

## Living FRIendly Summaries of the Body of Evidence using Epistemonikos (FRISBEE)

*Medwave* 2015;15(Suppl 3):e6337 doi: 10.5867/medwave.2015.6337

# Selective laser trabeculoplasty compared with medical treatment for the initial management of open angle glaucoma or ocular hypertension

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**Citation:** Pérez E, Rada G, Maul E. Selective laser trabeculoplasty compared with medical treatment for the initial management of open angle glaucoma or ocular hypertension. *Medwave* 2015;15(Suppl 3):e6337 doi: 10.5867/medwave.2015.6337

**Publication date:** 16/12/2015

## Abstract

Selective laser trabeculoplasty is a relatively new therapeutic alternative for the management of open angle glaucoma and ocular hypertension. On the other hand, medical treatment has robust data supporting its efficacy and has progressed in last decades with the introduction of prostaglandin analogues. To compare these two therapies, we searched Epistemonikos database, which is maintained by screening 30 databases, and identified four systematic reviews including four randomized and one non-randomized clinical trial. We combined the evidence using meta-analysis and generated a summary of findings table following the GRADE approach. We concluded that selective laser trabeculoplasty leads to a smaller absolute intraocular pressure reduction than medical treatment. However, it is not clear if there are differences in treatment success rate or need of additional antiglaucomatous interventions, because the certainty of the evidence is low.

## Problem

Open angle glaucoma and ocular hypertension are initially asymptomatic conditions that frequently course with additional optic nerve damage that may lead to progressive loss of visual field and irreversible blindness at an end stage if they are not treated appropriately. In clinical practice medical treatment is usually preferred as first line therapy, but laser trabeculoplasty or surgery are also valid options in selected patients as suggested by The American Academy of Ophthalmology [1].

Laser trabeculoplasty was first introduced in 1979, using argon laser [2]. A decade later, the procedure demonstrated to be as effective as timolol for intraocular pressure reduction in the initial management of open angle glaucoma or ocular hypertension [3]. Few years later

prostaglandin analogues were introduced and demonstrated to produce greater intraocular pressure reduction than timolol [4], with the advantage of requiring only once daily dosing. However, adherence to medical treatment remains an important problem as shown by recent reports of 25% of missed doses even when patients knew they were being monitored [5].

In this context, selective laser trabeculoplasty [6] could offer many theoretical advantages over argon laser trabeculoplasty such as easier application, and lower energy parameters that could reduce coagulative damage in trabecular meshwork. The latter has used as an argument to justify that the procedure can be repeated while the recommendation for argon laser trabeculoplasty

is against repeatability. There is evidence that the effectiveness of both interventions is similar [7], and despite only weak evidence of repeatability for selective laser trabeculoplasty [8], it is being used in clinical practice as a repeatable procedure without reports of intraocular pressure decompensation as previously seen with argon laser trabeculoplasty [9],[10].

Taking into account the introduction of new and better medications as well as selective laser trabeculoplasty a procedure that is easier to apply and potentially repeatable, we consider this effectiveness comparison of selective laser trabeculoplasty vs medical treatment for intraocular pressure reduction in open-angle glaucoma or ocular hypertension of great interest.

## Methods

We used Epistemonikos database, which is maintained by screening more than 30 databases, to identify systematic reviews and their included primary studies. With this information, we generated a structured summary using a pre-established format, which includes key messages, a summary of the body of evidence (presented as an evidence matrix in Epistemonikos), meta-analysis of the total of studies, a summary of findings table following the GRADE approach and a table of other considerations for decision-making.

### Key messages

- Selective laser trabeculoplasty results in less intraocular pressure reduction than medical treatment in patients with open angle glaucoma or ocular hypertension.
- It is not clear if there are differences in treatment success rate or need of additional antiglaucomatous interventions, because the certainty of the evidence is low.
- Both therapeutic alternatives are safe and cost-effective in certain settings. If there is optimal adherence, prostaglandin analogues might be the better option.
- However, regarding the outcome of absolute intraocular pressure reduction there are different results in published systematic reviews. This discrepancy is mainly due to differences in the primary studies included for meta-analysis.
- These results are in agreement with the main clinical guidelines, which suggest medical treatment as preferred initial therapy, considering laser trabeculoplasty as valid option in selected patients.

