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[Intervention Review]

Acupuncture for glaucoma

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ABSTRACT

Background

Glaucoma is a multi-factorial optic neuropathy characterized by an acquired loss of retinal ganglion cells at levels beyond normal age-related loss and corresponding atrophy of the optic nerve. Although many treatments are available to manage glaucoma, patients may seek complementary or alternative medicine approaches such as acupuncture to supplement their regular treatment. The underlying plausibility of acupuncture is that disorders related to the flow of Chi (traditional Chinese concept of vital force or energy) can be managed by stimulating relevant points on the body surface.

Objectives

To assess the effectiveness and safety of acupuncture compared with other treatments, no treatment, or placebo in patients with glaucoma.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL), which contains the Cochrane Eyes and Vision Trials Register (2018, Issue 11); Ovid MEDLINE; Embase.com; the Cumulative Index to Nursing and Allied Health Literature (CINAHL); the Allied and Complementary Medicine Database (AMED); PubMed; Latin American and Caribbean Literature on Health Sciences (LILACS); ZETOC; the *meta*Register of Controlled Trials (*m*RCT); ClinicalTrials.gov; the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP); and the National Center for Complementary and Alternative Medicine (NCCAM) website. We did not use any language or date restrictions in the search for trials. We last searched electronic databases on November 16, 2018, with the exception of NCCAM, which we last searched on July 14, 2010, and the *meta*Register of Controlled Trials (*m*RCT), which we last searched on January 8, 2013. We handsearched Chinese medical journals at Peking Union Medical College Library in April 2007.

We searched the Chinese Acupuncture Trials Register, the Traditional Chinese Medical Literature Analysis and Retrieval System (TCMLARS), the Chinese Biological Database (CBM), and the China National Knowledge Infrastructure (CNKI). We last searched Chinese electronic databases on November 19, 2018.

Selection criteria

We included randomized controlled trials (RCTs) in which one arm involved acupuncture treatment.

Data collection and analysis

Two review authors independently screened results, then extracted the data and assessed risk of bias for eligible trials.

Main results

We included three completed trials and one ongoing trial in the 2019 update of this review. The three completed trials, conducted in Taiwan and the United States, included participants with glaucoma or intraocular hypertension. The interventions investigated varied across trials. One trial compared auricular acupressure — a non-standard acupuncture technique — with the sham procedure in 33 patients. Another trial compared transcutaneous electrical nerve stimulation (TENS) with a sham procedure in 82 patients. The third trial compared 12 sessions of acupuncture on eye-points versus on non-eye-points in 22 patients. All three trials were rated at high risk of bias for at least one domain. The certainty of evidence across all outcomes was very low due to high risk of bias in at least one contributing study; substantial clinical heterogeneity and methodological heterogeneity; and imprecision of results.

One trial reported change in the visual field from baseline without any between-group comparison. Because of the quantity of missing data (50%), we did not calculate a between-group comparison, as the quantitative results are difficult to interpret.

All three trials reported data for estimation of reduction of intraocular pressure (IOP). However, time points of IOP measurement varied. For the trial comparing acupressure to a sham procedure, the difference in IOP reduction (measured in mm Hg) is estimated to be -3.70 (95% confidence interval [CI] -7.11 to -0.29) for the right eye and -4.90 (95% CI -8.08 to -1.72) for the left eye at four weeks, and -1.30 mm Hg (95% CI -4.78 to 2.18) for the right eye and -2.30 mm Hg (95% CI -5.73 to 1.13) for the left eye at eight weeks. For the trial comparing TENS to sham treatment, the difference reduction is estimated to be -2.81 (95% CI -3.8 to -1.84) for the right eye and -2.58 (95% CI -3.36 to -1.80) for the left eye immediately after treatment, -2.93 (95% CI -3.72 to -2.13) for the right eye and -3.56 (95% CI -4.35 to 2.78) for the left eye 30 minutes after treatment, and finally -3.61 (95% CI -4.47 to -2.75) for the right eye and -3.61 (95% -4.47 to -2.74) for the left eye. For the trial that compared acupuncture on eye-points versus non-eye-points, 11 out of 22 (50%) participants did not complete the treatment.

One trial reported data for estimation of visual acuity. When acupressure is compared to sham treatment, the difference in uncorrected visual acuity (UCVA, measured in logMAR) is estimated to be -0.01 (95% CI -0.24 to 0.22) for the right eye and -0.04 (95% CI -0.27 to 0.19) for the left eye at four months, and -0.03 logMAR (95% CI -0.27 to 0.21) for the right eye and -0.16 logMAR (95% CI -0.43 to 0.11) for the left eye at eight months. The difference in best corrected visual acuity (BCVA) is estimated to be 0.10 (95% CI -0.06 to 0.26) for the right eye and 0 (95% CI -0.14 to 0.14) for the left eye at four months, and -0.04 logMAR (95% CI -0.09 to 0.17) for the right eye and -0.04 logMAR (95% CI -0.18 to 0.10) for the left eye at eight months.

One trial reported progression of optic disc damage or nerve fiber layer loss without any between-group comparison. Because of the quantity of missing data (50%), we did not calculate a between-group comparison, as the quantitative results are difficult to interpret.

One trial reported adverse events in two patients (out of 22) who experienced needle sensitivity. However, the study did not report between-group comparisons. Because of the quantity of missing data (50%), we did not calculate a between-group comparison, as the quantitative results are difficult to interpret.

Authors' conclusions

At this time, it is impossible to draw reliable conclusions from available data to support the use of acupuncture for treatment of patients with glaucoma. Because of ethical considerations, RCTs comparing acupuncture alone with standard glaucoma treatment or placebo are unlikely to be justified in countries where the standard of care has already been established.

PLAIN LANGUAGE SUMMARY

Acupuncture as a treatment for people with glaucoma

What was the aim of this review?
This review aimed to assess whether acupuncture is useful and safe in treating people with glaucoma. We included in the review three completed trials and one ongoing trial.

What is the key message of this review?
At this time, it is impossible to draw reliable conclusions from available data to support the use of acupuncture for treatment of people with glaucoma.

What was studied in the review?
Glaucoma is a condition that damages the optic nerve and affects visual function. It is a major cause of blindness worldwide. Although many treatments are available, including eye drops, laser treatment, and surgical procedures, some people may seek complementary or alternative medicine approaches such as acupuncture to supplement their regular treatment.

What are the main results of the review?
The three completed studies were conducted in hospitals in Taiwan and the United States. These trials recruited participants with glaucoma or intraocular hypertension (higher than normal eye pressure). The trials differ greatly in the interventions compared, including auricular acupressure (a non-standard acupuncture technique), transcutaneous electrical nerve stimulation, and acupuncture on eye-points (12 sessions). Acupuncture may have a very small effect in reducing eye pressure, but the certainty of evidence is very low. One trial reported needle sensitivity. Trials provided no evidence of effect on visual field or visual acuity.

How up-to-date is this review?
Cochrane Review authors searched for studies that had been published up to November 16, 2018.

SUMMARY OF FINDINGS

Summary of findings for the main comparison.

Acupuncture compared with control interventions for glaucoma

Patient or population: participants with glaucoma or intraocular hypertension

Settings: outpatient

Intervention: acupuncture including auricular acupressure, transcutaneous electrical nerve stimulation on Pucan and Shenmai, and acupuncture on eye-points

Comparison: control interventions including sham treatments and acupuncture on non-eye-points

Outcomes	Descriptions	No. of participants (studies)	Quality of the evidence (GRADE)	Comments
Change in the visual field (short term)	Law 2015 did not report between-group comparisons for any outcomes examined in the trial. Because of the quantity of missing data (50%), we did not calculate a between-group comparison, as the quantitative results are difficult to interpret	22 (1 RCT)	⊕⊖⊖⊖ **very low**[a,b,c]	No relevant combinable data available for this outcome
Reduction in IOP (short term)	Her 2010: at 4 weeks—the time point at which acupressure treatment stopped—comparison of the acupressure group with the sham group revealed that the between-group difference in IOP (measured in mm Hg) was -3.70 (95% CI -7.11 to -0.29) for the right eye and -4.90 (95% CI -8.08 to -1.72) for the left eye. At 8 weeks, comparison of the acupressure group with the sham group revealed that the between-group difference in IOP reduction was -1.30 mm Hg (95% CI -4.78 to 2.18) for the right eye and -2.30 mm Hg (95% CI -5.73 to 1.13) for the left eye. No statistically significant difference in IOP was noted at any other follow-up time points Tsui-Yun 2016: immediately after TENS, comparison between TENS and sham treatment revealed greater reductions in IOP (measured in mm Hg) with TENS: -2.81 (95% CI -3.8 to -1.84) for the right eye and -2.58 (95% CI -3.36 to -1.80) for the left eye. Thirty minutes after TENS, values were -2.93 (95% CI -3.72 to -2.13) for the right eye and -3.56 (95% CI -4.35 to 2.78) for the left eye. Sixty minutes after TENS, values were -3.61 (95% CI -4.47 to -2.75) for the right eye and -3.61 (95% -4.47 to -2.74) for the left eye Law 2015 did not report between-group comparisons for any outcomes examined in the trial	137 (3 trials)	⊕⊖⊖⊖ **very low**[a,b,c]	No relevant combinable data available for this outcome
Change in visual acuity (short term)	One trial reported this outcome (Her 2010). No statistically significant difference in visual acuity was noted at any follow-up time points At 4 weeks, comparison of the acupressure group with the sham group revealed that the between-group difference in uncorrected visual acuity (UCVA, measured in logMAR) was -0.01 (95% CI -0.24 to 0.22) for the right eye and -0.04 (95% CI -0.27 to 0.19) for the left eye. The difference in best corrected visual acuity (BCVA, measured in logMAR) was 0.10 (95% CI -0.06 to 0.26) for the right eye and 0 (95% CI -0.14 to 0.14) for the left eye At 8 weeks, comparison of the acupressure group with the sham group revealed that the between-group difference in UCVA was -0.03 logMAR (95% CI	33 (1 trial)	⊕⊖⊖⊖ **very low**[a,b,c]	No relevant combinable data available for this outcome

	-0.27 to 0.21) for the right eye and -0.16 logMAR (95% CI -0.43 to 0.11) for the left eye. The difference in BCVA was -0.04 logMAR (95% CI -0.09 to 0.17) for the right eye and -0.04 logMAR (95% CI -0.18 to 0.10) for the left eye			
Progression of optic disc damage or nerve fiber layer loss (short term)	Law 2015 did not report between-group comparisons for any outcomes examined in the trial	22 (1 RCT)	⊕⊖⊖⊖ **very low**[a,b,c]	No relevant combinable data available for this outcome
Adverse events (short term)	In Law 2015, 2/22 patients experienced needle sensitivity	22 (1 RCT)	⊕⊖⊖⊖ **very low**[a,b,c]	No relevant combinable data available for this outcome

CI: confidence interval. **IOP**: intraocular pressure.

