not robust enough for us to determine which treatment is better.

The study did not investigate whether LPIp is better than no treatment to:

- slow disease progression;

- limit the need for medications;

- avoid the need for more laser or surgical treatment; or

- improve quality of life.

The study did not investigate unwanted events.

LPIp compared to travoprost 0.004% eye drops, as a secondary treatment

The evidence from one study on 80 people suggests that there may be little to no difference between the effects of LPIp and travoprost 0.004% on:

- disease progression;

- eye pressure;

- the need for medicines after 12 months; and

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- the need for further laser or surgical treatment.

The evidence further suggests that:

- unwanted effects are uncommon; and

- there may be little or no difference in the frequency of unwanted events between the two treatments.

The evidence was not robust enough for us to determine whether the treatments have different effects on the shape of the front of the eye.

We do not know which treatment works better to improve quality of life because no study investigated this.

What does this mean?
The evidence suggests that:

- LPIp may not be better than other treatments for chronic PAC; and

- unwanted events may be as common with LPIp as with other treatments for chronic PAC.

How up-to-date is this review?
The evidence in this Cochrane Review is current to December 2020.

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SUMMARY OF FINDINGS

Summary of findings 1. Summary of Findings

Laser peripheral iridoplasty with iridotomy versus iridotomy alone as a primary procedure

Patient or population: adults with PACS, PAC or PACG
Setting: hospital eye service
Intervention: LPIp[d] with PI
Comparison: PI alone

Outcomes	Comparator	Intervention	Relative Risk (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
Disease progression Follow-up: 24 months	No data available					
IOP Assessed with: Goldmann tonometry Follow-up: 24 months Units: mmHg, lower is better	The mean final IOP found in the control varied from **14.20 mmHg to 19.57 mmHg**.	The mean final IOP did not differ significantly between groups, with a mean final IOP of **0.39 mmHg greater** in the intervention group (95% CI -1.07 to 1.85).	-	174 (2 RCTs)	⊕⊕⊖⊖ Low[a]	Data reported at 3 and 12 months. Clinically significant difference in IOP = 2 mmHg or higher.
Additional medications required Follow-up: 24 months Units: № of medications, lower is better	The mean number of additional medications required in the control group was **0.90**.	The mean number of additional medications required did not differ significantly between groups, with an average of **0.10 more** medications required by the intervention group (95% CI -0.34 to 0.54).	-	126 (1 RCT)	⊕⊕⊖⊖ Low[a]	Data reported at 12 months
Complications Assessed with: clinical examination Follow-up: up to 24 months	The only severe complication encountered was 1 case of malignant glaucoma in the argon LPIp arm by Sun 2010. Overall complications were mild and uncommon in both studies, with no statistically significant difference between groups (complications encountered included: hyphema, post-laser IOP spikes, reduction in corneal endothelial cell count, non-significant reduction in visual acuity, transient atonic pupil, corneal endothelium burn, persistent uveitis).		Not estimable	206 (2 RCTs)	⊕⊕⊖⊖ Low[b]	Data reported at 3 and 12 months

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	-					
Further surgical or laser interventions Follow-up: 24 months	**230 per 1000**	**277 per 1000**	**RR 1.21** (0.66 to 2.21)	126 (1 RCT)	⊕⊕⊖⊖ Low[c]	Data reported at 12 months
Quality of life measures Follow-up: 24 months	No data available					
Anterior chamber morphology Assessed with: gonioscopy or AS-OCT Follow-up: 24 months	The mean final ACD found in the control group was **2.10 mm**.	The mean final ACD did not differ significantly between groups, with a mean final ACD of **0.00 mm greater** in the intervention group (95% CI -0.10 to 0.10).	Not estimable	48 (1 RCT)	⊕⊕⊖⊖ Low[a]	Data reported at 12 months
	-	-				
	-	-				

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
ACD: anterior chamber depth; **AS-OCT:** anterior segment optical coherence tomography; **CI:** confidence interval; **IOP:** intraocular pressure; **PAC:** primary angle closure; **PACG:** primary angle-closure glaucoma; **PACS:** PAC suspect; **RR**: Risk ratio; **OR:** Odds ratio.

GRADE Working Group grades of evidence
High-certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate-certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low-certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low-certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]We downgraded one level for risk of bias because participants, personnel and outcome assessors could not be masked. We downgraded a further level for a combination of imprecision (sample size was less than 400) and indirectness (no data were available at our pre-specified time point of 24 months and so we used available data at shorter follow-up which may not represent the situation at the longer follow-up).
[b]We downgraded one level for risk of bias because participants, personnel and outcome assessors could not be masked. We downgraded a further level for imprecision due to sparse data.
[c] We downgraded one level for risk of bias because participants, personnel and outcome assessors could not be masked. We downgraded a further level for a combination of imprecision (confidence intervals ranged from 0.66 to 1.21) and indirectness (no data were available at our pre-specified time point of 24 months and so we used available data at shorter follow-up which may not represent the situation at the longer follow-up).
[d]Argon laser was used in all instances of LPIp.

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Summary of findings 2. Summary of Findings

Laser peripheral iridoplasty as a secondary procedure versus no treatment

Patient or population: adults with PACS or PAC, and previous PI

Setting: hospital eye service

Intervention: LPIp[c]

Comparison: no further treatment

Outcomes	Comparator	Intervention	Relative Risk (95% CI)	№ of Participants (studies)	Quality of the evidence (GRADE)	Comments
Disease progression Follow-up: 24 months	No data available					
IOP Assessed with: Goldmann tonometry Follow-up: 24 months Units: mmHg, lower is better	The mean final maximum IOP found in the control group was **21.15 mmHg**. The mean final minimum IOP found in the control group was **14.54 mmHg**.	The mean final maximum IOP in the intervention group was significantly lower than that of the control (**1.81 mmHg lower**, 95% CI -3.11 to -0.51). The mean final minimum IOP did not differ significantly between groups, with an average of **0.31 mmHg lower** in the intervention group (95% CI -1.93 to 1.31)	-	22 (1 RCT)	⊕⊖⊖⊖ Very low[a]	Data reported at 3 months
Additional medications required Follow-up: 24 months	No data available					
Complications Follow-up: 24 months	No data available					
Further surgical or laser interventions Follow-up: 24 months	No data available					
Quality of life measures	No data available					

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Follow-up: 24 months					
Anterior chamber morphology Assessed with: AS-OCT images Follow-up: 24 months	Statistically significant widening was found for the intervention group in 43 of 48 AS-OCT parameters, and also in TIA measurements across all sectors. No AS-OCT measurements for the control group were reported.	Not estimable	22 (1 RCT)	⊕⊖⊖⊖ Very low[b]	Data reported at 3 months

AS-OCT: anterior segment optical coherence tomography; **IOP**: intraocular pressure; **PAC:** primary angle closure; **PACS:** suspected PAC; **PI:** peripheral iridotomy

GRADE Working Group grades of evidence
High-certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate-certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low-certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low-certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]We downgraded one level for risk of bias because participants, personnel and outcome assessors could not be masked. We downgraded a further level for imprecision (sample size was less than 400) and indirectness (no data were available at our pre-specified time point of 24 months and so we used available data at shorter follow-up which may not represent the situation at the longer follow-up).
[b]We downgraded two levels for risk of bias because participants, personnel and outcome assessors could not be masked, no comparison was made to the control group, and control measurements were not reported. We downgraded a further level for a combination of imprecision (sample size was less than 400) and indirectness (no data were available at our pre-specified time point of 24 months and so we used available data at shorter follow-up which may not represent the situation at the longer follow-up).
[c]Argon laser was used in all instances of LPIp.

Summary of findings 3. Summary of Findings

Laser peripheral iridoplasty as a secondary procedure versus medication

Patient or population: adults with PAC or PACG, and previous PI

Setting: hospital eye service

Intervention: LPIp[d]

Comparison: travoprost 0.004%

Outcomes	Comparator	Intervention	Relative Risk (95% CI)	№ of Participants (studies)	Quality of the evidence (GRADE)	Comments
Disease progression	The mean final vertical C/D ratio for the control group was **0.59**.	The mean final vertical C/D ratio did not differ significantly between groups, with an average of **0.03**	-	80 (1 RCT)	⊕⊕⊖⊖ Low[a]	Data reported at 12 months

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Assessed by: dilated assessment of the vertical C/D ratio using a 78 D lens Follow-up: 24 months Units: 0.00 to 1.00, higher indicating progression of the disease		**lower** in the intervention group (95% CI -0.11 to 0.05).				
IOP Assessed with: Goldmann tonometry Follow-up: 24 months Units: mmHg, lower is better	The mean change in IOP found in the control group was a reduction of **6.10 mmHg**.	The mean change in IOP did not differ significantly between groups, with an average reduction of **1.20 mmHg lower** in the intervention group (95% CI -2.87 to 0.47).	-	80 (1 RCT)	⊕⊕⊖⊖ Low[a]	Data reported at 12 months
Additional medications required Follow-up: 12 months	The mean number of additional medications required in the control group was **0.13**.	The mean number of additional medications required differed significantly between groups, with an average of **0.42 more** medications required by the intervention group (95% CI 0.23 to 0.61).	-	80 (1 RCT)	⊕⊕⊖⊖ Low[a]	Data reported at 12 months
Complications Assessed with: clinical examination Follow-up: up to 24 months	Overall complications were uncommon, and no severe complications were reported. Two cases of 'Post-laser IOP spike' were reported in the argon LPIp group (5%).		Not estimable	80 (1 RCT)	⊕⊕⊖⊖ Low[b]	Data reported at 12 months
Further surgical or laser interventions Follow-up: 24 months	There was one case of surgical intervention required in the intervention group (n = 40), compared with no cases in the control group (n = 40).		Not estimable	80 (1 RCT)	⊕⊕⊖⊖ Low[b]	Data reported at 12 months
Quality of life measures Follow-up: 24 months	No data available					
Anterior chamber morphology Assessed with: AS-OCT images for AOD, TISA, ARA, and mean angle width Follow-up: 24 months	Statistically significant widening was observed in AOD, TISA750 and ARA750 measurements for the intervention group. No measurements were reported for control participants.		Not estimable	80 (1 RCT)	⊕⊖⊖⊖ Very low[c]	Data reported at 12 months