### About the body of evidence for this question

<p>What is the evidence. See evidence matrix in Epistemonikos later</p>	<p>We found four systematic reviews [7],[11],[12],[13] that include four randomized clinical trials [14],[15],[16],[17] and one non randomized prospective study[18]. In this table and the summary in general, we only considered the randomized trials. Three of the four systematic reviews did a meta-analysis [7],[11],[19].</p>
<p>What types of patients were included</p>	<p>All of the randomized clinical trials included patients with ocular hypertension or primary open angle glaucoma. Two of them included also patients with secondary open angle glaucoma, particularly pseudoexfoliation glaucoma [14],[17] and pigment dispersion syndrome [17]. Only one study included patients with mixed mechanism open angle glaucoma with a narrow angle, if laser peripheral iridotomy was performed more than three months ago, but this study did not report the number of patients included with this diagnosis [14].</p> <p>All the studies included newly or recently diagnosed patients. Two of them also included patients previously controlled with medical treatment [14],[17]. There is no distinction by sex. Only two studies restricted age as inclusion criteria: one of them considered only patients under the age of 80 [16]; the other included patients between 25 and 82 years [14].</p> <p>All the studies excluded patients with previous laser procedure or ocular surgery disturbing the aqueous outflow.</p> <p>Three of the randomized clinical trials considered pregnancy as exclusion criteria [14],[15],[16].</p> <p>Studies included patients that belong to multiple ethnic groups: Chinese population [15], African or afro-Caribbean [17], white [14],[17] or non-white [14].</p> <p>Only one study established an upper limit of intraocular pressure, including patients with pressures between 24 and 34 mmHg in the higher eye, and 20 mmHg or more in the contralateral eye [14].</p>
<p>What types of interventions were included</p>	<p>All the studies compared selective laser trabeculoplasty with medical treatment.</p> <p>Regarding laser trabeculoplasty, all randomized clinical trials used similar procedures, with energy ranging from 0,2 to 1,7 mJ per application, adjusted according to patients characteristics and response, and applied over 360 degrees (approximately 100 non-overlapping laser spots).</p> <p>Regarding the extent of trabecular meshwork treated, one study [17] randomized patients into four groups, one receiving medical treatment, and other three groups treated with selective laser trabeculoplasty in different extent of trabecular meshwork: 360°, 180° and 90° respectively. This differs from the other three randomized clinical trials [14],[15],[16], which applied selective laser trabeculoplasty over 360° of trabecular meshwork. Only treatments performed over 360 degrees were considered for this summary.</p>

	<p>Medical treatment modality varied across studies. Two of the randomized clinical trials [16],[17] used exclusively latanoprost, a prostaglandin analogue. One study used [15] a variable combination of medicines including latanoprost, beta-blocker, pilocarpine and dorzolamide. The other randomized clinical trial [14] applied a flexible algorithm of treatment with sequential steps starting with prostaglandin analogues, then adding or substituting to beta-blocker, then brimonidine, and finally dorzolamide, brinzolamide or a fixed-combination dorzolamide-timolol.</p> <p>Follow up also varied across studies: one of the [15] followed patients for five years; two studies [14],[17] did for one year; and other study [16] for four to six months.</p>
<p>What types of outcomes were measured</p>	<p>The systematic reviews included here, analysed the following outcomes: absolute intraocular pressure reduction [7],[19], treatment success rate [7],[19] and need of additional antiglaucomatous interventions [19].</p> <p>There is heterogeneity in treatment success definition: one primary study [16] defined it as achieving an intraocular pressure reduction of 20% or more; other study [17] used two definitions, considering intraocular pressure reduction of 20% and 30% from baseline; one study [14] defined treatment success when achieving a target intraocular pressure reduction calculated by using a formula; other [15] defined it indirectly considering treatment failure when intraocular pressure was greater than 21 mmHg in follow up.</p> <p>Different adverse effects were evaluated by three of the randomized clinical trials [14],[15],[17]: ocular pain or discomfort [17], anterior chamber reaction [15], peripheral anterior synechiae [14], uveitis [14],[17], post-laser intraocular pressure spike [15],[17] and increase in trabecular meshwork pigmentation [15].</p>

### Summary of findings

This information is based on four randomized clinical trials including 271 eyes of 201 patients. All studies measured absolute intraocular pressure reduction and treatment success rate. Three of them [14],[15],[17] evaluated the need of additional antiglaucomatous interventions. The summary of finding is the following:

- Selective laser trabeculoplasty results in less intraocular pressure reduction than medical treatment in patients with open angle glaucoma or ocular hypertension. The certainty of evidence is high.
- It is not clear if there are differences in treatment success rate because the certainty of the evidence is very low for this outcome.
- It is not clear if there are differences in need of additional antiglaucomatous interventions, because the certainty of the evidence is very low.
- There is no report of relevant adverse effects for the studied treatment modalities.