GRADE Working Group grades of evidence.
High certainty: further research is very unlikely to change our confidence in the estimate of effect.
Moderate certainty: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low certainty: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low certainty: we are very uncertain about the estimate.

[a]High risk of bias in at least one contributing study.
[b]Substantial clinical heterogeneity and methodological heterogeneity.
[c]Imprecision of results.

BACKGROUND

Description of the condition

Glaucoma is a multi-factorial optic neuropathy characterized by an acquired loss of retinal ganglion cells at levels beyond normal age-related baseline loss and corresponding atrophy of the optic nerve (AAO 2015). Glaucoma is associated with distinctive patterns of visual dysfunction but is asymptomatic in its earlier stages. It is one of the leading causes of irreversible blindness worldwide (Friedman 2004; Quigley 2006; Tsai 2005).

Glaucoma is classified on the basis of anatomic features as open-angle (where the anterior chamber angle of the eye remains open) and angle-closure (with closure of the anterior chamber angle) glaucoma. Glaucoma is considered primary if the eye has no preexisting disease. Secondary forms of glaucoma are caused by various ocular or systemic diseases such as pigment dispersion syndrome and ocular trauma.

More than two million people in the United States are living with glaucoma; 80,000 of these individuals are legally blind as a result of the disease (Friedman 2004; Lee 2005; Martin 1985). It was estimated that 60.5 million people were affected by glaucoma in 2010 worldwide, and bilateral blindness was present in 4.5 million people with open-angle glaucoma (OAG) and in 3.9 million people with angle-closure glaucoma (Quigley 2006). The number of people with glaucoma worldwide is expected to increase to 111.8 million in 2040, disproportionately affecting people residing in Asia and Africa (Tham 2014). The prevalence of glaucoma is higher in the elderly, among persons of African descent, and in people with diabetes, hypertension, or myopia (Lee 2005; Quigley 2006).

Primary open-angle glaucoma (POAG) is the most common type of glaucoma (Friedman 2004). POAG usually has an insidious onset and progresses slowly and painlessly, affecting one or both eyes. Because central vision is relatively unaffected until late in the disease, visual loss generally progresses without symptoms. Diagnosis of POAG is based on evidence of optic nerve damage presented as a structural abnormality of the optic disc or retinal nerve fiber layer, or as the presence of characteristic abnormalities in the visual field. Additional criteria include a normal appearing open anterior chamber angle and absence of secondary causes of glaucoma. Although most patients with glaucoma exhibit increased intraocular pressure (IOP) upon repeated measurement, some may have IOP that is within the average range (AAO 2015).

Patients may present with acute elevation of IOP, when the entire circumference of the anterior chamber angle is obstructed suddenly. Intermittent closure of the anterior chamber angle may lead to chronic angle-closure glaucoma (AAO 2015).

Diagnosis of angle-closure glaucoma can be achieved by gonioscopy, which is an examination of the structure and width of the anterior chamber angle. Angle-closure glaucoma is reserved for eyes in which glaucomatous optic neuropathy or visual field defect is evident in the presence of angle closure.

Description of the intervention

Treatment options

Current treatments for glaucoma are directed at lowering IOP because IOP is the only known risk factor that can be treated with the beneficial effect of reducing progression of visual field loss (AGIS 2000; CNTGSG 1998; Gordon 2002; Heijl 2002).

Pharmacological therapy

Treatment of patients with glaucoma usually begins with topical antiglaucoma medications. Prostaglandin analogs are the most frequently prescribed initial eye drops for lowering IOP in patients with glaucoma because they are efficacious and well tolerated, and are instilled once daily (AAO 2015; Li 2016; Marquis 2005; van der Valk 2005). They lower IOP by increasing the uveoscleral outflow of aqueous humor. Other agents include beta-blockers, alpha2-adrenergic agonists, parasympathomimetics, topical and oral carbonic anhydrase inhibitors, and two newer classes of antiglaucoma agents—rho kinase (ROCK) inhibitors and nitric oxide. Nitric oxide is molecularly combined with another hypotensive agent as a single molecule that breaks down to individual molecules inside the eye. Parasympathomimetics, rho kinase inhibitors, and nitric oxide lower IOP by increasing trabecular outflow. The remaining agents work mainly by decreasing aqueous humor formation. Parasympathomimetic (miotic) agents such as pilocarpine affect pupil size or accommodation and are reserved for use in patients who do not respond to other topical antiglaucoma medications (AAO 2015; Lee 2005).

Choice of medical therapy depends on the IOP-lowering efficacy of the agent, as well as its potential cost, side effects, and dosing schedules. Thus, a strict stepwise approach may not be followed. If target IOP is not achieved by one medication, then switching or adding medications should be considered, depending on whether the individual patient has responded to the first medication (AAO 2015). Medical interventions for POAG are the topic of a published Cochrane systematic review (Vass 2007).

Laser therapy

An alternative or additive treatment to glaucoma medication is laser trabeculoplasty (AAO 2015). Laser trabeculoplasty lowers IOP by mechanically stimulating the trabecular meshwork to reduce its resistance to the outflow of aqueous humor (Lee 2005). A Cochrane Review on laser trabeculoplasty for OAG has been published (Rolim de Moura 2007).

Incisional surgery

If the patient's IOP cannot be controlled with medications, incisional filtering surgery can be considered (AAO 2015). Filtering surgery reduces IOP by creating a new channel that improves the outflow of the aqueous humor. Trabeculectomy is the most commonly performed surgical procedure. An opening created in the anterior chamber angle allows the aqueous humor to flow from the anterior chamber into a space beneath the conjunctiva under the surface of the eye. The problem most often associated with this surgery is growth of scar tissue, which may cause an obstruction in this artificial channel that blocks aqueous humor drainage, and the IOP-lowering effect may decrease gradually with time. Other vision-threatening complications include overfiltration, hypotony, bleeding, and infection.

In addition to trabeculectomy, non-penetrating surgical procedures such as viscocanalostomy and deep sclerectomy have been developed. These techniques avoid full-thickness penetration into the anterior chamber of the eye. Fewer complications have

been reported, but their effectiveness in lowering IOP may be limited compared with that of trabeculectomy (Netland 2001). A Cochrane Review comparing medical and surgical interventions for glaucoma has been published (Burr 2012).

Glaucoma drainage devices

Tube and plate drainage devices could be used to maintain drainage of aqueous humor in spite of subconjunctival scarring (Burr 2012; Lim 1998). Glaucoma drainage devices are usually recommended in cases where trabeculectomy is unlikely to succeed. A Cochrane Review of these devices has been published (Tseng 2017).

Minimally invasive glaucoma surgery

Minimally invasive glaucoma surgery (MIGS) refers to a group of newer surgical procedures performed by using an ab interno approach and required minimal or no manipulation of the conjunctiva or the sclera. MIGS can be divided into four main approaches, including increasing trabecular outflow by bypassing the juxtacanalicular trabecular meshwork, increasing uveoscleral outflow via suprachoroidal pathways, reducing aqueous production from the ciliary body, and creating a subconjunctival drainage pathway. Some MIGS procedures were approved by the regulatory bodies to be performed only in conjunction with cataract surgery. A suite of Cochrane Reviews on various MIGS have been initiated (Hu 2016; King 2019; Le 2019; Otarola 2017; Sandhu 2017).

Other procedures

Alternative microsurgical procedures performed on the trabecular meshwork such as trabecular aspiration, goniocurettage, laser trabecular ablation, and trabeculotomy have been described as means of lowering IOP in OAG. These techniques are not widely used, and their safety and effectiveness are not known (Burr 2012).

Although many treatments are available, glaucoma is a chronic condition for which no cure is known. Some patients may seek complementary or alternative medicine such as acupuncture to supplement their regular treatment.

Acupuncture

Acupuncture is a branch of traditional Chinese medicine that has been used for more than 2000 years in the treatment of various illnesses. In traditional Chinese medicine, the body is seen as representing a delicate balance of two opposing and inseparable forces: yin and yang. Yin represents the cold, slow, or passive principle, and yang represents the hot, excited, or active principle. An imbalance in these two opposing forces is associated with blockage in the flow of Chi (vital force or energy), which leads to various illnesses. Chi flows along pathways known as meridians with acupuncture points on the human body that connect with them (NCCAM 2007). The underlying philosophy of acupuncture is that disorders related to the flow of Chi can be prevented or treated by stimulating the relevant acupuncture points on the body surface. These points are stimulated typically by inserting needles; however, related techniques such as manual (acupressure), electrical, or laser stimulation of acupuncture points are often included under this term (Rhee 2002).