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Units: mm for AS-OCT measurements	

AS-OCT: anterior segment optical coherence tomography;**IOP:** intraocular pressure; **PAC:** primary angle closure; **PACS:** suspected PAC; **PI:** peripheral iridotomy

GRADE Working Group grades of evidence
High-certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate-certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low-certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low-certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]We downgraded one level for risk of bias because participants, personnel and outcome assessors could not be masked. We downgraded a further level for a combination of imprecision (sample size was less than 400) and indirectness (no data were available at our pre-specified time point of 24 months and so we used available data at shorter follow-up which may not represent the situation at the longer follow-up).
[b]We downgraded one level for risk of bias because participants, personnel and outcome assessors could not be masked. We downgraded a further level for imprecision due to sparse data.
[c]We downgraded two levels for risk of bias because participants, personnel and outcome assessors could not be masked, no comparison was made to the control group, and control measurements were not reported. We downgraded a further level for a combination of imprecision (sample size was less than 400) and indirectness (no data were available at our pre-specified time point of 24 months and so we used available data at shorter follow-up which may not represent the situation at the longer follow-up).
[d]Argon laser was used in all instances of LPIp.

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BACKGROUND

Description of the condition

'Angle closure' refers to the occlusion of the trabecular meshwork by the peripheral iris, preventing aqueous outflow (Kanski 2011). Chronic appositional contact between these two structures is thought to allow adherence, known as peripheral anterior synechiae (PAS), which is one of the hallmarks of primary angle-closure glaucoma (PACG) (Lee 2006). Other indicators, such as elevated intraocular pressure (IOP) are also used in the identification of the disease. In 2002, Foster and colleagues proposed a classification system for categorising cases of angle closure (Foster 2002). The American Academy of Ophthalmology adopted their system in 2015 (Prum 2016), and we use it throughout this review (see Table 1.)

Glaucoma is a group of disorders which shows a distinctive and potentially progressive optic neuropathy, characterised by structural damage to the optic nerve and associated visual field loss (Kanski 2011). Glaucoma is the second leading cause of blindness worldwide. The number of people with glaucoma was estimated to be 76 million in 2020 and is expected to increase to 111.8 million by 2040 (Tham 2014). A quarter of cases are due to PACG. While open-angle glaucoma is more common than PACG, blindness is a more likely consequence of PACG (Tham 2014). Prevalence of PACG is higher in East Asians and Chinese populations and in women. In European populations, the prevalence of ACG is 0.4% of the adult population (Day 2012). PACG presents a serious health concern worldwide, and over 32 million cases are predicted by the year 2040 (Tham 2014).

Treatment of PAC

The main aims of treatment in people with chronic angle closure are to remove the underlying pathophysiological mechanism inducing closure and to reduce intraocular pressure (IOP) (Amerasinghe 2008). Currently, the first-line treatment for primary angle closure (PAC) is Nd:YAG laser peripheral iridotomy (NICE 2016), which involves the use of a laser to make a single hole in the peripheral iris (Le 2018). Peripheral iridotomy is thought to resolve the mechanism of 'pupillary block', whereby the pupillary iris makes a seal with the lens posteriorly, preventing the flow of aqueous humour into the anterior chamber (Gazzard 2003). Peripheral iridotomy was first developed in 1956. Since then, it has gone through a range of changes in modality (Khuri 1973; Pollack 1984).

In at least a third of cases of PAC, the anterior chamber angle remains appositionally closed after an iridotomy. The use of secondary line treatment options to widen the anterior chamber angle, such as laser peripheral iridoplasty (LPIp) or lens extraction (NICE 2016), is then considered. LPIp, originally coined 'laser gonioplasty', was first introduced in the 1970s (Kimbrough 1979), and can potentially be done with other types of laser that have a thermal effect. Its efficacy in the treatment of chronic angle closure is the focus of this review.

Description of the intervention

LPIp involves the placement of contraction burns in the extreme iris periphery. One or two burns are placed at each clock hour position circumferentially using an iridotomy lens (Kanski 2011). Precise parameters used appear to vary, with spot size ranging from 150 to 500 µm and power from 100 to 300 mW, for a duration of 0.4 to 0.5 s (Babighian 2018; Kanski 2011; Ramakrishnan 2016). Various laser modalities have been used, such as argon, krypton and diode lasers (Huang 2015; Muller 2016; Sassani 1993).

How the intervention might work

Several mechanisms have been proposed to explain the way in which LPIp opens the anterior chamber angle. The classic model suggests that the laser causes contraction of the iris stroma peripheral to the burn, between the burn and the trabecular meshwork, physically pulling open the angle (Ritch 1992; Ritch 2007). Histopathological reports further describe this as a result of the heat shrinkage of collagen, followed by contraction of a fibroblastic membrane formed at the site of injury (Sassani 1993). More recently, studies have placed emphasis on the cross-sectional thinning of the iris stroma at areas subjected to laser, which could contribute to a wider angle recess (Liu 2013). While peripheral iridotomy primarily acts by resolving pupillary block, LPIp could help to resolve chronic angle closure from other mechanisms including plateau iris syndrome (Gazzard 2003; Ritch 2007).

Why it is important to do this review

LPIp is typically used when a primary peripheral iridotomy does not successfully open an angle in PAC disease (Peng 2011). Previous systematic reviews have found inconclusive evidence regarding the use of LPIp in the treatment of chronic PAC cases. The previous version of this review was only able to analyse one randomised controlled trial (Ng 2012). This update aims to review the available literature to establish whether any further conclusions can be drawn.

OBJECTIVES

To assess the effectiveness of laser peripheral iridoplasty in the treatment of people with chronic angle closure, when compared to laser peripheral iridotomy, medical therapy or no further treatment.

METHODS

Criteria for considering studies for this review

Types of studies

We included only randomised controlled trials (RCTs) in the review.

Types of participants

Inclusion criteria

Participants must have had either suspected or confirmed primary angle closure (PACS and PAC respectively), or primary chronic angle-closure glaucoma (PACG).

No restrictions were applied with regards to gender, age or ethnicity of participants.

Participants were not excluded due to a history of resolved acute angle closure or previous laser peripheral iridotomy.

Exclusion criteria

- Secondary causes of angle closure
- Cases of acute angle closure attack

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Types of interventions

We included RCTs which compared the use of iridoplasty with medical treatment, laser peripheral iridotomy, or no further treatment. We also included RCTs which assessed a combined intervention of both laser peripheral iridotomy and peripheral laser iridoplasty at a single sitting.

Included trials focused on the use of iridoplasty in either the primary or secondary management of chronic angle closure (defined as people diagnosed with PACS, PAC or PACG).

Comparators

The comparators used were laser iridotomy alone, pharmaceutical treatment or no treatment.

Types of outcome measures

Primary outcomes

Percentage of cases found to have disease progression at two years, defined as either: a) change in stage of the disease (PACS to PAC to PACG); or b) worsening of glaucomatous damage among participants with PACG. As highlighted in Table 1, disease progression is based on clinical examination, including IOP and gonioscopy for PACS to PAC; and structural assessment of the optic disc and visual field testing for PAC to PACG.

Secondary outcomes

- IOP (intraocular pressure - measured using Goldmann applanation tonometry)
- The number of IOP-lowering medications required
- Complication rate and type (e.g. hyphema, persistently elevated IOP, change in corneal endothelial cell count (CECC), change in best corrected visual acuity (BCVA), etc.)
- Further surgical or laser interventions (e.g. a filtering procedure or phacoemulsification)
- Quality of life measures (e.g. National Eye Institute Visual Function Questionnaire (NEI-VFQ) or EuroQOL - 5 Dimension (EQ-5D) instrument, as reported in the trial)
- Anatomical change in the anterior chamber (measured clinically or using imaging techniques, such as anterior segment optical coherence tomography, AS-OCT)

Search methods for identification of studies

Electronic searches

The following resources were searched. There were no restrictions to language or year of publication. The date of the search was 20 December 2020.

- Cochrane Central Register of Controlled Trials (CENTRAL; 2020, Issue 12) (which contains the Cochrane Eyes and Vision Trials Register) in the Cochrane Library (searched 20 December 2020) (Appendix 1).
- MEDLINE Ovid (1946 to 20 December 2020) (Appendix 2).
- Embase Ovid (1974 to 20 December 2020) (Appendix 3).
- PubMed (1948 to 20 December 2020) (Appendix 4).
- National Institute for Health and Care Excellence (NICE) (www.nice.org.uk; searched 20 December 2020) (Appendix 5).
- US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (www.clinicaltrials.gov; searched 20 December 2020) (Appendix 6).
- World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp; searched 20 December 2020) (Appendix 7).

Searches had no language restriction but only English language studies were included. The unrestricted search revealed one Korean language study as a possible inclusion.

Searching other resources

We did not carry out formal checking of topic-specific journals. However, on a cursory search of the journal in which the Korean language study was published, we also found another study. Both of the Korean studies have been noted in the Discussion section of this review, but are awaiting full assessment.

Data collection and analysis

Throughout data collection and analysis, we used standard methods proposed by Cochrane.