<b>Selective laser trabeculoplasty compared to medical treatment in open angle glaucoma or ocular hypertension.</b>				
<b>Patients</b>		Newly diagnosed open angle glaucoma or ocular hypertension		
<b>Intervention</b>		360° Selective laser trabeculoplasty		
<b>Comparison</b>		Medical treatment		
Outcomes	Absolute effect*		Relative effect (95% CI)	Certainty of the evidence (GRADE)
	WITH medical treatment	WITH selective laser trabeculoplasty		
	Difference: patients per 1000			
Absolute intraocular pressure reduction	Mean absolute intraocular pressure reduction was 8.20 mmHg	Mean absolute intraocular pressure reduction was 7 mmHg	MD -1.20 (-1.69 to -0.71)	⊕⊕⊕⊕ <sup>1,2</sup> High
	Difference: 1.20 mmHg less absolute intraocular pressure reduction with laser trabeculoplasty (Margin of error: 0.71 to 1.69 mmHg less reduction)			
Treatment success rate	646 per 1000	578 per 1000	RR 0.89 (0.74 to 1.07)	⊕○○○ <sup>3,4</sup> Very low
	Difference: 68 eyes less per 1000 (Margin of error: 167 less to 45 more)			
Eyes underwent additional antiglaucomatous interventions	216 per 1000	233 per 1000	RR 1.16 (0.52 to 2.62)	⊕○○○ <sup>3,4</sup> Very low
	Difference: 17 eyes more per 1000 (Margin of error: 104 less to 350 more)			

RR: Risk ratio.  
MD: Mean difference.  
Margin of error = 95% confidence interval (CI).  
GRADE: evidence grades of the GRADE Working Group (see later in this article).

\* The risk **WITH medical treatment** based on the risk in the control group of the trials. The risk **WITH selective laser trabeculoplasty** (and its margin of error) is calculated from the relative effect (and its margin of error).

1 Studies have small risk of bias, and studies with higher weights have low risk, that is why we did not decrease the certainty of the evidence regarding this concept.  
2 There is heterogeneity in the medical treatment modality used, however all studies included prostaglandin analogues as first line treatment, which is in line with actual clinical practice. Particularly, the study with most weight for this outcome [16] used only latanoprost. We did not decrease the certainty of the evidence for this reason.  
3 Results are inconsistent for this outcome, some studies favour medical treatment and others selective laser trabeculoplasty, none of them significantly. Definition of treatment success varies between the studies, as well as the criteria to decide necessity of additional antiglaucomatous interventions.  
4 There is imprecision in the results with large margin of error covering important beneficial effects for both therapies between different studies.

## About the certainty of the evidence (GRADE)\*

⊕⊕⊕⊕

**High:** This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different† is low.

⊕⊕⊕○

**Moderate:** This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different† is moderate

⊕⊕○○

**Low:** This research provides some indication of the likely effect. However, the likelihood that it will be substantially different† is high.

⊕○○○

**Very low:** This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different† is very high.

\*This concept is also called 'quality of the evidence' or 'confidence in effect estimates'.

† Substantially different = a large enough difference that it might affect a decision.



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## Other considerations for decision-making

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### To whom this evidence does and does not apply

- This evidence applies to patients with newly diagnosed open angle glaucoma or ocular hypertension, regardless of baseline intraocular pressure or patient age at disease presentation.
- This evidence excludes patients with previous laser procedure or ocular surgery disturbing the aqueous outflow as well as pregnant patients.

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### About the outcomes included in this summary

- Evidence about patients' preferences in glaucoma treatment shows that visual outcome related to the risk of moderate visual loss (defined as inability to drive a car) and long-term blindness are the most important events that patients want to prevent. There is no clear preference about the treatment modality used, whether medical or surgical [20].
- Despite the fact that visual outcome is not systematically measured in the primary studies included in this review (just one evaluated visual field and visual acuity), there is evidence that intraocular pressure reduction significantly delays progression of glaucoma, including visual field impairment [21].
- The outcomes measured by these studies are centred on intraocular pressure, a very relevant factor used in clinical practice to define treatment success or need of further therapy, especially in patients with early stages of disease to whom this evidence may apply.
- However, it would be ideal to count with primary studies of longer follow up and systematically measuring relevant outcomes such as visual acuity, visual field, cup/disc ratio and adverse effects.