The exact mechanism of the effects of acupuncture is far from clearly delineated. People have tried to explain how acupuncture works within the framework of Western medicine. Of the different mechanisms of action proposed (Cho 2006; Moffet 2006), the dominant one suggests that acupuncture stimulates the release of neurochemicals (usually endogenous opioids or serotonin). "Gate theory" or segmental effects is another proposed mechanism for analgesia. In the "gate theory," sensory input from acupuncture blocks or interferes with nociceptive pain signals at the spinal level. In addition, involuntary body functions are regulated by the autonomic nervous system. Examples of such functions include heart rate, blood pressure, postmenopausal vasomotor symptoms, and respiration. Review of the results of studies on different body systems treated with acupuncture recently led to the proposal of a model termed the broad sense hypothalamus-pituitary-adrenal (BS-HPA) axis. This model hypothesizes that the central nervous system is essential for processing the effects of acupuncture by modulating the autonomic nervous system, the neuroimmune system, and hormone regulation. Different mechanisms proposed so far might be viewed as part of an elaborate interaction among different systems of the body.

Animal models and small samples of human studies have shown the ocular effects associated with acupuncture. Studies have reported potentially beneficial effects of IOP reduction, improvement in central visual acuity, increased ocular blood flow, preservation of normal waveform characteristics of multi-focal electroretinography (mfERG), alteration of visual function tested by the visual evoked potential (VEP), and increased retinal nerve growth factor (Chan 2005; Chu 2002; Naruse 2000; Pagani 2006; Sagara 2006).

Why it is important to do this review

A cross-sectional study among the US population in 1998 indicated that prevalence of the use of acupuncture among people reporting use of complementary medicine for glaucoma was 1.8% (1/54) (Rhee 2001; Rhee 2002). In a cross-sectional survey of patients with established glaucoma in two major urban hospitals in Canada, 207 patients (13.7%, out of 1516 patients) reported current or past use of complementary medicine specifically for glaucoma, and among them seven patients (3.4%) reported past or present use of acupuncture for glaucoma (Wan 2012). A comprehensive collection and summary of currently available clinical trials will provide the best evidence to determine whether acupuncture is effective and safe in treating patients with glaucoma.

OBJECTIVES

To assess the effectiveness and safety of acupuncture compared with other treatments, no treatment, or placebo in patients with glaucoma.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomized controlled trials (RCTs).

Types of participants

We included trials enrolling participants of any age and sex with any type of glaucoma, as diagnosed in the included trials.

Types of interventions

We defined *acupuncture* as the stimulation of acupuncture points by any method, including needle insertion, acupressure, and surface electrical and laser stimulation. We included trials that compared acupuncture therapy with other treatments, no treatment, or placebo for treating patients with any type of glaucoma. We also included trials that compared different types of acupuncture therapy, as well as trials that compared acupuncture in combination with another treatment versus the other treatment alone.

Types of outcome measures

Primary outcomes

- Difference between treatment groups regarding change in the visual field from baseline, as measured by any methods used in the included trials

Secondary outcomes

- Reduction in IOP
- Change in visual acuity
- Progression of optic disc damage or nerve fiber layer loss

Timing of outcome assessment was as follows.

- Short term: outcomes up to one year.
- Long term: outcomes longer than one year.

Adverse effects

We planned to include all systemic and ocular adverse effects related to acupuncture or other treatments as reported in the included trials. Specific adverse effects of interest were:

- pain and bleeding due to placement of the acupuncture needle;
- reduction in visual acuity;
- cataract formation;
- infection;
- punctured organs; and
- legal blindness (visual acuity of 20/200 or worse in the better eye with corrective lenses, or visual field restriction to 20 degrees diameter or less [tunnel vision] in the better eye).

Quality of life measures

We planned to summarize quality of life data by using any validated measures presented in included trials.

Economic data

We planned to summarize cost-benefit analyses and other data on economic outcomes.

Follow-up

We did not impose any restrictions based on the length of follow-up.

Search methods for identification of studies

Electronic searches

The Cochrane Eyes and Vision Information Specialist searched the following electronic databases for RCTs and controlled clinical trials, with no restrictions on language or year of publication. Electronic databases were last searched on November 16, 2018, with the exception of NCCAM, which was last searched on July 14, 2010; the *m*RCT, which was last searched on January 8, 2013; and the Chinese databases, which were last searched on November 19, 2018.

- Cochrane Central Register of Controlled Trials (CENTRAL; 2018, Issue 11) (which contains the Cochrane Eyes and Vision Trials Register), in the Cochrane Library (searched November 16, 2018) (Appendix 1).
- MEDLINE Ovid (1946 to November 16, 2018) (Appendix 2).
- Embase.com (1947 to November 16, 2018) (Appendix 3).
- Cumulative Index to Nursing and Allied Health Literature (CINAHL) (January 1937 to November 16, 2018) (Appendix 4).
- Allied and Complementary Medicine Database (AMED) (January 1985 to November 16, 2018) (Appendix 5).
- PubMed (1948 to November 16, 2018) (Appendix 6).
- Latin American and Caribbean Health Sciences Literature Database (LILACS) (1982 to November 16, 2018) (Appendix 7).
- ZETOC (January 1993 to November 16, 2018) (Appendix 8).
- *meta*Register of Controlled Trials (*m*RCT) (www.controlled-trials.com) (last searched January 8, 2013) (Appendix 9).
- US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (www.clinicaltrials.gov; searched November 16, 2018) (Appendix 10).
- World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp; searched November 16, 2018) (Appendix 11).
- National Center for Complementary and Alternative Medicine (NCCAM) website (http://nccam.nih.gov) (last searched July 14, 2010) (Appendix 12).
- Chinese Acupuncture Trials Register (searched November 19, 2018) (Appendix 13).
- Traditional Chinese Medical Literature Analysis and Retrieval System (TCMLARS) (searched November 19, 2018) (Appendix 14).
- Chinese Biological Database (CBM) (searched November 19, 2018) (Appendix 15).
- China National Knowledge Infrastructure (CNKI) (searched November 19, 2018) (Appendix 16).

Searching other resources

We searched the reference lists of included trials. An ad hoc manual search of Chinese medical journals *(Beijing Journal of Traditional Chinese Medicine, Shanghai Journal of Traditional Chinese Medicine, Liaoning Journal of Traditional Chinese Medicine, Zhejiang Journal of Medicine, Jiangxi Journal of Traditional Chinese Medicine, Journal of Clinical Acupuncture, Shanghai Journal of Acupuncture, Chinese Journal of Practical Ophthalmology)* was conducted by Dr. Yuanbo Liang and colleagues at Peking Union Medical College Library in 2013.

Data collection and analysis

Selection of studies

Two review authors independently assessed the titles and abstracts obtained by the searches. We classified each citation as "definitely exclude," "unclear," or "definitely include." We obtained full texts

of all potentially or definitely related articles and determined their final eligibility. We resolved discrepancies between the two review authors through discussion. We found evidence in the literature that many of the so called RCTs were not truly randomized in the field of complementary medicine (Oh 2007). For this reason, for potentially eligible studies identified after full-text screening, we contacted study authors by email on February 22, 2019, and again on March 6, 2019, to ask about their approaches to random sequence generation and allocation concealment to confirm trial eligibility. We excluded trials if the email information was not available/valid, or if study authors did not respond to our inquiries. We documented the excluded studies and the reasons for exclusion in the Characteristics of excluded studies table.

Data extraction and management

Two review authors independently extracted study characteristics and data for the primary and secondary outcomes onto paper data collection forms developed by Cochrane Eyes and Vision. We resolved discrepancies through discussion. One review author entered all data into Review Manager 5 (RevMan 5) (Review Manager 2014). The second review author independently checked the data entered. We did not contact study authors for missing outcome data.

Assessment of risk of bias in included studies

Two review authors independently assessed included trials for four types of bias. We rated each domain as having low, high, or unclear risk of bias in accordance with Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2017).

Selection bias

Selection bias, in the context of RCT, refers to "systematic differences between baseline characteristics of the groups that are compared (Higgins 2017)." We assessed methods of sequence generation and allocation concealment.

Performance bias

Performance bias refers to "systematic differences between groups in the care that is provided (Higgins 2017)." We examined masking of outcome assessment, in which persons responsible for assessing outcomes were unaware of the assigned intervention. Masking of participants and care providers may not be feasible in trials on this topic, and hence is not used as a measure of quality.

Attrition bias

Attrition bias refers to "systematic differences between groups in withdrawals from a study (Higgins 2017)." We assessed follow-up times and losses to follow-up in each group. We examined reasons for losses to follow-up (e.g., withdrawals, dropouts, protocol deviations) and how losses of participants were handled. We also assessed whether the analysis was conducted on an intention-to-treat basis, that is, whether participants were analyzed in the group to which they were randomly assigned.

Detection bias

Detection bias refers to "systematic differences between groups in how outcomes are determined (Higgins 2017)." We examined masking of outcome assessment.

Data synthesis

We followed the guidelines pertaining to data synthesis provided in Chapter 9 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Deeks 2017). For dichotomous outcomes, we planned to calculate a summary risk ratio. For continuous outcomes, we planned to calculate the mean difference. For cross-over trials, we planned to use estimates that correctly accounted for the correlation between outcomes from the same individual. Before combining the data, we planned to assess clinical and methodological heterogeneity by examining the characteristics and methodological quality of each trial. To assess the amount of statistical heterogeneity, we planned to use forest plots, results of the Chi^2 test for statistical heterogeneity, and the value of I^2. If we detected no substantial statistical heterogeneity (i.e., I^2 value < 60%), and if we noted no clinical or methodological heterogeneity among trials, we planned to combine the results in a meta-analysis using a random-effects model. We planned to use a fixed-effect model if we identified three or fewer trials. When substantial heterogeneity was present, we planned not to combine trial results but to present them in a tabulated summary.

We assessed the certainty of evidence using the GRADE approach and presented the findings in a "Summary of findings" table. Outcomes assessed were change in the visual field, reduction in IOP, change in visual acuity, progression of optic disc damage or never fiber layer loss, and adverse events.

Sensitivity analysis

We planned to conduct sensitivity analyses to examine the impact of exclusion of trials of lower methodological quality if at least two trials were included.