Selection of studies

One review author first removed duplicate papers, after which two review authors independently assessed the titles and abstracts of the remaining discrete papers. We labelled each record as 'relevant', 'possibly relevant' or 'not relevant', and we put aside the 'relevant' and 'possibly relevant' papers for full-text review. Discrepancies were discussed between the two review authors where required, and a joint decision made.

The full-text copies of the papers which passed initial screening were then read independently by two review authors to ascertain whether they met the inclusion criteria. These were marked as 'Yes', or 'No', with discrepancies discussed and resolved between the two authors.

We generated a populated PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart (Moher 2009), which presents the study selection process (Figure 1).

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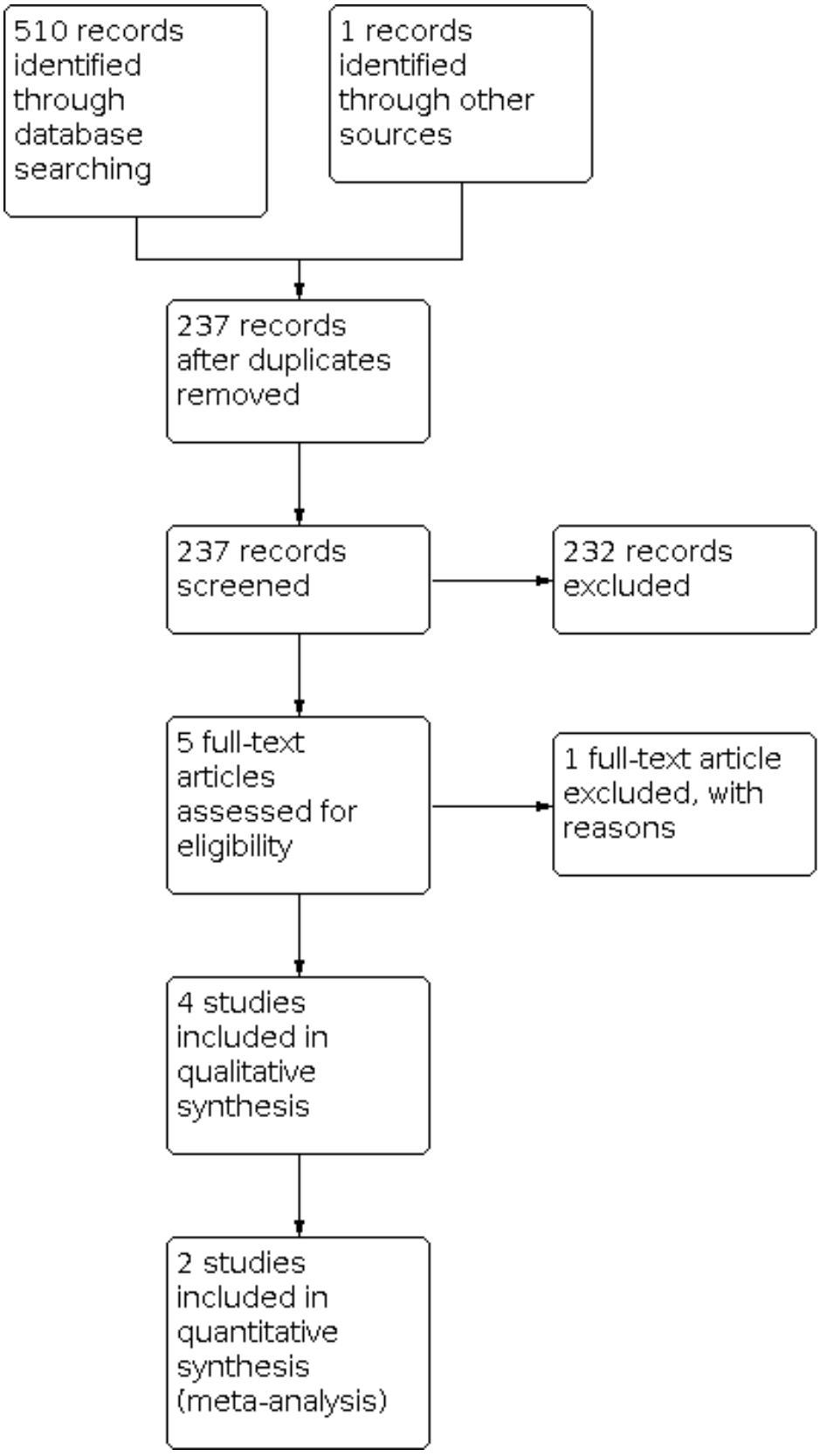
Figure 1. PRISMA Flow diagram of studies



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Data extraction and management

One review author extracted the relevant data from each included study using extraction tables created with guidance from Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2019, hereafter referred to as the *Cochrane Handbook*). Outcome data were extracted as specified in the Methods section. A second review author subsequently checked the extracted data.

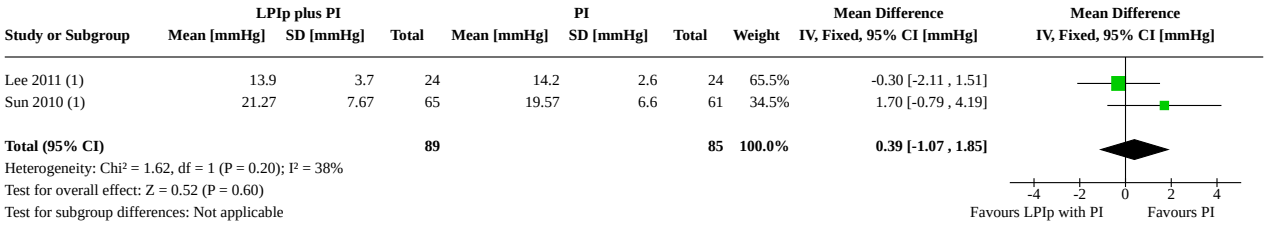
Assessment of risk of bias in included studies

Two review authors independently used Cochrane's Risk of Bias 1 tool (RoB 1) to assess the quality of the included RCTs (Higgins 2019). RCTs were rated as either 'low risk', 'unclear risk, or 'high risk', with details for each parameter included in the relevant Characteristics of included studies table. Any discrepancies were discussed between the two review authors and an agreement reached. RCTs were assessed for the following criteria: use of random sequence generation and allocation concealment (selection bias); blinding (masking) of participants and researchers (performance bias); masking of outcome assessment (detection bias); incomplete outcome data (attrition bias); and selective outcome reporting (reporting bias).

Measures of treatment effect

Measurement of treatment effect was determined using the risk ratio measure for dichotomous outcome variables, while the mean difference measure was used for continuous outcome variables. All results were presented with 95% confidence intervals. It was only possible to calculate a pooled measurement of effect estimate for one outcome (Figure 2).

Figure 2. Forest plot of comparison: 1 Argon LPIp with PI vs PI alone, outcome: 1.1 Mean change in intraocular pressure (IOP)



Footnotes
(1) Argon laser was used in all instances of LPIp

Unit of analysis issues

The unit of analysis was the participant, and was not a major concern for this review as very little meta-analysis could be performed. Lee 2011 was the only study to use a within-person RCT design, randomising one eye to argon LPIp with peripheral iridotomy, and the other to peripheral iridotomy alone. The authors ensured that both eyes were classified as having a similar level of disease (both eyes were categorised as PACS as part of their inclusion criteria) before a random selection between the eyes was made to determine the intervention and control eyes. Baseline parameters for eyes from each group were given in their table 1, and groups were well matched. It is unclear, however, whether any statistical correction was performed to mitigate the risk of bias with taking repeated measurements.

In order to deal with cross-over studies, cluster trials or multiple treatment arms, we followed the recommendation given in Chapter 8 of the *Cochrane Handbook* (Higgins 2019).

Dealing with missing data

We planned to handle missing data in accordance with the *Cochrane Handbook* recommendations. Some data which investigators planned to collect in two of the included RCTs were not included in their results section. For example, Narayanaswamy 2016 did not include change in anterior chamber depth (ACD) at 12 months, and Bourne 2017 did not include P values for some of the trial's IOP results. However, we decided that this information was not key to the review. There was enough information available to reach our conclusions, and thus we decided that contacting trial authors about these data was unnecessary.

Assessment of heterogeneity

We assessed heterogeneity by examining the characteristics of the included studies, in order to determine whether a meta-analysis could be carried out or whether a narrative synthesis would be more appropriate. As many outcome measures could not be pooled (see Data synthesis), Chi^2 and I^2 values could not often be calculated. A Chi^2 value of 1.62 and I^2 value of 38% (P = 0.20) was generated for the final mean IOP outcome of those studies which assessed LPIp with peripheral iridotomy, versus peripheral iridotomy alone as a primary procedure, suggesting a low level of heterogeneity between these studies. Therefore, a fixed-effect model of meta-analysis was used.

Assessment of reporting biases

As the number of included studies was fewer than 10, we could not use a funnel plot using standard error values to assess the risk of publication bias.

Data synthesis

We could not perform a quantitative synthesis (meta-analysis) for many of the outcomes assessed, as there were not enough relevant high-quality RCTs available with sufficient homogeneity between studies. Several distinct methods of assessing the intervention against a comparator were identified, and separated into appropriate subsections. We performed a narrative synthesis of the majority of outcomes.

A sufficient level of homogeneity was present in the studies which assessed LPIp with peripheral iridotomy, versus peripheral

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iridotomy alone as a primary procedure, to allow a pooled estimate for the final mean IOP to be generated. Adverse effects were also reported by these studies and pooled estimates for these can be found in Table 2.

Subgroup analysis and investigation of heterogeneity

Both a high level of clinical diversity and methodological diversity was evident between the included RCTs, resulting in an inability to perform meta-analysis on the majority of reported outcomes. In total, 15 discrete outcome variables were reported with a high disparity in those reported by each study (see Table 3). For example, many differing variables were used to assess anterior chamber morphology, and did not lend themselves to the generation of pooled estimates.