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### Balance between benefits and risks, and certainty of the evidence

- In this evidence there is no report of relevant adverse effects for the therapies evaluated, so they may be both considered safe alternatives.
- Nevertheless, there are case reports and series that describe adverse effects of selective laser trabeculoplasty such as subconjunctival haemorrhage, hyphema, corneal haze, cystoid macular edema, choroidal effusion, and more. Most of them were transient or could be resolved with simple medication [7].
- One of the most important side effects reported for laser trabeculoplasty is peripheral anterior synechiae because they are not reversible through medical treatment and could lead to an impaired intraocular pressure reduction effect. Fortunately it is a rare event with selective laser trabeculoplasty [7].

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### Resource considerations

- While medical treatment needs life-long application, selective laser trabeculoplasty could substitute or reduce the number of medications required to achieve disease control [7] hence decreasing treatment costs while the effect of the procedure persists. However, the costs of the laser device acquisition and maintenance should also be considered.
- From a patient out of pocket payments perspective, specially in a resource limited setting, the strategy of a one-time laser surgery intervention following self-referral could be highly cost-effective [22]. However, in an optimal adherence setting, prostaglandin analogues would have better cost-effectiveness to treat patients with newly diagnosed open angle glaucoma [23].

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### Differences between this summary and other sources

- Our conclusions regarding treatment success rate are concordant with the identified systematic reviews [7],[11],[12],[19].
  - However, regarding absolute intraocular pressure reduction there are differences in the results obtained by the different published meta-analyses [7],[11],[19]. Our results are in agreement with one of the systematic reviews [19], but differ from other two [7],[11]. This is mainly due to differences in the primary studies included in the meta-analysis for this outcome. Both of the systematic reviews that obtained results discordant to ours [7],[11] excluded one of the randomized clinical trials [17] and one of these reviews [11] also included a non-randomized prospective study [18]. The other meta-analysis concordant to our results [19], did not consider one of the primary studies [16].
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Our review is the only one including data of the four published randomized clinical trials in the meta-analysis for this outcome.

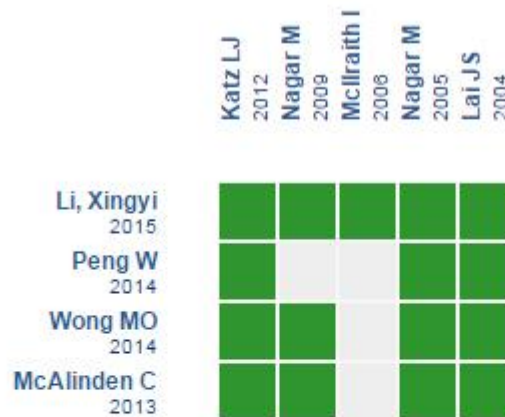
- Our conclusions are consistent with the main clinical guidelines of glaucoma management. In summary, they suggest medical treatment as first line therapy, but that laser trabeculoplasty can be considered as initial therapy in selected patients, especially who cannot or will not use medical treatment [1],[24],[25],[26],[27],[28].

#### Could this evidence change in the future?

- It is unlikely that the results of absolute intraocular pressure reduction change substantially in the future because the high certainty of evidence.
- New studies could clarify if there are differences in treatment success rates or need of additional antiglaucomatous interventions. We are not aware of ongoing studies answering this question.

#### How we conducted this summary

Using automated and collaborative means, we compiled all the relevant evidence for the question of interest and we present it as a matrix of evidence.



Starting from any systematic review, Epistemonikos builds a matrix based on existing connections in the database.

The author of the matrix can select relevant information for a specific health question (typically in PICOD format) in order to display the information set for the question.

The *rows* represent systematic reviews that share at least one primary study, and *columns* display the studies.

The boxes in green correspond to studies included in the respective reviews.

Follow the link to access the **interactive version**: [Selective laser trabeculoplasty versus medical treatment for open angle glaucoma and ocular hypertension](#)



## Notes

The upper portion of the matrix of evidence will display a warning of "new evidence" if new systematic reviews are published after the publication of this summary. Even though the project considers the periodical update of these summaries, users are invited to comment in *Medwave* or to contact the authors through email if they find new evidence and the summary should be updated earlier. After creating an account in Epistemonikos, users will be able to save the matrixes and to receive automated notifications any time new evidence potentially relevant for the question appears.

The details about the methods used to produce these summaries are described here <http://dx.doi.org/10.5867/medwave.2014.06.5997>.

Epistemonikos foundation is a non-for-profit organization aiming to bring information closer to health decision-makers with technology. Its main development is Epistemonikos database ([www.epistemonikos.org](http://www.epistemonikos.org)).

These summaries follow a rigorous process of internal peer review.

### Conflicts of interest

The authors do not have relevant interests to declare.

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