RESULTS

Description of studies

Results of the search

The initial electronic searches for the first version of this review revealed 28 distinct titles and abstracts, of which two appeared to be relevant and led to review of the full articles. We excluded both studies because they were not RCTs (Kumar 1994; Nesterov 1997). We identified 13 reports through handsearching, none of which met our inclusion criteria. An updated search in March 2010 yielded 15 abstracts and two clinical trials. None were relevant to the scope of the review. The updated search in January 2013 yielded 14 abstracts and one ongoing trial; one completed trial — Her 2010 — and one ongoing trial — JPRN 2009 — were included in the 2013 update.

The update search in 2018 yielded 560 distinct titles and abstracts, of which 30 appeared to be relevant and underwent full-text review. We identified 18 potentially eligible studies after full-text screening, only 12 of which provided email information. We contacted authors of these 12 studies by email to inquire about their approaches to random sequence generation and allocation concealment. We were able to confirm eligibility of two trials (Her 2010; Tsui-Yun 2016). Her 2010 was included in the 2013 update. Tsui-Yun 2016 is a new trial. Authors of the remaining 10 trials did not respond to our inquiries. In addition, we identified one trial that was conducted by an author (SL) of this systematic review (Law 2015).

In summary, in the 2019 update, we have included three completed trials—Her 2010; Law 2015; Tsui-Yun 2016—and one ongoing trial—JPRN 2009.

See Figure 1 for the study flow diagram.

Figure 1. Study flow diagram.

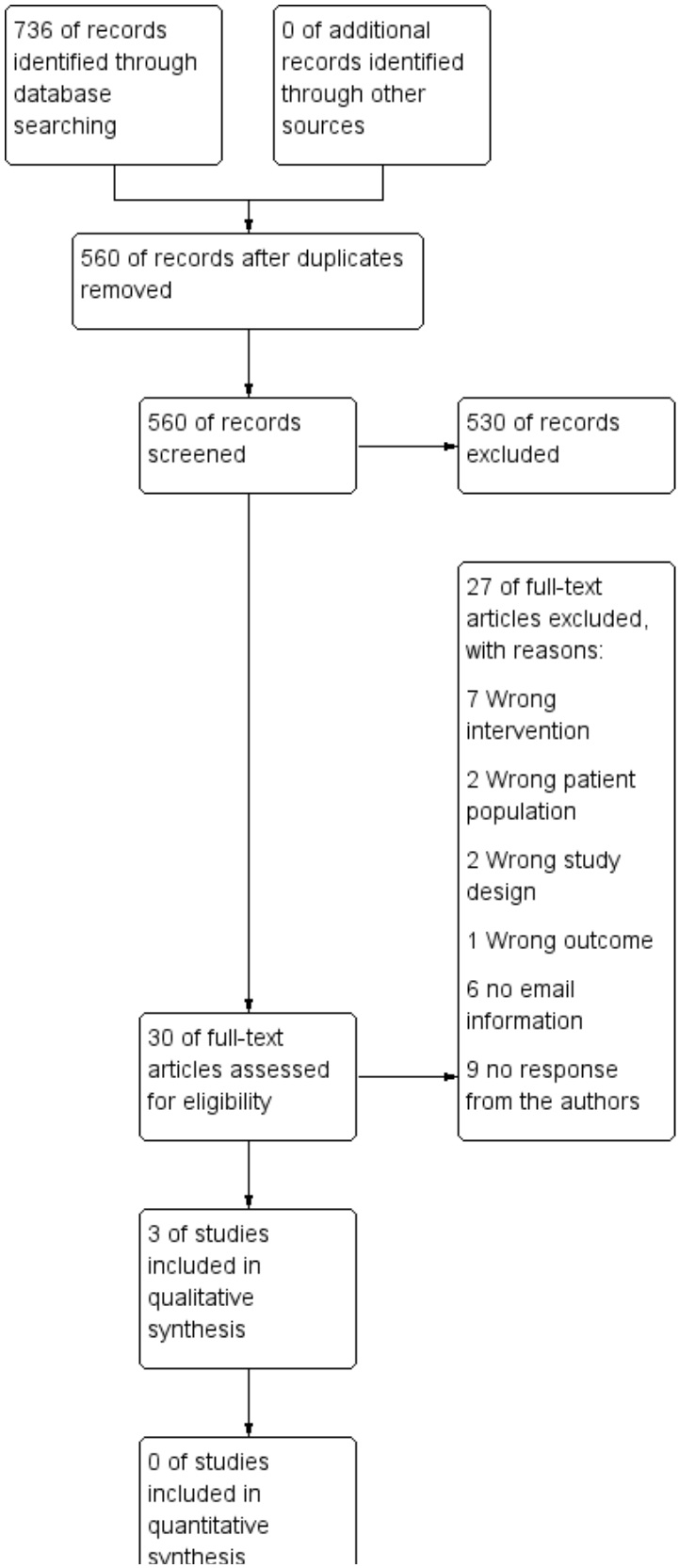
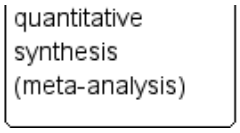


Figure 1. (Continued)



Included studies

We described details of these three trials in the Characteristics of included studies table.

Types of participants

The three completed trials were conducted in hospitals in Taiwan and the United States, including a total of 137 participants (ranging from 22 and 33 to 82 participants) with glaucoma or intraocular hypertension. Researchers compared different acupuncture approaches (Her 2010; Law 2015; Tsui-Yun 2016). Eligibility criteria varied across trials. Laser surgery generally was not allowed for trial participants.

Specifically, Her 2010 included 33 participants 30 years of age or older who had primary open-angle glaucoma, chronic angle-closure glaucoma, normal-tension glaucoma, ocular hypertension, or secondary glaucoma in one or both eyes who had been treated for at least one year.

Tsui-Yun 2016 included 82 participants 20 years of age or older who had glaucoma or intraocular hypertension in one or both eyes and IOP above 22 mm Hg. This trial excluded patients if they had undergone the following surgeries or had the following conditions: laser surgery for glaucoma or myopia; inflammation of eyes; intraocular hypertension caused by cataract or other eye disease; two or more injected and/or systemic medications that lowered IOP; and end-stage glaucoma.

Law 2015 included 22 participants 18 years of age or older who had primary open-angle glaucoma and stable IOP with no use of any alternative therapy, no history of surgical or laser intervention for glaucoma or failed interventions within the prior three years, no cardiovascular or neurological disease or bleeding disorder, and no retinal abnormality or non-glaucomatous optic neuropathy. This trial excluded patients if they had secondary glaucoma.

Types of interventions

Acupuncture procedures were different among the three trials, including acupressure, transcutaneous electrical nerve stimulation (TENS), and needle acupuncture. Comparators also differed across trials, including sham treatment and needle acupuncture on non-eye-points. Treatment duration ranged from 20 minutes to 12 weeks.

Specifically, in the Her 2010 trial, participants were randomly assigned to the auricular acupressure group or the sham group. Patients in the acupressure group received "stimulator tapping" and massage of the "auricular points (kidney, liver, and eye) over the right ear at our first course of outpatient clinic." Tapping stimulation was administered. Over a four-week period, patients regularly massaged their ears using thumb and index finger "twice per day for nine minutes each time (three minutes/each point)." At four weeks' follow-up, patients stopped acupoint tapping and no further massages were given. Patients in the sham group received "stimulator tapping but no massage at the sham auricular points." All other treatment modalities were the same as those used for the acupressure group.

In the Tsui-Yun 2016 trial, the treatment group "was treated with direct current on acupoints of Pucan and Shenmai through TENS (electrodes) for 20 min." The control group "was subjected to TENS electrodes on the same acupoints, but without direct current."

In the Law 2015 trial, participants were randomly assigned to 12 sessions (over 6 to 12 weeks) of acupuncture on eye-points or on non-eye-points followed by cross-over after a washout period of four weeks.

Types of outcomes

Change in the visual field from baseline

One trial assessed visual field, with achromatic automated perimetry, with the 24-2 Standard Swedish Interactive Threshold Algorithm (Law 2015). Visual field measurements were obtained at the baseline visit, within one week of completion of the first series of 12 sessions, and within one week before and after the second series of 12 sessions.

Reduction in IOP

All three trials assessed IOP. Her 2010 and Law 2015 measured IOP with a Goldmann applanation tonometer. Tsui-Yun 2016 measured IOP with a pneumotonometer. Time points of measurement varied. Her 2010 measured IOP 10 minutes before and after treatment, and at weeks 1, 2, 3, 4, and 8 of follow-up. Law 2015 measured diurnal IOP at the baseline visit, within one week of completion of the first series of 12 sessions (over 6 to 12 weeks), and within one week before and after the second series of 12 sessions. Tsui-Yun 2016 measured IOP at baseline and immediately and 30 and 60 minutes after treatment.

Change in visual acuity

Two trials measured visual acuity (Her 2010; Law 2015). Both trials measured visual acuity with a visual acuity chart. However, time points of measurement varied. Specifically, Her 2010 measured visual acuity 10 minutes before and after treatment, and at weeks 1, 2, 3, 4, and 8 of follow-up. Law 2015 measured visual acuity at the baseline visit, within one week of completion of the first series of 12 sessions (over 6 to 12 weeks), and within one week before and after the second series of 12 sessions.

Progression of optic disc damage or nerve fiber layer loss

One trial assessed the optic disc using confocal scanning laser ophthalmoscopy (Law 2015). Optic disc measurements were obtained at the baseline visit and within one week of completion of the second acupuncture series.

Adverse events

One trial recorded adverse events throughout the study (Law 2015).

Excluded studies

See the Characteristics of excluded studies table for details.

Risk of bias in included studies

See Figure 2 for a summary of the risk of bias assessment.

Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

Allocation

Random sequence generation

We rated all three trials as having low risk of bias for random sequence generation.

Allocation concealment

We rated Tsui-Yun 2016 as having unclear risk of bias for allocation concealment because the method used to conceal allocation was not described in the article. Contacting study authors did not reveal any new information. We rated the other two trials as having low risk of bias.