In addition, as previously mentioned, several different comparators and methods of assessing the intervention were utilised, and we decided it was inappropriate to synthesise these results cumulatively. Instead, the results were separated into three groups and discussed individually. Subgroup analysis could not be performed due to a paucity of available data.

Sensitivity analysis

We planned for sensitivity analyses to be conducted to assess the influence of a high risk of reporting bias (found using the RoB1 tool), unpublished data, and industry-funded data (funding bias) on effect sizes. However, this could not be done due to the small number of trials, with different comparators, making meta-analysis unfeasible for the majority of outcome measures.

Summary of findings and assessment of the certainty of the evidence

We used the GRADE system to assess the quality of the evidence (see Quality of the evidence). We followed the methods outlined in Section 8.5 and Chapter 12 of the *Cochrane Handbook* (Higgins 2019, Higgins 2020), regarding the use of GRADEpro software (GRADEpro GDT).

We included a 'Summary of findings' table for each of the following three methods of assessing the intervention.

- Laser peripheral iridoplasty with iridotomy versus iridotomy alone as a primary procedure.
- Laser peripheral iridoplasty as a secondary procedure versus no treatment.
- Laser peripheral iridoplasty as a secondary procedure versus medication.

We included the following outcomes, where measured.

- Disease progression
- IOP
- Additional medications
- Complications
- Further surgical or laser interventions
- Quality of life measures
- Anterior chamber morphology, including extent of peripheral anterior synechiae (PAS)

The certainty of the evidence was assessed using the five GRADE domains: methodological limitations of the studies; inconsistency of effect; imprecision; indirectness; and publication bias. Concerns were rated as 'not serious', 'serious' or 'very serious'.

RESULTS

Description of studies

An overview of study attributes can be found in the Characteristics of included studies table.

Results of the search

For this update, a search of the databases on 20 December 2020 returned a total of 510 records (Figure 1). After removing 273 duplicates, 237 distinct records remained to be screened. We excluded a further 232 records based on their titles and abstracts, leaving five papers for full-text assessment. Of these five, one was a case report and was thus excluded, while the remaining four were confirmed as inclusions.

We identified two Korean language studies, which are awaiting full assessment (Characteristics of studies awaiting classification).

Included studies

We have included four RCTs in this review (Bourne 2017; Lee 2011; Narayanaswamy 2016; Sun 2010).

Design of studies

The studies by Bourne 2017, Lee 2011 and Narayanaswamy 2016 were parallel group RCTs, including two separate groups for each arm. Lee 2011 was a within-person RCT: one eye underwent peripheral iridotomy alone, while the other eye underwent both laser peripheral iridotomy and argon LPIp.

Participants

Three studies (Sun 2010, Narayanaswamy 2016 and Bourne 2017), enrolled 158 participants (158 eyes), 80 participants (80 eyes), and 22 participants (22 eyes) respectively, while Lee 2011 enrolled 24 participants (48 eyes).

Most participants were from an Asian population, with participants from China (Sun 2010), Singapore (Narayanaswamy 2016) and South Korea (Lee 2011). Bourne 2017 recruited participants from the UK.

Controls and Interventions

All studies used argon LPIp as their mode of delivering LPIp. Sun 2010 randomised each arm to either peripheral iridotomy alone or peripheral iridotomy with argon LPIp (argon LPIp was performed two to five days following peripheral iridotomy). Bourne 2017 randomised post-peripheral iridotomy participants with a persistently occludable angle on gonioscopy to either argon LPIp or no further treatment. Lee 2011 also compared peripheral iridotomy alone to peripheral iridotomy with argon LPIp (the intervention eye underwent peripheral iridotomy and argon LPIp at the same sitting). Narayanaswamy 2016 compared argon LPIp to medical therapy (travoprost) in post-peripheral iridotomy participants with a persistently occludable angle on gonioscopy.

Outcomes

The outcomes assessed have been listed in Table 3.

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Sun 2010 and Narayanaswamy 2016 conducted a final measurement of outcomes at 12 months, while Bourne 2017 and Lee 2011 conducted their final measurement at 3 months.

Excluded studies

We excluded one study because it was an observational study comparing a group which had undergone argon LPIp in one time period, with a matched group from an earlier period (Cho 2017).

Risk of bias in included studies

We assessed the risk of bias for the included studies, with the findings summarised in Figure 3 and Figure 4.

Figure 3. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

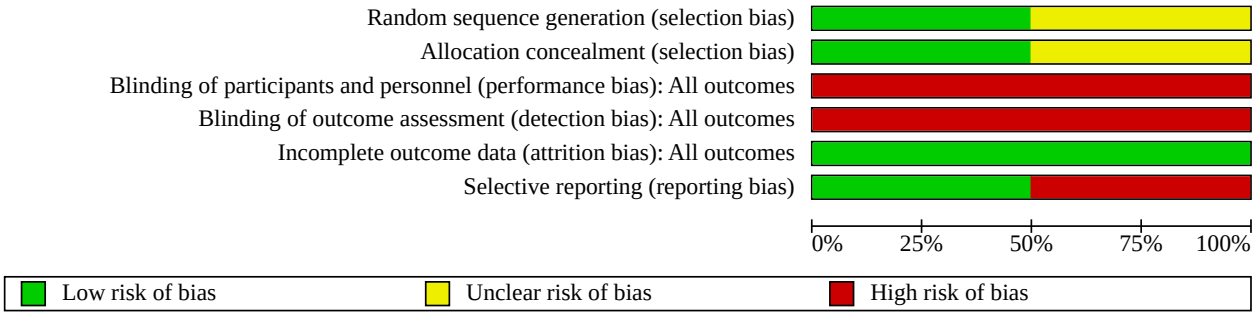
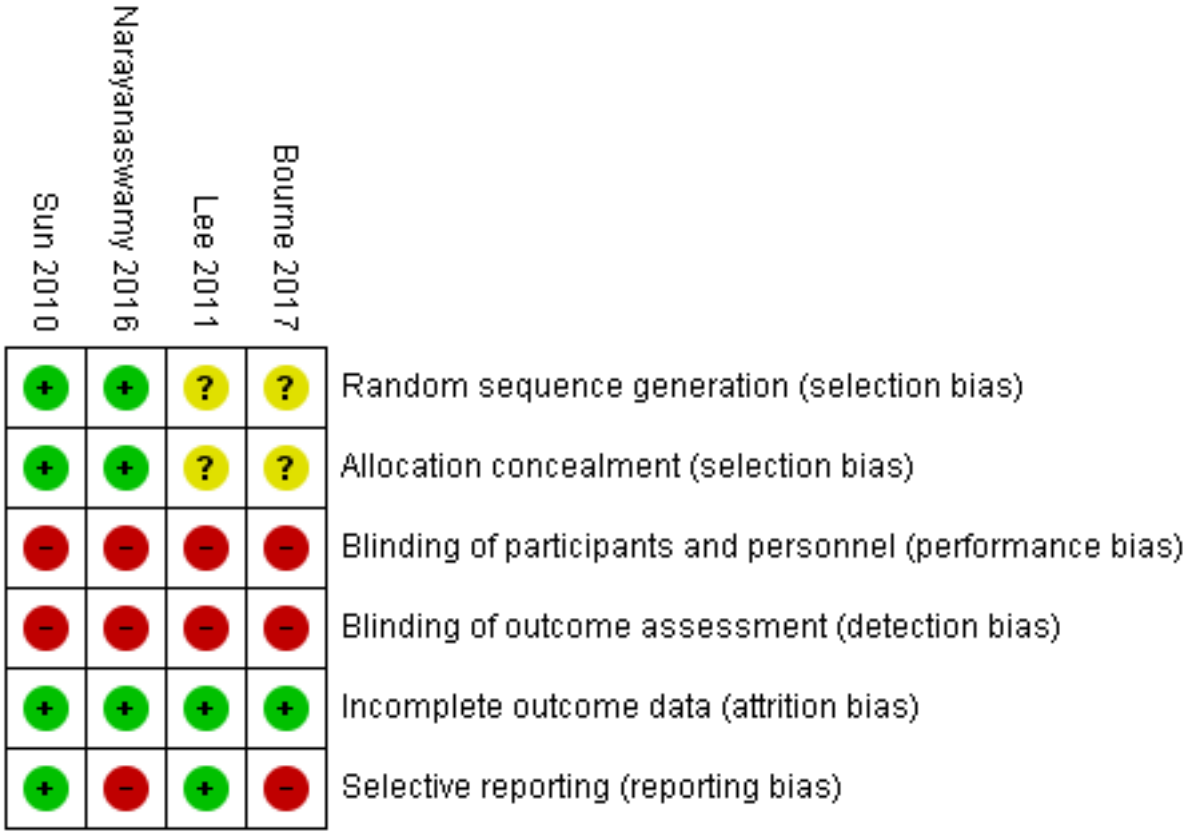


Figure 4. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



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Allocation

Random sequence generation was used by Narayanaswamy 2016 via the use of pre-allocated codes, and by Sun 2010 using a random number generator. We assessed both of these as 'low risk'. Both Lee 2011 and Bourne 2017 commented on having randomised participants but did not specify their randomisation process and therefore were marked as 'unclear risk'. Concealment of allocations before assignment was ensured by Narayanaswamy 2016 using sealed envelopes opened at the point of assignment. Sun 2010 had very well-matched groups, and so were judged to be at 'low' risk of bias. Lee 2011 and Bourne 2017 did not include a comparison of the two arms, or mention concealment measures and so were marked as 'unclear risk'.

Blinding

None of the participants nor researchers from all four trials were masked to which intervention the participants had received. Thus, all trials were marked as high risk.