Blinding

Blinding of participants and personnel

We rated Tsui-Yun 2016 as having high risk of bias for blinding of personnel because only participants were masked in the trial. We rated the other two trials as having low risk of bias.

Blinding of outcome assessment

We rated Her 2010 and Tsui-Yun 2016 as having high risk of bias for blinding of outcome assessment because outcome assessors were not masked in the trials. We rated the remaining trial as having low risk of bias.

Incomplete outcome data

We rated Law 2015 as having high risk of bias for incomplete outcome data because 11 out of 22 (50%) participants did not complete the study. We rated the other two trials as having low risk of bias.

Selective reporting

We rated all three studies as having unclear risk of bias for selective reporting because the original protocols were not available, although the outcomes prespecified in the methods section were reported in the results section (Her 2010; Law 2015; Tsui-Yun 2016).

Effects of interventions

See: **Summary of findings for the main comparison**

Clinical heterogeneity made comparisons or meta-analyses of included trials impossible. We therefore summarized the effects of interventions on each outcome by trial.

Change in the visual field from baseline

Law 2015 did not report between-group comparisons for any outcomes examined in the trial. Because 11 out of 22 (50%) participants did not complete the treatment, we did not calculate a between-group comparison, as the quantitative results are difficult to interpret. The certainty of evidence is very low, downgraded for high risk of bias, imprecision, and inconsistency.

Reduction in IOP

Her 2010 did not report between-group comparisons for any outcomes examined in the trial. We re-analyzed data reported at four weeks and at eight weeks. At four weeks—the time point at which acupressure treatment stopped—comparison of the acupressure group with the sham group revealed that the between-group difference in IOP (measured in mm Hg) was -3.70 (95% confidence interval [CI] -7.11 to -0.29) for the right eye and -4.90 (95% CI -8.08 to -1.72) for the left eye. At eight weeks—the longest follow-up time point in the study—comparison of the acupressure group with the sham group revealed that the between-group difference in IOP reduction was -1.30 mm Hg (95% CI -4.78 to 2.18) for the right eye and -2.30 mm Hg (95% CI -5.73 to 1.13) for the left eye. No statistically significant difference in IOP was noted at any other follow-up time points.

Tsui-Yun 2016 also did not report between-group comparisons for any outcomes examined in the trial. We re-analyzed data reported immediately, 30 minutes, and 60 minutes after TENS. Immediately after TENS, comparison between TENS and sham treatment revealed greater reductions in IOP (measured in mm Hg) in TENS: -2.81 (95% CI -3.8 to -1.84) for the right eye and 2.58 (95% CI -3.36 to -1.80) for the left eye. Thirty minutes after TENS, values were -2.93 (95% CI -3.72 to -2.13) for the right eye and -3.56 (95% CI -4.35 to 2.78) for the left eye. Sixty minutes after TENS, values were -3.61 (95% CI -4.47 to -2.75) for the right eye and -3.61 (95% -4.47 to -2.74) for the left eye.

Law 2015 did not report between-group comparisons for any outcomes examined in the trial. Because of the quantity of missing data, we did not calculate a between-group comparison, as the quantitative results are difficult to interpret. The certainty of evidence is very low, downgraded for high risk of bias, imprecision, and inconsistency.

Change in visual acuity

Her 2010 did not report between-group comparisons for any outcomes examined in the trial. We re-analyzed data reported at four weeks and at eight weeks. At four weeks—the time point at which acupressure treatment stopped—comparison of the acupressure group with the sham group revealed that the between-group difference in uncorrected visual acuity (UCVA, measured in logMAR) was -0.01 (95% CI -0.24 to 0.22) for the right eye and -0.04 (95% CI -0.27 to 0.19) for the left eye. The difference in best corrected visual acuity (BCVA, measured in logMAR) was 0.10 (95% CI -0.06 to 0.26) for the right eye and 0 (95% CI -0.14 to 0.14) for the left eye. At eight weeks—the longest follow-up time point in the study—comparison of the acupressure group with the sham group revealed that the between-group difference in UCVA was -0.03 logMAR (95% CI -0.27 to 0.21) for the right eye and -0.16 logMAR (95% CI -0.43 to 0.11) for the left eye. The difference in BCVA was -0.04 logMAR (95% CI -0.09 to 0.17) for the right eye and -0.04 logMAR (95% CI -0.18 to 0.10) for the left eye. No statistically significant difference in visual acuity was noted at any other follow-up time points. The certainty of evidence is very low, downgraded for high risk of bias, imprecision, and inconsistency.

Progression of optic disc damage or nerve fiber layer loss

Law 2015 did not report between-group comparisons for any outcomes examined in the trial. Because of the quantity of missing data, we did not calculate a between-group comparison, as the quantitative results are difficult to interpret. The certainty of evidence is very low, downgraded for high risk of bias, imprecision, and inconsistency.

Adverse events

In Law 2015, two participants experienced needle sensitivity. However, this study did not report between-group comparisons for any outcomes examined in the trial. Because 11 out of 22 (50%) participants did not complete the treatment, the quantitative results are difficult to interpret. The certainty of evidence is very low, downgraded for high risk of bias, imprecision, and inconsistency.

DISCUSSION

Acupuncture, which originated in China more than 2000 years ago, is one of the oldest medical procedures in the world (NCCAM 2007). Over the past two decades, acupuncture has grown in popularity in the United States and in other Western countries. Between 2002 and 2012, the numbers of acupuncture users and licensed acupuncturists increased by 50% and 100%, respectively. According to the 2012 National Health Interview Survey (N = 33,373 respondents), 7.4% of respondents reported having had acupuncture before, and the proportion of current acupuncture users (within the preceding 12 months) increased from 1.1% to 1.7% in 2002 and 2012 (Cui 2017).

In accordance with this trend, some patients with glaucoma may seek acupuncture as a supplement or an alternative to their traditional glaucoma management. The certainty of evidence is very low for all outcomes assessed, and the quantitative results should be interpreted carefully. One completed trial suggests that

although intraocular pressure (IOP) in the acupressure group was statistically lower than that in the sham group at four weeks' follow-up, the difference was not statistically significant at any other follow-up time points, including the longest follow-up time (eight weeks). Further, the difference in visual acuity between the two groups was not statistically significant at any follow-up time point. Another completed trial suggests that the reduction in IOP in the treatment group receiving electrical stimulation of acupoints was statistically greater than that in the control group without electrical stimulation immediately, 30 minutes, and 60 minutes after treatment. However, long-term efficacy and safety were unclear. Results from the third completed trial, which compared effects of 12 sessions of acupuncture on eye-points versus on non-eye-points, were difficult to interpret because half of participants did not complete the treatment. All together, limited information from randomized controlled trials (RCTs) highlights the gap in existing evidence. The effectiveness of acupuncture as a therapeutic modality for glaucoma could not be established at this point.

AUTHORS' CONCLUSIONS

Implications for practice

At this time, it is impossible to draw reliable conclusions from available data to support the use of acupuncture for treatment of patients with glaucoma. Most patients with glaucoma currently cared for by ophthalmologists do not use non-traditional therapy.

Implications for research

Because of ethical considerations, RCTs comparing acupuncture alone with standard glaucoma treatment or placebo are unlikely to be justified in the near future in countries where the standard of care has already been established. However, trials in which acupuncture in combination with another glaucoma treatment is compared with the other glaucoma treatment alone might be of interest. It would be valuable for researchers and clinicians who are experienced in acupuncture to agree on certain basic standards for administration of acupuncture in clinical trials. Adequate data on IOP, central visual acuity, contrast sensitivity, visual field changes, optic nerve and retinal nerve fiber layer analysis, ocular blood flow, pattern electroretinography (PERG), multi-focal ERG, visual evoked potential (VEP), multi-focal visual evoked potential (mfVEP), potential harms, visual-related quality of life, and economic outcomes will facilitate appropriate evaluation of the effectiveness and safety of acupuncture.

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CHARACTERISTICS OF STUDIES

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

Her 2010

Methods	**Study design:** RCT **Study date:** not reported **Number randomized (total and per group):** 33 participants in total; 16 participants (28 glaucoma eyes) in the auricular acupressure group and 17 participants (32 glaucoma eyes) in the sham group **Number analyzed (total and per group):** 33 participants in total; 16 participants (28 glaucoma eyes) in the auricular acupressure group and 17 participants (32 glaucoma eyes) in the sham group **Exclusions and loss to follow-up:** 0 **Study follow-up:** 8 weeks
Participants	**Country:** Taiwan **Age (mean ± SD, range), years:** 73.6 ± 9.1 in the acupressure group, 76.3 ± 10.5 in the sham group **Gender:** 3/16 in the acupressure group and 4/17 in the sham group are female **Inclusion criteria:** age 30 years or older; history of unilateral or bilateral glaucoma or ocular hypertension that has been treated for at least 1 year **Exclusion criteria:** laser trabeculoplasty in the past; filtering surgery for glaucoma in the past; persistent ocular inflammation within the past year; start of or adjustment to the use of any systemic med-

Her 2010 *(Continued)*

	ication that affects the IOP within 3 months; end-stage glaucoma with impending phthisis bulbi; no detectable IOP because of poor psychological condition
Interventions	**Treatment or intervention 1:** auricular acupressure **Control or intervention 2:** sham group **General procedures (e.g., pre-op or post-op tests, medications, procedures):** "Patients in the acupressure group received 'stimulator tapping' and massage of the auricular points (kidney, liver, and eye) over the right ear at our first course of outpatient clinic. Tapping stimulation was administered using a 1-mm alloy ball (Magrain; Sakamura, Kyoto, Japan) designed for acupressure, which was applied to the surface of the auricular acupoints. Subsequently, over a 4-week period, patients regularly massaged their ears using thumb and index finger (squeezing each side of the ear with inward pressure from opposing finger and thumb) twice per day for 9 minutes each time (3 minutes/each point). A regular follow-up was performed and the side for tapping, left ear or right ear, was alternated weekly. After 4 weeks of follow-up, tapping of the acupoints was discontinued and no further massages were given. The investigators re-evaluated IOP, uncorrected visual acuity, and best corrected visual acuity at the 8-week follow-up conducted at the clinic. Patients in the sham group received stimulator tapping but no massage at the sham auricular points (wrist, shoulder, and jaw). All other treatment modalities were the same as those for the acupressure group"
Outcomes	**Primary outcome(s):** IOP and visual acuity with or without glasses were measured **Secondary outcome(s):** N/A **Measurements taken, specify intervals at which outcomes assessed:** "IOP was measured with a Goldmann applanation tonometer (Haag-Streit AG, Koeniz, Switzerland). Visual acuity was examined with a 6-m visual acuity chart. Glaucomatous eyes were used for analysis of IOP, as were eyes with better than 0.01 (decimal) visual acuity. All visual acuity data were transformed to the LogMAR (MAR¼minimal angle resolution) form for analysis" **Unit of analysis (individual or eye):** eye or individual (1 eye per person was used for the analysis) **Other issues with outcome assessment (e.g., quality control for outcomes if any):** N/A
Notes	**Funding source(s):** National Science Counsel of Taiwan (NSC 97-2320-B-039-022-MY3 and NSC 98-2815-C-039-097-B), Department of Health, Executive Yuan, Taiwan (DOH98-TD-F-113-098011), and China Medical University (CMU98-CT-10), Taichung, Taiwan **Publication language:** English

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Method used to generate random sequence was not described in the article. After contacting the study author, we received the following information: "We used computer to generate 40 (our original expected patient collection numbers) simple randomized allocation sequences. We then assigned patients to 'control' or 'trial' group according to their clinic visit order. So we knew the next patient would be assigned to which group, but we didn't know who would be the next one (patient's visit order was arranged by the clinic assistant, who didn't know the randomized allocation sequences). The patient him-/herself would not know which group he/she would be assigned"
Allocation concealment (selection bias)	Low risk	Method used to conceal allocation was not described in the article. We considered that allocation was adequately concealed after contacting the study authors because "patient's visit order was arranged by the clinic assistant, who didn't know the randomized allocation sequences"

Her 2010 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Masking of participants and personnel was not described in the article. After contacting the study author, we received the information that "patients were blinded of their treatment group whereas the outcome assessors were not blinded"
Blinding of outcome assessment (detection bias) All outcomes	High risk	See above
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up was reported
Selective reporting (reporting bias)	Unclear risk	Original protocol was not available
Other bias	Low risk	No other bias was identified

Law 2015

Methods	**Study design:** cross-over RCT **Study date:** not reported **Number randomized (total and per group):** 22 participants in total; 11 participants (11 glaucoma eyes) in the eye-point acupuncture group and 11 participants (11 glaucoma eyes) in the non-eye-point acupuncture group **Number analyzed (total and per group):** 11 participants in total **Exclusions and loss to follow-up:** 11 participants did not complete the study **Study follow-up:** 13 weeks
Participants	**Country:** United States **Age (mean ± SD, range), years:** 63.7 ± 14.3 in total **Gender:** 8/11 are female **Inclusion criteria:** primary open-angle glaucoma; age 18 years or older; stable intraocular pressures (< 2 mm Hg variation in the last 2 follow-up visits over a period of at least 3 months and without alteration of glaucoma therapy for 6 months); no use of any alternative therapy including cannabis; no history of surgical or laser intervention for glaucoma or failed interventions within the prior 3 years; no cardiovascular or neurological disease or bleeding disorder; no retinal abnormality or non-glaucomatous optic neuropathy **Exclusion criteria:** secondary glaucomas were excluded, including pigmentary dispersion, pseudoexfoliation, and uveitic, steroid-induced, or traumatic glaucoma
Interventions	**Treatment or intervention 1:** acupuncture on eye-points **Control or intervention 2:** acupuncture on non-eye-points **General procedures (e.g., pre-op or post-op tests, medications, procedures):** "Acupuncture was performed by an experienced, licensed acupuncturist. Two groups of acupuncture points were evaluated. One group of points was related to the eye or used to treat eye diseases according to traditional Chinese acupuncture theory (eye-points). The 4 eye-points were UB2, GB37, Liv3, and LI4. The second group of acupuncture points was not eye related and is traditionally used to treat non-ocular dis-

Law 2015 *(Continued)*

	ease (non-eye-points). The 4 non-eye-points were St36, St38, Sp6, and UB60. Acupuncture needles were placed on points on both sides of the body. Sterile stainless steel disposable acupuncture needles (1-inch 36-gauge needles and 1/2-inch 38-gauge needles) were used. A sensation of numbness and mild aching at the acupoint (traditionally termed ''De Qi'') was elicited as an indication of proper needle placement. Each acupuncture needle [was] left in place for 20 minutes while the patient rested on a 45-degree-reclined examination chair, without electric or laser stimulation of the needle or moxibustion. Patients were randomly assigned (by flipping a coin) to receive 1 acupuncture series, either the eye-points or non-eye-points, for 12 sessions over 6–12 weeks (1–2 sessions per week) and then were crossed over to receive the other acupuncture series (12 sessions over 6–12 weeks) with a washout period of 4 weeks in between. Glaucoma medical therapy was not altered at any time during the study"
Outcomes	**Primary outcome(s):** IOP **Secondary outcome(s):** vital signs, visual acuity, visual field, optic disc, RNFL thickness measurements **Measurements taken, specify intervals at which outcomes assessed:** "BP, HR, and IOP were measured 15 minutes before and after each treatment session. Diurnal IOP measurement and automated visual field measurements were obtained at the baseline visit, within 1 week of completion of the first series of 12 sessions, and within 1 week before and after the second series of 12 sessions. Optic disc (HRT) and RNFL measurements (SD OCT) were obtained at the baseline visit and within 1 week of completing the second acupuncture series. Adverse reactions were recorded throughout the study period **Unit of analysis (individual or eye):** eye or individual (1 eye per person was used for the analysis) **Other issues with outcome assessment (e.g., quality control for outcomes if any):** N/A
Notes	**Funding source(s):** Oppenheimer Seed Grants in Complementary, Alternative, and Integrative Medicine, University of California Los Angeles, David Geffen School of Medicine, Los Angeles, California **Publication language:** English

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Patients were randomly assigned by flipping a coin
Allocation concealment (selection bias)	Low risk	The allocation sequence was not predictable
Blinding of participants and personnel (performance bias) All outcomes	Low risk	"Patients and research personnel, except the licensed acupuncturist, were masked"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"Patients and research personnel, except the licensed acupuncturist, were masked"
Incomplete outcome data (attrition bias) All outcomes	High risk	11 out of 22 (50%) participants did not complete the treatment
Selective reporting (reporting bias)	Unclear risk	Original protocol was not available
Other bias	Low risk	No other bias was identified

Tsui-Yun 2016

Methods	**Study design:** RCT **Study date:** not reported **Number randomized (total and per group):** 82 participants in total; 40 participants in the direct current group and 42 participants in the control group **Number analyzed (total and per group):** 82 participants in total; 40 participants in the direct current group and 42 participants in the control group **Exclusions and loss to follow-up:** 0 **Study follow-up:** 60 minutes
Participants	**Country:** Taiwan **Age (mean ± SD, range), years:** 54.0 ± 19.4 in the direct current group, 56.1 ± 20.0 in the control group **Gender:** 27/40 in the acupressure group and 20/42 in the sham group are female **Inclusion criteria:** age ≥ 20 years; intraocular pressure > 22 mm Hg; 1 one or both eyes with glaucoma or intraocular hypertension; not pregnant; no cancer diagnosed; clear consciousness (mentally normal and without a mental illness); minimum education level of junior high school; capable of communication (speaking Chinese or Taiwanese); agreed to participate in the experiment and signed the informed consent with guarantee of full participation in the experiment **Exclusion criteria:** laser surgery for glaucoma or myopia; inflammation of eyes; intraocular hypertension caused by cataract or other eye disease; ≥ 2 injected and/or systemic medications that lowered IOP; end stage of glaucoma (severe optic neuropathy); unclear consciousness; unco-operative during the experiment; unwilling to sign the informed consent; unable to participate throughout the entire experimental period
Interventions	**Treatment or intervention 1:** direct current **Control or intervention 2:** control **General procedures (e.g., pre-op or post-op tests, medications, procedures):** "The IOPs of all participants were measured. The experimental group was treated with DC on acupoints of Pucan (BL 61) and Shenmai (BL 62) through transcutaneous electrical nerve stimulation (TENS) for 20 min while the control group was subjected to TENS electrodes on the same acupoints, but without DC. Another IOP measurement was immediately taken. After 30 min, a third IOP measurement was taken, and IOP was also measured after 60 min"
Outcomes	**Primary outcome(s):** IOP **Secondary outcome(s):** N/A **Measurements taken, specify intervals at which outcomes assessed:** "The IOPs of all participants were measured. The experimental group was treated with DC on acupoints of Pucan (BL 61) and Shenmai (BL 62) through TENS for 20 min while the control group was subjected to TENS electrodes on the same acupoints, but without DC. Another IOP measurement was immediately taken. After 30 min, a third IOP measurement was taken, and IOP was also measured after 60 min" **Unit of analysis (individual or eye):** eye **Other issues with outcome assessment (e.g., quality control for outcomes if any):** N/A
Notes	**Funding source(s):** N/A

Tsui-Yun 2016 *(Continued)*

Publication language: English

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Method used to generate random sequence was not described in the article. After contacting the study author, we received the following information: "randomization by computer"
Allocation concealment (selection bias)	Unclear risk	Method used to conceal allocation was not described in the article, and the study author did not inform our research team about their method of allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	High risk	Only participants were masked from their intervention group
Blinding of outcome assessment (detection bias) All outcomes	High risk	Only participants were masked from their intervention group
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up was reported
Selective reporting (reporting bias)	Unclear risk	Original protocol was not available
Other bias	Low risk	No other bias was identified

BP: blood pressure.
DC: direct current.
HR: heart rate.
HRT: Heidelberg Retinal Tomography.
IOP: intraocular pressure.
N/A: not applicable.
RCT: randomized controlled trial.
RNFL: retinal nerve fiber layer.
SD: standard deviation.
SD OCT: spectral domain optical coherence tomography.
TENS: transcutaneous electrical nerve stimulation.