As mentioned, all studies encountered difficulty in removing bias due to the inability to mask personnel to the iridoplasty scars. Narayanaswamy 2016 masked the researchers to some of the results they were obtaining by concealing the scale of the tonometer when IOP measurements were taken; these were subsequently read by an assistant. Sun 2010 also reported masking of IOP measurements, as well as assessment of visual acuity and automated perimetry, but did not specify the methods used. Despite attempts to reduce bias by some trials, we assessed all studies as 'high risk' because concealment was not possible for other measurements, such as gonioscopy.

Incomplete outcome data

All participants in Lee 2011 and Bourne 2017 were followed to study completion. Losses to follow-up were similar in both groups in Sun 2010 (20.8% peripheral iridotomy, 19.8% argon LPIp with peripheral iridotomy; 32 lost in total of 158 enrolled) and were included in a separate 'last observation carried forward' analysis. Narayanaswamy 2016 only had one loss to follow-up, from the argon LPIp group, which was also included in a 'last observation carried forward' analysis. However, this does not seem to have been done separately from the main analysis. As all studies had a low number of losses to follow-up, or accounted for any significant number of losses, we assessed all as 'low' risk of bias.

Selective reporting

Sun 2010 and Narayanaswamy 2016 were both prospectively registered (on the Chinese Clinical Trial Register and ClinicalTrials.gov respectively), while Bourne 2017 and Lee 2011 did not appear to have registered their trials. Sun 2010 and Lee 2011 reported fully on all outcomes specified in their methods, and were marked as 'low' risk of bias. Narayanaswamy 2016 included the baseline values for most AS-OCT parameters (mean angle width, angle opening distance (AOD), trabecular-iris space area (TISA), angle recess area (ARA), and iris thickness). However, they did not report the final raw values, or P values for the travoprost group, if measured. The change in anterior chamber depth (ACD) was also not reported, despite measurement at baseline. Bourne 2017 did not report AS-OCT values at three months for the control group, only comparing pre- and post-argon LPIp values. Therefore, we assessed both Narayanaswamy 2016 and Bourne 2017 as 'high' risk of bias.

Other potential sources of bias

We identified no other potential sources of bias in the included studies.

Effects of interventions

See: **Summary of findings 1** Summary of Findings; **Summary of findings 2** Summary of Findings; **Summary of findings 3** Summary of Findings

Laser peripheral iridoplasty with iridotomy versus iridotomy alone as a primary procedure

The use of argon LPIp with iridotomy as a primary procedure was used by two studies as their intervention (Lee 2011; Sun 2010).

Primary outcome

Neither study collected data for the primary outcome of interest for this review.

Secondary outcomes

Intraocular pressure (IOP)

There was no difference in IOP lowering efficiency between LPIp and control groups. Lee 2011 assessed IOP at one hour, day, week, and one month as well as three months post-intervention, but no evidence of effect was observed in the argon LPIp group at three months (mean difference (MD) 0.30 lower, 95% confidence interval (CI) -2.11 to 1.51). A later assessment at 12 months was made by Sun 2010, who also found no evidence of effect in the argon LPIp group (MD 1.70 mmHg higher, 95% CI -0.79 to 4.19). Results from both studies were pooled, giving a combined mean difference of 0.39 mmHg (Analysis 1.1, 95% CI -1.07 to 1.85; I^2 = 38%; 2 studies, 174 participants; low-certainty evidence).

Additional medications

Sun 2010 reported on the mean number of additional glaucoma medications prescribed at 12 months. No evidence of effect was observed in the use of argon LPIp over the control (MD 0.10, 95% CI -0.34 to 0.54; 126 participants, low-certainty evidence).

Complications

Complications were reported by both studies, but were varied in nature. Both Lee 2011 and Sun 2010 noted a similar risk of bleeding between groups, with Lee 2011 reporting that 4% of participants in both groups developed 'hyphema'. Sun 2010 reported on 'iris haemorrhage', which was present in 11.7% of participants in the argon LPIp with peripheral iridotomy group, and 12.3% of participants in the peripheral iridotomy group.

'Post-laser IOP spikes' were present in 16.9% of participants in the peripheral iridotomy group and 17.3% of participants in the argon LPIp with peripheral iridotomy group in Sun 2010, while Lee 2011 noted 33% in both groups. However, Lee 2011 classified an IOP spike as an increase of 5 mmHg or higher, while Sun 2010 classified a spike as an IOP of 30 mmHg or higher.

Sun 2010 assessed best corrected visual acuity (BCVA) at 12 months and found no difference in final median BCVA between groups (P = 0.410 peripheral iridotomy alone, P = 0.431 argon LPIp with

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peripheral iridotomy). Sun 2010 also assessed corneal endothelial cell count (CECC) at 12 months and found no evidence of effect in the argon LPIp group, over the control group (MD -93.54 cells/mm^2, 95% CI -230.77 to 43.69; 126 participants, low-certainty evidence).

Other complications reported by Lee 2011 included 'persistent uveitis' (8% in the peripheral iridotomy alone group versus 4% in the argon LPIp with peripheral iridotomy group) and 'transient atonic pupil' (occurred in a single participant of the argon LPIp with peripheral iridotomy group, 4%). Sun 2010 reported two cases of 'corneal endothelial burn' in the peripheral iridotomy alone group (2.6%), and one case of malignant glaucoma in the argon LPIp with peripheral iridotomy group (1.2%).

Extent of peripheral anterior synechiae (PAS)

Sun 2010 examined the extent of peripheral anterior synechiae (PAS) at baseline and 12 months. While finding a significant improvement in both groups ($P < 0.001$), the authors found no difference between groups ($P = 0.473$).

Further surgical or laser interventions

The need for further surgery was assessed by Sun 2010 at 12 months, who found no evidence of effect in the argon LPIp group over controls (risk ratio (RR) 1.21, 95% CI 0.66 to 2.21; 126 participants, low-certainty evidence).

Quality of life measures

Data regarding quality of life measures were not collected by the authors of either study.

Anterior chamber morphology

Anterior chamber angle (ACA), anterior chamber volume (ACV) and anterior chamber depth (ACD) were measured by Lee 2011 at three months using a Pentacam®. Argon LPIp showed no evidence of effect over peripheral iridotomy alone in any of these parameters (ACD: MD 0.00 mm, 95% CI -0.10 to 0.10; ACV: MD 2.20 mm, 95% CI -7.23 to 11.63; and ACA: MD 0.86 mm, 95% CI -1.47 to 3.19; 24 participants, 48 eyes; very low-certainty evidence for all measurements).

Summary of effects

No evidence of effect was found for the use of argon LPIp alongside peripheral iridotomy over the control group for the included outcome measures. We created an 'Adverse effects' table (Table 2) to better summarise any differences in complication rate between groups. Overall complications were uncommon, and severe complications were rare.

Laser peripheral iridoplasty as a secondary procedure versus no treatment

The use of argon LPIp as a secondary procedure versus no treatment was examined by one included study (Bourne 2017).

Primary outcome

Bourne 2017 did not collect data for the primary outcome of interest for this review.

Secondary outcomes

Intraocular pressure (IOP)

Bourne 2017 measured IOP hourly between 9:00 and 16:00 in order to obtain diurnal IOP (DIOP) results at baseline and three months. At three months, they found the mean difference in maximum IOP in the intervention group to be 1.81 mmHg lower than the control (95% CI -3.11 to -0.51; (19.34 mmHg argon LPIp, 21.15 mmHg peripheral iridotomy alone)) suggesting a clinically significant reduction in participants post-argon LPIp. However, no evidence of effect was observed for mean minimum values (MD -0.31, 95% CI -1.93 to 1.31), and P values were not included comparing the two groups. GRADE evidence for the final maximum and minimum IOP measurements was very low-certainty.

Additional medication

The authors did not collect data regarding the use of additional medications.

Complications

The authors did not collect data regarding adverse events.

Further surgical or laser interventions

The authors did not collect data regarding any requirement for further surgical or laser intervention.

Quality of life measures

The authors did not collect data regarding quality of life measures.

Anterior chamber morphology

Bourne 2017 reported AOD, TISA and ARA at three months, by the analysis of AS-OCT images. Measurements were taken at 500 µm and 750 µm from the scleral spur, for eight sectors. Statistically significant widening was found in the argon LPIp group for all AOD, ARA and TISA parameters at three months, excluding Inferior AOD500 and 750, Supero-nasal and Supero-temporal ARA500 and Inferonasal ARA750 (5 of 48). Trabecular iris angle (TIA) measurements were also measured by Bourne 2017, and widening was found to be statistically significant in all sectors. However, the GRADE certainty of this evidence was very low, and no AS-OCT measurements for the control group (peripheral iridotomy alone) were reported.

Summary of effects

While there was no difference in final mean minimum IOP values between groups, a clinically significant reduction in maximum IOP values was observed in the LPIp group. While this evidence was of very low-certainty, it showed a reduced range of diurnal IOP in those having undergone the intervention. The evidence regarding change in AS-OCT parameters was very unclear. Although statistically significant increases were reported in the intervention group, the evidence was of very low-certainty, and no AS-OCT measurements for the control group were reported.

Laser peripheral iridoplasty as a secondary procedure versus medication

The use of argon LPIp as a secondary procedure versus travoprost 0.004% was examined by one included study (Narayanaswamy 2016).

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Primary outcome

Narayanaswamy 2016 assessed the primary outcome of progression of the disease state via measurement of vertical cup-to-disk ratio (C/D ratio). Argon LPIp showed no evidence of greater effect in preventing disease progression when compared to travoprost (MD -0.03, 95% CI -0.11 to 0.05; 80 participants; low-certainty evidence).

Secondary outcomes

Intraocular pressure (IOP)

Narayanaswamy 2016 reported that participants from the travoprost group achieved a statistically significantly lower mean IOP at 12 months, when compared to those in the argon LPIp group (17.7 mmHg versus 19.2 mmHg, P = 0.02), despite no difference at baseline (P = 0.61). However, when assessing the mean change in IOP at 12 months, no evidence of a greater effect in the travoprost group was noted (MD -1.20, 95% CI -2.87 to 0.47; 80 participants; low-certainty evidence).

Additional medications

The mean number of glaucoma medications prescribed at 12 months was assessed by Narayanaswamy 2016. No evidence of effect was shown for argon LPIp over the travoprost group: a mean difference of 0.42 additional medications was required by the intervention group at 12 months (95% CI 0.23 to 0.61; 80 participants; low-certainty evidence).

Complications

No serious adverse events were reported. Narayanaswamy 2016 reported two cases of 'post-laser IOP spike' in their argon LPIp arm (5%). An IOP spike was classified as an increase of 5 mmHg or higher.

Extent of peripheral anterior synechiae (PAS)

The extent of peripheral anterior synechiae (PAS) was measured at 12 months. Narayanaswamy 2016 reported a decrease in the travoprost group (P = 0.03), while noting an increase in the extent of PAS in the argon LPIp group (mean progression by 0.9 clock hours, P = 0.03).

Further surgical or laser interventions

The need for further surgery was assessed by Narayanaswamy 2016 at 12 months, who reported one case in the intervention group alone, with none in the control group (80 participants; low-certainty evidence).

Quality of life measures

The authors did not collect data regarding quality of life measures.

Anterior chamber morphology

Narayanaswamy 2016 assessed anterior chamber morphology at 12 months, by the analysis of AS-OCT images. Statistically significant widening was reported in AOD500 and 750, TISA750 and ARA750 values (P < 0.001 for all) for the argon LPIp group. However, measurement of effect could not be calculated due to a paucity of available data, and results were not included for control participants, despite measurement at baseline. Mean angle width was also reported to be significantly increased in the argon LPIp group versus the travoprost group (1.6 versus 2.0 Shaffer angle, P = 0.001), while no change in iris thickness (750 µm and 2000 µm) was observed (P = 0.43 and P = 0.34 respectively). All evidence was of low GRADE certainty.

Summary of effects

No evidence of greater effect of LPIp was noted for the included outcomes. The evidence regarding change in AS-OCT parameters was unclear, Although statistically significant increases were reported in the intervention group, the evidence was of low certainty, and many control group measurements were not reported at 12 months. No serious adverse events were reported in either group, but a greater number of medications was required by the argon LPIp group at 12 months.

DISCUSSION

Summary of main results

In this review, the results of four RCTs assessing the efficacy of argon LPIp as an intervention have been presented. Overall, the included studies have produced insufficient evidence to support the use of argon LPIp in people with chronic angle closure. Only one study reported results pertaining to the primary outcome (by assessing vertical C/D ratio) and found no statistical difference between groups (Narayanaswamy 2016). No data were reported regarding progression of visual field loss, patient views or quality of life. The IOP lowering efficacy of argon LPIp was similar or worse than other options explored.

Overall, the results suggest that argon LPIp may be safe, however no long term follow up data was reported beyond 12 months. The incidence of severe complications reported by three RCTs was rare for all participants across control and intervention groups, regardless of the specific intervention utilised.

Conflicting results were reported regarding the change in extent of peripheral anterior synechiae (PAS) in the argon LPIp groups post-intervention (Narayanaswamy 2016; Sun 2010). Sun 2010 reported a reduction in the extent of PAS post-argon LPIp while Narayanaswamy 2016 reported an increase. This contradiction is possibly explained by differences in gonioscopy technique (the use or absence of indentation). A small change in the extent of PAS is unlikely to be clinically relevant.

Two studies found no evidence of effect of argon LPIp in the reduction of IOP when compared to control groups, whether used as a primary or secondary procedure (Lee 2011; Sun 2010). Another study comparing argon LPIp with medication reported a greater reduction in IOP in their control participants; however, the mean change was not significantly different between groups (Narayanaswamy 2016). One study assessed diurnal IOP, and found a reduction in the range of diurnal IOP values in their argon LPIp group compared to that at baseline, and to that of the peripheral iridotomy control group (Bourne 2017). However, the clinical relevance of a reduction in IOP fluctuation is uncertain.

Anterior chamber morphology was assessed using a wide range of parameters. Widening of the majority of AOD, TISA and ARA measurements post-argon LPIp was reported by Bourne 2017 and Narayanaswamy 2016. However, control data were absent and evidence was of a low or very low certainty. TIA and mean angle width were examined by single studies and found to be significantly widened. However, the measure of effect could also not be assessed

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for these outcomes. Finally, mean ACA, ACV and deepest ACD were assessed by Lee 2011 who found no difference in measure of effect between argon LPIp and peripheral iridotomy alone.

We identified two Korean language studies, and extracted information from their abstracts only (their characteristics are outlined in the Characteristics of studies awaiting classification table). Park 2011 compared laser peripheral iridotomy alone to argon LPIp with peripheral iridotomy. It is not clear whether this study is a RCT or just a comparison of two groups of unequal number (11 and 14). Baseline IOP was disparate between groups (15.0 mmHg versus 18.9 mmHg). However, no difference in IOP reductions was noted between the peripheral iridotomy alone and the argon LPIp with peripheral iridotomy groups (1.5 mmHg and 1.1 mmHg respectively). The main outcome measure reported in the abstract was widening of anterior chamber angle. Change in IOP is not mentioned in the English language abstract.

The second study, by Kim 2003, is a RCT comparing peripheral iridotomy alone to argon LPIp with peripheral iridotomy, with 30 participants per group. The English language abstract and a graph of results showed an advantage of combined treatment at 2 and 4 months (when comparing 'success' defined as IOP < 21 mmHg without the use of medication), while only showing a just significant advantage at 6 and 8 months (both having P = 0.047) and no difference at 12 months.

An observational study by Cho and colleagues was excluded (Cho 2017). It compared people who had undergone argon LPIp with peripheral iridotomy between April and August 2015, with an earlier group who had undergone peripheral iridotomy alone between October 2014 and March 2015. The participants in the earlier group were matched for age, gender and iridotrabecular contact index, but not IOP. The changes in IOP were not significantly different between groups.

Overall completeness and applicability of evidence

Of the four studies included, only Narayanaswamy 2016 measured direct progression of the disease, by assessing C/D ratio, while no studies assessed progression of visual field scotoma.

A varied range of secondary outcomes were reported by the included studies, which made it difficult to collate the evidence. Of the outcomes shared by the studies, high variation in findings was evident, which may be due in part to the small sample sizes of some of the included studies. Findings may also differ as a result of the differing methods of study design (both regarding the methods of interventions and comparators used), as well as the short follow-up period of some of the studies (three months in half of the included studies). Meta-analysis was not feasible.

Most participants were recruited from an Asian population, with participants from China, Singapore and Korea (Lee 2011; Narayanaswamy 2016; Sun 2010), with only 7% of participant eyes from a European population (Bourne 2017). Differences in anterior segment physiology between ethnic groups could hinder the applicability of the results found to non-Asian populations.

Quality of the evidence

The five GRADE domains (methodological limitations of the studies, inconsistency of effect, imprecision, indirectness, and publication bias) were used to assess the quality of the evidence obtained from the included studies. Concerns were rated as 'not serious', 'serious' or 'very serious'.

Methodological limitations of the studies

All trials had a high risk of bias concerning the lack of ability to mask (blind) participants and personnel to the intervention received, and the ability to mask the assessor to the outcomes measured. Two trials showed small instances of selective reporting (Bourne 2017; Narayanaswamy 2016). There was a lack of specification of the randomisation and allocation process by two studies (Bourne 2017; Lee 2011). All studies included results of cases lost to follow-up where applicable. Therefore, we rated our concerns regarding this GRADE domain as 'serious'.

Indirectness

Three of the four included trials did not assess the primary outcome, disease progression. However, the participants, intervention and comparators used by all studies all provide direct evidence to the clinical question at hand. The parameters used to measure morphology of the anterior chamber varied between studies; despite this, no serious indirectness was found in the outcome measures assessed. Therefore, we rated our concerns regarding this GRADE domain as 'not serious'.

Imprecision

The total number of participants included in all the trials was 252 participants (276 eyes). Some outcomes were only measured by a single trial: C/D ratio by Narayanaswamy 2016; and BCVA and CECC by Sun 2010. However, these studies had larger sample sizes (80 and 126, respectively) and followed participants to 12 months. Therefore, we rated our concerns regarding this GRADE domain as 'not serious'.

Inconsistency

A significantly greater number of medications was required by the control group in one study (Narayanaswamy 2016), which also noted a decrease in the extent of PAS in the control group, yet an increase in the intervention group. This contrasts to another study, which found no significant difference between intervention and control groups concerning both outcomes (Sun 2010). However, different comparators were used (travoprost and peripheral iridotomy alone, respectively).

IOP was measured by all four studies. Two found no significant difference between groups at 3 months (Lee 2011), and 12 months (Sun 2010), while a third found a reduced range of DIOP in the intervention group (P values not given) (Bourne 2017). The last study, Narayanaswamy 2016, found a significantly lower mean IOP at 12 months in their comparator group. However, as mentioned, this trial used a different comparator. Therefore, we rated our concerns regarding this GRADE domain as 'serious'.

Likelihood of publication bias

No unpublished data were available for analysis. Of the published studies, no financial conflicts of interest were declared. Published studies did not exclusively show positive findings. Therefore, we rated our concerns regarding this GRADE domain as 'not serious'.