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

Study	Reason for exclusion
Hao 2014	Not a randomized controlled trial
He 2017	Not a randomized controlled trial
Huang 2014	No response from study authors to our inquiries about whether the study was a randomized controlled trial
Huo 2009	Acupuncture as defined in this review was not used

Study	Reason for exclusion
Jiang 1996	Not a randomized controlled trial
Kumar 1994	Non-randomized comparative study; acupuncture as defined in this review was not used
Leszczynska 2018	No response from study authors to our inquiries about whether the study was a randomized controlled trial
Li 2008	Outcomes prespecified in this review were not measured
Li 2017	Acupuncture as defined in this review was not used
Liu 2013	No response from study authors to our inquiries about whether the study was a randomized controlled trial
Luo 2018	Acupuncture as defined in this review was not used
Nesterov 1997	Non-randomized comparative study; acupuncture as defined in this review was not used
Rao 2016	No response from study authors to our inquiries about whether the study was a randomized controlled trial
Tang 2015	No response from study authors to our inquiries about whether the study was a randomized controlled trial
Wang 2016	No response from study authors to our inquiries about whether the study was a randomized controlled trial
Wang 2017	No response from study authors to our inquiries about whether the study was a randomized controlled trial
Wu 2010	No response from study authors to our inquiries about whether the study was a randomized controlled trial
Wu 2108	No response from study authors to our inquiries about whether the study was a randomized controlled trial
Xu 2012	Not a randomized controlled trial
Yan 2012	Not a randomized controlled trial
Yang 2018	Acupuncture as defined in this review was not used
Yin 2012	Acupuncture as defined in this review was not used
Zhang 2002	No patients with glaucoma
Zhang 2003	No patients with glaucoma
Zhang 2009	No contact information to verify whether the study was a randomized controlled trial
Zhang 2014	Acupuncture as defined in this review was not used
Zhao 2018	Acupuncture as defined in this review was not used

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

JPRN 2009

Trial name or title	Acupuncture for Glaucoma
Methods	This is an interventional, parallel, randomized study
Participants	Inclusion criteria: patients with glaucoma treated for at least 1 year with ocular hypotensive medication Exclusion criteria: laser trabeculoplasty, any ocular surgery; inflammation within 1 year; other abnormal ocular condition; starting or adjusting the use of any systemic medication affecting intraocular pressure (IOP) within 3 months
Interventions	Patients will be randomly assigned to standard treatment or standard treatment plus acupuncture
Outcomes	• IOP • Blood flow volume of eyeball
Starting date	10/27/2009
Contact information	t-seki@m.tains.tohoku.ac.jp
Notes	

APPENDICES

Appendix 1. CENTRAL search strategy

#1 MeSH descriptor: [Glaucoma] explode all trees
#2 glaucom*
#3 MeSH descriptor: [Intraocular Pressure] explode all trees
#4 (intra*ocular or ocular) near/3 (hypertension* or tension* or pressur*)
#5 MeSH descriptor: [Ocular Hypertension] explode all trees
#6 IOP
#7 {or #1-#6}
#8 MeSH descriptor: [Acupuncture] explode all trees
#9 MeSH descriptor: [Acupuncture Therapy] explode all trees
#10 MeSH descriptor: [Medicine, Chinese Traditional] explode all trees
#11 MeSH descriptor: [Bloodletting] explode all trees
#12 MeSH descriptor: [Acupressure] explode all trees
#13 acupunctur* or acupressur*
#14 (meridian* or moxi*)
#15 (electrostimulat* or electroacupunctur*)
#16 (electro* next/1 (stimulat* or acupunctur*))
#17 acupoint*
#18 (erjian or taiyang or EX-HN6 or EX-HN5)
#19 body needl*
#20 (bloodletting or blood-letting or pricking blood)
#21 (Ear-apex or temporal region)
#22 qi
#23 ((chinese near/3 medicin*) or TCM)
#24 {or #8-#23}
#25 #7 and #24

Appendix 2. MEDLINE (Ovid) search strategy

1. Randomized Controlled Trial.pt.
2. Controlled Clinical Trial.pt.
3. (randomized or randomised).ab,ti.
4. placebo.ab,ti.
5. drug therapy.fs.
6. randomly.ab,ti.
7. trial.ab,ti.
8. groups.ab,ti.
9. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8
10. exp animals/ not humans.sh.
11. 9 not 10
12. exp glaucoma/
13. glaucom*.tw.
14. exp intraocular pressure/
15. ((intra?ocular or ocular) adj3 (hypertension* or tension* or pressur*)).tw.
16. Ocular Hypertension/
17. IOP.tw.
18. or/12-17
19. exp Acupuncture/
20. exp Acupuncture Therapy/
21. exp Medicine, Chinese Traditional/
22. exp Acupressure/
23. (acupunctur* or acupressur*).tw.
24. (meridian* or moxi*).tw.
25. (electrostimulat* or electroacupunctur*).tw.
26. (electro* adj1 (stimulat* or acupunctur*)).tw.
27. acupoint*.tw.
28. exp Bloodletting/
29. (erjian or taiyang or EX-HN6 or EX-HN5).tw.
30. body needl*.tw.
31. (bloodletting or blood-letting or pricking blood).tw.
32. (Ear-apex or temporal region).tw.
33. qi.tw.
34. ((chinese adj3 medicin*) or TCM).tw.
35. or/19-34
36. 18 and 35
37. 11 and 36

The search filter for trials at the beginning of the MEDLINE strategy is from the published paper by Glanville 2006.

Appendix 3. Embase.com search strategy

#1 'randomized controlled trial'/exp
#2 'randomization'/exp
#3 'double blind procedure'/exp
#4 'single blind procedure'/exp
#5 random*:ab,ti
#6 #1 OR #2 OR #3 OR #4 OR #5
#7 'animal'/exp OR 'animal experiment'/exp
#8 'human'/exp
#9 #7 AND #8
#10 #7 NOT #9
#11 #6 NOT #10
#12 'clinical trial'/exp
#13 (clin* NEAR/3 trial*):ab,ti
#14 ((singl* OR doubl* OR trebl* OR tripl*) NEAR/3 (blind* OR mask*)):ab,ti
#15 'placebo'/exp
#16 placebo*:ab,ti
#17 random*:ab,ti
#18 'experimental design'/exp
#19 'crossover procedure'/exp

#20 'control group'/exp
#21 'latin square design'/exp
#22 #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21
#23 #22 NOT #10
#24 #23 NOT #11
#25 'comparative study'/exp
#26 'evaluation'/exp
#27 'prospective study'/exp
#28 control*:ab,ti OR prospectiv*:ab,ti OR volunteer*:ab,ti
#29 #25 OR #26 OR #27 OR #28
#30 #29 NOT #10
#31 #30 NOT (#11 OR #23)
#32 #11 OR #24 OR #31
#33 'glaucoma'/exp
#34 'intraocular pressure'/exp
#35 'intraocular pressure abnormality'/de
#36 'ocular ischemic syndrome'/exp
#37 glaucom*:ab,ti
#38 ((intra*ocular OR ocular) NEAR/3 (hypertension* OR tension* OR pressur*)):ab,ti
#39 iop:ab,ti
#40 #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39
#41 'acupuncture'/exp
#42 'chinese medicine'/exp
#43 'bloodletting'/exp
#44 'acupuncture needle'/exp
#45 'acupressure'/exp
#46 'chinese medicine'/exp
#47 acupunctur*:ab,ti OR acupressur*:ab,ti
#48 (electro* NEAR/1 (stimulat* OR acupunctur*)):ab,ti
#49 electrostimulat*:ab,ti OR electroacupunctur*:ab,ti
#50 acupoint*:ab,ti
#51 erjian:ab,ti OR taiyang:ab,ti OR 'ex hn6':ab,ti OR 'ex hn5':ab,ti
#52 'ear apex':ab,ti OR 'temporal region':ab,ti
#53 bloodletting:ab,ti OR 'blood letting':ab,ti OR 'pricking blood':ab,ti
#54 (body NEXT/1 needl*):ab,ti
#55 meridian*:ab,ti OR moxi*:ab,ti
#56 qi:ab,ti
#57 (chinese NEAR/3 medicin*):ab,ti OR tcm:ab,ti
#58 #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57
#59 #40 AND #58
#60 #32 AND #59

Appendix 4. CINAHL (EBSCO) search strategy

S1 (MH "Glaucoma+")
S2 TI (glacuom*) OR AB (glacuom*)
S3 (MH "Intraocular Pressure")
S4 TI ((intra*ocular OR ocular) N3 (hypertension* OR tension* OR pressur*)) OR AB ((intra*ocular OR ocular) N3 (hypertension* OR tension* OR pressur*))
S5 (MH "Ocular Hypertension+")
S6 TI (IOP) OR AB (IOP)
S7 S1 OR S2 OR S3 OR S4 OR S5 OR S6
S8 (MH "Acupuncture+")
S9 (MH "Medicine, Chinese Traditional+")
S10 (MH "Acupressure+")
S11 (MH "Medicine, Oriental Traditional+")
S12 TI (acupunctur* OR acupressur*) OR AB (acupunctur* OR acupressur*)
S13 TI (meridian* OR moxi*) OR AB (meridian* OR moxi*)
S14 TI (electrostimulat* OR electroacupunctur*) OR AB (electrostimulat* OR electroacupunctur*)
S15 TI (electro* N1 (stimulat* OR acupunctur*)) OR AB (electro* N1 (stimulat* OR acupunctur*))
S16 TI (acupoint*) OR AB(acupoint*)
S17 TI (erjian OR taiyang OR EX-HN6 OR EX-HN5) OR AB (erjian OR taiyang OR EX-HN6 OR EX-HN5)