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Potential biases in the review process

In this review, we followed the steps for conducting a systematic review, as outlined by Cochrane, to prevent bias wherever possible. We expanded the search strategies used in previous iterations of this review in order to ensure all relevant studies could be identified, and we searched a wide variety of locations. As outlined in the methods section, several review authors independently searched for, and assessed the risk of bias of, included studies, and extracted data were checked by another author.

We identified two potentially relevant studies. However, as they were published in Korean and translation was not available, these could not be included in the synthesis of the review.

Agreements and disagreements with other studies or reviews

Not applicable, as there are no other current reviews.

AUTHORS' CONCLUSIONS

Implications for practice

LPIp is currently used as a second-line treatment option in people with remaining appositional angle closure after peripheral iridotomy. The results obtained from the four included RCTs do not provide enough evidence to suggest that argon LPIp confers any additional benefit to the use of peripheral iridotomy alone in reducing IOP and subsequently preventing the progression of the disease process, whether when used as a primary or secondary intervention. A low incidence of severe complications was reported by three RCTs across all groups. Findings suggest that anterior chamber morphology may be positively impacted by argon LPIp. However, there is no evidence of significant reduction in IOP after argon LPIp and thus there is no evidence to support the use of LPIp in the management of chronic angle closure glaucoma.

Implications for research

The results of the included trials suggest argon LPIp provides little to no benefit over comparators in the management of people with chronic angle closure. Despite uncertainties, the existing evidence does not justify research efforts in further trials of argon LPIp as an intervention in cases of chronic angle closure.

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CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Bourne 2017

Study characteristics

Methods	**Study design:** parallel group RCT
	Study date: not reported
	Number randomised (total and per group): 22 in total; 11 per group

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Bourne 2017 *(Continued)*

	Number analysed (total and per group): 22 in total; 11 per group
	Exclusions and losses to follow-up: nil
	Study follow-up: 3 months
Participants	**Country:** UK
	Age (mean ± SD), years: not reported
	Ethnicity: Caucasian (understood to be white)
	Recruitment: consecutive enrolment
	Inclusion criteria: bilateral PAC, PACS, or a combination
	Exclusion criteria: 'Any other ocular comorbidity'; resolution of gonioscopically occludable angle following PI
Interventions	**Control:** no further treatment
	Intervention: argon LPIp
Outcomes	**Primary outcomes:** angle parameters: AOD, TISA, ARA, TIA, IT
	Secondary outcomes: IOP
Notes	**Funding source:** Hinchingbrooke Hospital Ophthalmology Research Fund
	Competing interests: none declared
	Publication language: English
	Trial registered: unregistered
	Sample size and power calculations: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	“consecutive patients … were recruited to the IMPACT study”
		“LPI procedures were performed … a randomly allocated eye of each patient”
		“The second randomisation … took place 3 months post-LPI”
		Randomisation process not specified
Allocation concealment (selection bias)	Unclear risk	Allocation process not specified
Blinding of participants and personnel (performance bias) All outcomes	High risk	Masking not possible (iridoplasty scars)
Blinding of outcome assessment (detection bias) All outcomes	High risk	Masking not possible (iridoplasty scars)
Incomplete outcome data (attrition bias)	Low risk	All participants completed the trial

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Bourne 2017 *(Continued)*
All outcomes

Selective reporting (reporting bias)	High risk	P values not provided for several IOP results

Lee 2011

Study characteristics	
Methods	**Study design:** within-person RCT **Study date:** not reported **Number randomised (total and per group):** 24 participants; 24 eyes per group **Number analysed (total and per group):** 24 participants; 24 eyes per group **Exclusions and losses to follow-up:** nil **Study follow-up:** 3 months
Participants	**Country:** South Korea **Age (mean ± SD), years:** not reported **Ethnicity:** not reported **Recruitment:** consecutive and prospective enrolment **Inclusion criteria:** bilateral PACS **Exclusion criteria:** IOP > 21 mmHg using GAT; the presence of PAS; GON such as neuroretinal rim notching and/or thinning and/or disc haemorrhage and an associated retinal nerve fibre layer defect; visual field defects indicative of GON; a previous episode of acute angle closure attack; secondary angle closure
Interventions	**Control:** PI alone on a randomly selected eye, one week prior to the intervention **Intervention:** PI combined with argon LPIp in a single sitting, on the fellow eye
Outcomes	**(Primary vs. secondary outcomes not specified)** **Outcomes:** IOP, complications, angle parameters (mean anterior chamber depth (ACD), anterior chamber volume (ACV), anterior chamber angle (ACA), topographic ACD analysis)
Notes	**Funding source:** not reported **Competing interests:** none declared **Publication language:** English **Trial registered:** unregistered **Sample size and power calculations:** not reported

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**

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Lee 2011 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Randomisation process not specified
Allocation concealment (selection bias)	Unclear risk	Randomisation process not specified
Blinding of participants and personnel (performance bias) All outcomes	High risk	Masking not possible (iridoplasty scars)
Blinding of outcome assessment (detection bias) All outcomes	High risk	Masking not possible (iridoplasty scars)
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants were followed to study completion
Selective reporting (reporting bias)	Low risk	All outcomes were fully reported on

Narayanaswamy 2016

Study characteristics	
Methods	**Study design:** parallel group RCT **Study date:** October 2007 to March 2012 **Number randomised (total and per group):** 80; 40 per group **Number analysed (total and per group):** 80; 40 per group **Exclusions and losses to follow-up:** 1 loss to follow-up, included in analysis **Study follow-up:** 12 months
Participants	**Country:** Singapore **Age (mean ± SD), years:** intervention: 65.2 ± 7.8; control: 65.8 ± 6.4 **Ethnicity:** not reported **Recruitment:** Singapore National Eye Centre and the Department of Ophthalmology, National University Hospital were involved **Inclusion criteria:** ≥ 40 years of age, diagnosed with PAC or PACG prior to PI; gonioscopically occludable angle following PI; untreated IOP of 22 to 30 mmHg 1 month post-PI **Exclusion criteria:** IOP > 30 mmHg; history of a previous acute PAC; secondary causes of angle closure (e.g. subluxed lens, uveitis, trauma, or neovascular glaucoma; vertical cup-to-disc ratio of 0.9 or more, or visual field constriction involving the central 10 of the visual field; visual acuity less than 20/40 resulting from cataract; or previous intraocular surgery, laser trabeculoplasty, refractive surgery, or argon LPIp; > 6 clock hours of PAS and a CECC < 1000 cells/mm2
Interventions	**Intervention:** argon LPIp

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Narayanaswamy 2016 *(Continued)*

	Control: prostaglandin analogue therapy (travoprost 0.004%)
Outcomes	**Primary:** IOP (complete success = IOP without medication, qualified success = with medication) **Secondary:** change in IOP and % change; angle parameters: AOD, TISA, ARA; complications; number of medications; PAS
Notes	**Funding source:** National Medical Research Council, Singapore, Republic of Singapore (grant no.: NMRC/TCR/002-SERI/2008) AMO Singapore Pte. Ltd, Singapore, Republic of Singapore (unrestricted grant) **Competing interests:** none declared **Publication language:** English **Trial registered:** ClinicalTrials.gov (Identifier: NCT00980473) **Sample size and power calculations:** reported: a calculated sample size of 40 participants in each arm was required to show a difference of 30%, with a power of 80% and a target α level of 0.05.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"The block randomisation method was designed by an independent clinical executive. Subjects were randomised based on pre-allocated codes placed in sealed envelopes that were opened during the randomisation visit by a trial coordinator"
Allocation concealment (selection bias)	Low risk	Randomisation was conducted by an independent person. Codes were only revealed during the randomisation visit.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Masking of iridoplasty scars not possible
Blinding of outcome assessment (detection bias) All outcomes	High risk	Masking of iridoplasty scars not possible "…the scale of the tonometer was concealed from the examiner. The IOP values were documented by an assistant"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Losses to follow-up were very few, and included in a 'Last observation carried forward' analysis
Selective reporting (reporting bias)	High risk	Change in ACD not reported at 12 months

Sun 2010

Study characteristics

Methods	**Study design:** parallel group RCT **Study date:** 1 October 2005 to 31 October 2006

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Sun 2010 *(Continued)*

	Number randomised (total and per group): 158 total; 77 control, 81 intervention **Number analysed (total and per group):** 126 total; 61 control (79.2%), 65 intervention (80.2%) **Exclusions and losses to follow-up:** 32 total lost to follow-up; 16 control, 16 intervention **Study follow-up:** 12 months
Participants	**Country:** China **Age (mean ± SD), years:** control: 63 ± 8; intervention: 65 ± 8 **Ethnicity:** not reported **Recruitment:** consecutive cases of PAC and PACG were invited **Inclusion criteria:** age ≥ 40; > 0.5 clock hours PAS; occludable angle (non-visibility of the posterior trabecular meshwork of ≥ 270 degrees without indentation); ability to undergo examination and laser procedures **Exclusion criteria:** unwillingness or inability to provide consent, or inability to return for scheduled visits; history or signs of acute angle closure (dilated and fixed pupil, sector atrophy of iris, pigmentary dusting of corneal endothelium, and glaukomflecken); prior intraocular surgical treatment; history or signs of trauma to the eye; any other ocular disorders that may have an effect on the structure or function of the drainage angle, such as uveitis and lens dislocation
Interventions	**Intervention:** PI and argon LPIp **Control:** PI alone
Outcomes	**Primary vs. secondary outcomes not specified** **Outcomes:** IOP; number of medications; PAS; complications (including requirement of further surgery); BCVA
Notes	**Funding source:** grant from the 'National 11th five-year plan Science and Technology' **Competing interests:** none declared **Publication language:** English **Trial registered:** Chinese Clinical Trial Register (Identifier: ChiCTR-TRC-00000034) **Sample size and power calculations:** reported: a calculated sample size of 63 in each arm was required to detect a 2.5 mmHg difference in IOP between groups (standard deviation [SD], 5 mmHg), with a power of 0.8 and type I error of 0.05. 76 cases needed to be recruited in each group, when an estimated loss to follow-up of 20% was taken into account.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Consecutive cases …were invited to participate" "The ophthalmologists who made the diagnoses were not aware of the treatment assignment" "Eligible patients were randomised …into 1 of 2 treatment arms …using a random number table"
Allocation concealment (selection bias)	Low risk	"Eligible patients were randomised by a research assistant … using a random number table"

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Sun 2010 *(Continued)*

		Concealment method not specified, but control and intervention groups well matched
Blinding of participants and personnel (performance bias) All outcomes	High risk	"The ophthalmologist who performed the follow-up examination could not be masked"
Blinding of outcome assessment (detection bias) All outcomes	High risk	"The ophthalmologist who performed the follow-up examination could not be masked" "The examiner did not have access to the previous IOP or gonioscopy records" "Technicians who performed IOP examination, refraction test, and automated perimetry also were masked"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Losses to follow-up were reported, and data pertaining to these participants were included in a separate 'Last observation carried forward' analysis. 16 participants were lost in each group (20.8% PI alone, 19.8% argon LPIp with PI)
Selective reporting (reporting bias)	Low risk	All outcomes were reported

AOD: angle opening distance
ARA: angle recess area
BCVA: best corrected visual acuity
GAT: Goldmann applanation tonometry
GON: glaucomatous optic neuropathy
IOP: intraocular pressure
IT: iris thickness
LPIp: laser peripheral iridoplasty
PAC: primary angle closure
PACG: primary angle-closure glaucoma
PAS: peripheral anterior synechiae
PI: peripheral iridotomy
RCT: randomised controlled trial
TISA: trabecular-iris space area

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Cho 2017	Observational study rather than a randomised controlled trial

Characteristics of studies awaiting classification *[ordered by study ID]*

Kim 2003

Methods	**Study design:** parallel group RCT **Study date:** 2003 **Number randomised (total and per group):** 63 total; 33 control, 30 intervention **Number analysed (total and per group):** 63 total; 33 control (100%), 30 intervention (100%) **Exclusions and losses to follow-up:** none specified in English language abstract

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Kim 2003 *(Continued)*

	Study follow-up (months): 12 months
Participants	**Country:** South Korea **Age (mean ± SD), years:** 62.9 ± 11.8 control; 65.9 ± 8.5 intervention **Gender:** M = 9, F = 24 control; M = 5, F = 25 intervention **Ethnicity:** not specified in English **Recruitment:** people with PACG who required laser therapy **Inclusion criteria:** not specified in English **Exclusion criteria:** not specified in English
Interventions	**Intervention:** argon LPIp + PI **Control:** PI alone
Outcomes	**Primary vs. secondary outcomes not specified** **Outcomes:** IOP, otherwise not specified in English
Notes	**Funding source:** not specified in English **Competing interests:** not specified in English **Publication language:** Korean

Park 2011

Methods	**Study design:** within-person RCT **Study date:** 2011 **Number randomised (total and per group):** (17 participants) 25 eyes total; 11 control, 14 intervention **Number analysed (total and per group):** (17 participants) 25 eyes total; 11 control, 14 intervention **Exclusions and losses to follow-up:** none specified in English language abstract **Study follow-up:** not specified in English (IOP reported at 6 months)
Participants	**Country:** South Korea **Age (mean ± SD), years:** not specified in English **Ethnicity:** not specified in English **Recruitment:** people with "narrow angles" recruited **Inclusion criteria:** not specified in English **Exclusion criteria:** not specified in English
Interventions	**Intervention:** argon LPIp + PI **Control:** PI alone

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Park 2011 *(Continued)*

Outcomes	**Primary vs. secondary outcomes not specified** **Outcomes:** IOP, AOD, ARA, TISA, ACD, otherwise not specified in English
Notes	**Funding source:** not specified in English **Competing interests:** not specified in English **Publication language:** Korean

ADDITIONAL TABLES

Table 1. Categorising angle closure

Criteria (Yes/No: Y/N)	**Primary angle-closure suspect**	**Primary angle closure**	**Primary angle-closure glaucoma**
≥ 180 degrees of iridotrabecular contact	Y	Y	Y
Peripheral anterior synechiae or elevated intraocular pressure	N	Y	Y
Optic neuropathy	N	N	Y

Table 2. Adverse effects

Complication	**No of eyes (studies)**	**Control (PI alone) group**	**Intervention (argon LPIp with PI) group**	**Risk Ratio**	**95% CI**	**P value**
Hyphema	206 (2)	10 cases (of 101) 100 per 1000	10 cases (of 105) 95 per 1000	0.96	0.42 to 2.21	P = 0.9272
Transient IOP spike	206 (2)	21 cases (of 101) 200 per 1000	24 cases (of 105) 229 per 1000	1.10	0.65 to 1.85	P = 0.7202
Persistent uveitis 1/52 post LPIp	48 (1)	2/24 83 per 1000	1/24 42 per 1000	0.50	0.05 to 5.15	P = 0.5603
Transient atonic pupil	48 (1)	0 cases (of 24)	1 case (of 24) 42 per 1000	3.00	0.13 to 70.17	P = 0.4946
Corneal endothelial burns	158[a] (1)	2 cases (of 77) 26 per 1000	0 cases (of 81) 0 per 1000	0.19	0.01 to 3.90	P = 0.2816
Malignant glaucoma	158[a] (1)	0 cases (of 77) 0 per 1000	1 case (of 81) 12 per 1000	2.85	0.12 to 69.01	P = 0.5188

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Table 2. Adverse effects *(Continued)*

Requirement for surgery	126 (1)	14 cases (of 61) 230 per 1000	18 cases (of 65) 277 per 1000	1.21	0.66 to 2.22	P = 0.5428
Corneal endothelial cell count	126 (1)	Mean change 2667.62 to 2704.28 (61 cases)	Mean change 2641.14 to 2610.74 (65 cases)	-	-	-
Visual acuity	126 (1)	Median worsening by 0.05 (61 cases)	Median worsening by 0.05 (65 cases)	-	-	-

[a]Sun 2010 reported data for all enrolled participants for these outcomes (158).

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Table 3. Outcome measures by study

	Outcome measures (Reported Yes/No: Y/N)														
Study	**C/D ratio**	**BCVA**	**IOP**	**PAS**	**Number of medications**	**Complications**	**AOD**	**TISA**	**ARA**	**TIA**	**IT**	**CECC**	**ACD**	**ACA**	**ACV**
Sun 2010	Y	Y	Y	Y	Y	Y	N	N	N	N	N	Y	N	N	N
Lee 2011	N	N	Y	N	N	Y	N	N	N	N	N	N	Y	Y	Y
Narayanaswamy 2016	N	N	Y	Y	Y	Y	Y	Y	Y	N	N	N	N	N	N
Bourne 2017	N	N	Y	N	N	N	Y	Y	Y	Y	Y	N	N	N	N

ACD/A/V: anterior chamber depth/angle/volume
AOD: angle opening distance
ARA: angle recess area
BCVA: best corrected visual acuity
C/D ratio: cup-to-disk ratio
CECC: corneal endothelial cell count
IOP: intraocular pressure
IT: iris thickness
PAS: peripheral anterior synechiae
TIA: trabecular-iris angle
TISA: trabecular-iris space area

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WHAT'S NEW

Date	Event	Description
1 December 2020	New citation required and conclusions have changed	Three new trials have been included in this update (Bourne 2017; Lee 2011, Narayanaswamy 2016).
1 December 2020	New search has been performed	New lead author, James Bayliss taken on for update of review.

HISTORY

Protocol first published: Issue 3, 2007
Review first published: Issue 3, 2008

Date	Event	Description
14 December 2011	New citation required but conclusions have not changed	Issue 2, 2012: One new trial (Sun 2010) was included in the review and the review text was updated accordingly.
14 December 2011	New search has been performed	Issue 2, 2012: Electronic searches were updated.
24 April 2008	Amended	Converted to new review format.
23 November 2007	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

JB: co-ordinated update of review; screened initial search results and full-text copies; appraised quality and extracted data from papers; drafted updated review text; involved in revision and editing of current manuscript.

NW: screened initial search results and full-text copies; appraised quality of papers; checked extraction of data from papers; provided experience in systematic approach; involved in revision and editing of current manuscript.

WSN: performed previous work that provided the foundation for the updated review; involved in revision and editing of current manuscript.

AAB: conceived the review question; provided a clinical perspective; performed previous work that provided the foundation for the updated review; involved in revision and editing of current manuscript.

DECLARATIONS OF INTEREST

JB: None known
WSN: None known
NW: None known
AAZ: None known

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

- The title was changed from chronic angle-closure glaucoma to angle closure for the first version of the published review (Ng 2012). Angle closure refers to people with narrow angles, angle closure and angle-closure glaucoma.
- The outcome measures assessed were expanded to include 'complication rate', and the outcome 'opening of the anterior chamber angle' was expanded to include any anatomical change in the anterior chamber angle (such as with AS-OCT).
- The original protocol sought to include any assessment of LPIp as an intervention whether primary or secondary, however did not specify this explicitly. This was updated to add clarity for the current version of the review, as three new studies were identified which assessed argon LPIp using a variety of different methods.

INDEX TERMS

Medical Subject Headings (MeSH)

Bias; Chronic Disease; Glaucoma, Angle-Closure [drug therapy] [*surgery]; Intraocular Pressure; Iris [*surgery]; Laser Therapy [*methods] [statistics & numerical data]; Lasers, Gas [therapeutic use]; Randomized Controlled Trials as Topic

MeSH check words

Adult; Humans

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