S18 TI ("body needl*") OR AB ("body needl*")
S19 TI (bloodletting OR "blood letting" OR "pricking blood") OR AB (bloodletting OR "blood letting" OR "pricking blood")
S20 TI ("Ear apex" OR "temporal region") OR AB ("Ear apex" OR "temporal region")
S21 TI (qi) OR AB (qi)
S22 TI ((chinese N3 medicin*) OR TCM) OR AB ((chinese N3 medicin*) OR TCM)
S23 (S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22)
S24 S7 AND S23

Appendix 5. AMED search strategy

1. exp Glaucoma/
2. exp Ocular hypertension/
3. glaucom*.tw.
4. ((intra?ocular or ocular) adj3 (hypertension* or tension* or pressur*)).tw.
5. IOP.tw.
6. 1 or 2 or 3 or 4 or 5
7. exp Acupuncture/
8. exp Acupuncture therapy/
9. exp Traditional medicine chinese/
10. exp Acupressure/
11. (acupunctur* or acupressur*).tw.
12. (meridian* or moxi*).tw.
13. (electrostimulat* or electroacupunctur*).tw.
14. (electro* adj1 (stimulat* or acupunctur*)).tw.
15. acupoint*.tw.
16. exp Bloodletting/
17. (erjian or taiyang or EX-HN6 or EX-HN5).tw.
18. body needl*.tw.
19. (bloodletting or blood letting or pricking blood).tw.
20. (Ear-apex or temporal region).tw.
21. qi.tw.
22. ((chinese adj3 medicin*) or TCM).tw.
23. 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22
24. 6 and 23

Appendix 6. PubMed search strategy

1. ((randomized controlled trial[pt]) OR (controlled clinical trial[pt]) OR (randomised[tiab] OR randomized[tiab]) OR (placebo[tiab]) OR (drug therapy[sh]) OR (randomly[tiab]) OR (trial[tiab]) OR (groups[tiab])) NOT (animals[mh] NOT humans[mh])
2. glaucom*[tw]
3. ((intraocular[tw] OR ocular[tw]) AND (hypertension*[tw] OR tension*[tw] OR pressur*[tw]))
4. IOP[tw]
5. #2 OR #3 OR #4
6. (acupunctur*[tw] OR acupressur*[tw])
7. (meridian*[tw] OR moxi*[tw])
8. (electrostimulat*[tw] OR electroacupunctur*[tw])
9. (electro*[tw] AND (stimulat*[tw] OR acupunctur*[tw]))
10. acupoint*[tw]
11. (erjian[tw] OR taiyang[tw] OR EX-HN6[tw] OR EX-HN5[tw])
12. body needl*[tw]
13. (bloodletting[tw] OR blood letting[tw] OR pricking blood[tw])
14. (Ear-apex[tw] OR temporal region[tw])
15. qi[tw]
16. ((Chinese[tw] AND medicin*[tw]) OR TCM[tw])
17. #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16
18. #5 AND #17
19. #1 AND #18
20. Medline[sb]
21. #19 NOT #20

Appendix 7. LILACS search strategy

(Glaucoma$ OR MH:C11.525.381$ OR "Ocular Hypertension" OR "Hipertensión Ocular" OR "Hipertensão Ocular" OR MH:C11.525$ OR "Intraocular Pressure" OR "Presión Intraocular" OR "Pressão Intra-Ocular" OR MH:G14.440$ OR IOP OR "intraocular hypertension" OR "intraocular tension" OR "intraocular pressure" OR "ocular tension" OR "ocular pressure") AND (Acupunctur$ OR MH:H02.004$ OR MH:HP3.018.069$ OR MH:E02.190.044$ OR Chinese Traditional Medicine OR TCM OR "Medicina China Tradicional" OR "Medicina Tradicional Chinesa" OR "Zhong Yi Xue" OR "Chung I Hsueh" OR MH:E02.190.488.585.520$ OR MH:I01.076.201.450.654.558.520$ OR Bloodletting OR Venodisección OR Sangria OR MH:E02.800.558.500$ OR Meridian$ OR moxi$ OR electrostimulat$ OR electroacupunctur$ OR electro-stimulat$ OR electro-acupunctur$ OR acupoint$ OR acupressure$ OR erjian OR taiyang OR EX-HN6 OR EX-HN5 OR "body needling" OR bloodletting OR blood-letting OR "pricking blood" OR Ear-apex OR "temporal region" OR qi)

Appendix 8. ZETOC search strategy

glaucoma* acup*
glaucoma* electrostimulate
glaucoma* electroacupuncture
glaucoma* Chinese medicine
glaucoma* bloodletting
glaucoma* traditional medicine
"ocular hypertension" acup*
"ocular hypertension" electrostimulate
"ocular hypertension" electroacupuncture
"ocular hypertension" Chinese medicine
"ocular hypertension" bloodletting
"ocular hypertension" traditional medicine

Appendix 9. *meta*Register of Controlled Trials search strategy

acupuncture and glaucoma

Appendix 10. ClinicalTrials. gov search strategy

(Glaucoma OR glaucomas OR "ocular hypertension") AND (acupuncture OR acupressure OR electrostimulate OR electroacupuncture OR acupoint OR bloodletting OR Chinese medicine OR traditional medicine)

Appendix 11. ICTRP search strategy

glaucoma AND acupuncture OR glaucoma AND acupressure OR glaucoma AND electrostimulate OR glaucoma AND electroacupuncture OR glaucoma AND acupoint OR glaucoma AND bloodletting OR glaucoma AND Chinese medicine OR glaucoma AND traditional medicine

glaucomas AND acupuncture OR glaucomas AND acupressure OR glaucomas AND electrostimulate OR glaucomas AND electroacupuncture OR glaucomas AND acupoint OR glaucomas AND bloodletting OR glaucomas AND Chinese medicine OR glaucomas AND traditional medicine

"ocular hypertension" AND acupuncture OR "ocular hypertension" AND acupressure OR "ocular hypertension" AND electrostimulate OR "ocular hypertension" AND electroacupuncture OR "ocular hypertension" AND acupoint OR "ocular hypertension" AND bloodletting OR "ocular hypertension" AND Chinese medicine OR "ocular hypertension" AND traditional medicine

Appendix 12. National Center for Complementary and Alternative Medicine website search strategy

acupuncture and glaucoma

Appendix 13. Chinese Acupuncture Trials Register search strategy

(青光眼 OR 眼压) AND (针灸 OR 针刺 OR 穴位 OR 电针 OR 电刺激 OR 放血)

Appendix 14. TCMLARS (SinoMed) search strategy

(青光眼 OR 眼压) AND (针灸 OR 针刺 OR 穴位 OR 电针 OR 电刺激 OR 放血)

Appendix 15. Chinese Biomedical Literature Service System (SinoMed) search strategy

(青光眼 OR 眼压) AND (针灸 OR 针刺 OR 穴位 OR 电针 OR 电刺激 OR 放血)

Appendix 16. CNKI search strategy

(青光眼 OR 眼压) AND (针灸 OR 针刺 OR 穴位 OR 电针 OR 电刺激 OR 放血)

WHAT'S NEW

Date	Event	Description
29 January 2020	New citation required but conclusions have not changed	Issue 2 2020: Electronic searches have been updated
29 January 2020	New search has been performed	Issue 2 2020: We included two new trials (Law 2015; Tsui-Yun 2016) and one ongoing trial (JPRN 2009) in this update

HISTORY

Protocol first published: Issue 2, 2006
Review first published: Issue 4, 2007

Date	Event	Description
18 April 2013	New citation required but conclusions have not changed	Issue 5, 2013: we included one new trial and one ongoing trial in this update. Seven Chinese trials were added as awaiting assessment, and these will be assessed for eligibility in the next update
18 April 2013	New search has been performed	Issue 5, 2013: electronic searches were updated
8 July 2010	New search has been performed	Issue 9 2010: updated searches did not yield any new trials
11 October 2008	Amended	Review was converted to new review format
30 July 2007	New citation required and conclusions have changed	We made substantive amendments

CONTRIBUTIONS OF AUTHORS

Conceiving the review: TL.
Designing the review: SL, TL.
Co-ordinating the review: TL.
Collecting data for the review:
- Designing search strategies: Cochrane Eyes and Vision editorial base.
- Undertaking searches: Cochrane Eyes and Vision editorial base.
- Screening search results: SL, TL, LW.
- Organizing retrieval of papers: SL, TL, LW.
- Screening retrieved papers against inclusion criteria: SL, TL, LW.
- Appraising quality of papers: SL, TL, LW.
- Extracting data from papers: SL, TL, LW.
- Writing to authors of papers for additional information: SL, TL, LW.
- Providing additional data about papers: SL, TL.
- Obtaining and screening data on unpublished studies: SL, TL.

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Interpreting data:
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- Providing a policy perspective: SL.

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DECLARATIONS OF INTEREST

No financial conflicts of interest have been declared, and the review authors declare that they do not have any association with any parties who may have vested interests in the results of this review. SL was the Principal Investigator of one of the included trials. He was involved in screening the search results but did not participate in data abstraction or risk of bias assessment for this trial.

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  The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the Systematic Reviews Programme, NIHR, NHS, or the Department of Health.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We included only RCTs in this review, although the protocol also specified quasi-RCTs. In the current update, we excluded studies with no confirmation from study authors that the studies were randomized; we also added a "Summary of findings" table. We documented all adverse events reported.

INDEX TERMS

Medical Subject Headings (MeSH)

Acupuncture Therapy [*methods]; Acupuncture, Ear; Glaucoma [*therapy]; Randomized Controlled Trials as Topic

MeSH check words

Humans