

Published in final edited form as:

Cochrane Database Syst Rev. ; (4): CD006030. doi:10.1002/14651858.CD006030.pub2.

Acupuncture for glaucoma

Simon K Law¹ and Tianjing Li²

¹Los Angeles, USA

²Cochrane Eyes and Vision Group US Project, Johns Hopkins Bloomberg School of Public Health, Baltimore, USA

Abstract

Background—Glaucoma is a multifactorial optic neuropathy in which there is an acquired loss of retinal ganglion cells at levels beyond normal age-related loss and corresponding atrophy of the optic nerve. Although there are many existing treatments, glaucoma is a chronic condition. Some patients may seek complementary or alternative medicine such as acupuncture to supplement their regular treatment. The underlying plausibility of acupuncture is that disorders related to the flow of Chi (the traditional Chinese concept translated as vital force or energy) can be prevented or treated by stimulating the relevant points on the body surface.

Objectives—The objective of this review was to assess the effectiveness and safety of acupuncture in people with glaucoma.

Search methods—We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (which contains the Cochrane Eyes and Vision Group Trials Register) (*The Cochrane Library* 2010, Issue 3), MEDLINE (January 1950 to March 2010), EMBASE (January 1980 to March 2010), Latin American and Caribbean Literature on Health Sciences (LILACS) (January 1982 to March 2010), ZETOC (January 1993 to March 2010), Allied and Complementary Medicine Database (AMED) (January 1985 to March 2010), the *meta*Register of

Simon K Law 100 Stein Plaza 2-235 Los Angeles CA 90095 USA Law@jsei.ucla.edu.

Contributions of authors Conceiving the review: TL

Designing the review: SL, TL

Coordinating the review: TL

Data collection for the review

- Designing search strategies: Cochrane Eyes and Vision Group editorial base

- Undertaking searches: Cochrane Eyes and Vision Group editorial base

- Screening search results: SL, TL

- Organizing retrieval of papers: SL, TL

- Screening retrieved papers against inclusion criteria: SL, TL

- Appraising quality of papers: SL, TL

- Extracting data from papers: SL, TL

- Writing to authors of papers for additional information: SL, TL

- Providing additional data about papers: SL, TL

- Obtaining and screening data on unpublished studies: SL, TL

Data management for the review

- Entering data into RevMan: SL, TL

- Analysis of data: SL, TL

Interpretation of data

- Providing a methodological perspective: TL

- Providing a clinical perspective: SL

- Providing a policy perspective: SL

Writing the review: SL, TL

Performing previous work that was the foundation of the current study: SL

Declarations of interest There are no financial conflicts of interest and the authors declare that they do not have any associations with any parties who may have vested interests in the results of this review.

Controlled Trials (*m*RCT) (www.controlled-trials.com), ClinicalTrials.gov (www.clinicaltrials.gov) and the National Center for Complementary and Alternative Medicine web site (NCCAM) (<http://nccam.nih.gov>). There were no language or date restrictions in the search for trials. The electronic databases were last searched on 23 March 2010 with the exception of NCCAM which was last searched on 14 July 2010. We also handsearched Chinese medical journals at Peking Union Medical College Library in April 2007.

Although the Cumulative Index to Nursing and Allied Health Literature (CINAHL), the Chinese Acupuncture Trials Register, the Traditional Chinese Medical Literature Analysis and Retrieval System (TCMLARS), and the Chinese Biological Database (CBM) were searched for the original review, we did not search these databases for the 2010 review update.

Selection criteria—We planned to include randomized and quasi-randomized clinical trials in which one arm of the study involved acupuncture treatment.

Data collection and analysis—Two authors independently evaluated the search results against the inclusion and exclusion criteria. Discrepancies were resolved by discussion.

Main results—We found no randomized clinical trials and subsequently no meta-analysis was conducted. Evidence was limited to a few case series of small sample size.

Authors' conclusions—At this time, it is impossible to draw reliable conclusions from the available data to support the use of acupuncture for the treatment of glaucoma. Since most glaucoma patients currently cared for by ophthalmologists do not use non-traditional therapy, the clinical practice decisions will have to be based on physician judgement and patients' value given this lack of data in the literature.

Background

Introduction

Glaucoma is a multifactorial optic neuropathy in which there is an acquired loss of retinal ganglion cells at levels beyond normal age-related baseline loss and corresponding atrophy of the optic nerve (AAO 2000). Although asymptomatic in its earlier stages, the disease is nevertheless one of the leading global causes of irreversible blindness (Tsai 2005).

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

Epidemiology

It is estimated that more than two million people in the United States currently have glaucoma, of whom 80,000 are legally blind as a result of the disease (Friedman 2004; Lee 2005; Martin 1985). Based on a review of published data with the use of prevalence models combined with United Nation population projections, it is estimated that by 2010, 60.5 million people will be affected by glaucoma, and bilateral blindness will be present in 4.5 million people with open-angle glaucoma (OAG) and 3.9 million people with angle-closure glaucoma (Quigley 2006).

The prevalence of glaucoma is higher in some subsets of the population such as the elderly, persons of African descent, and people with diabetes, hypertension, or myopia (Lee 2005). Persons of African descent in the United States were four to five times more likely to develop OAG than were white people. The prevalence of OAG among individuals of African descent ranges from 1.23% in people aged 10 to 49 years old to 11.26% in those 80 years of age or

older. The incidence of OAG for all ages is 1.1 per 100,000 per year among white populations and 3.9 per 100,000 per year among black populations (Lee 2005; Quigley 1997).

Description of the condition

Primary open-angle glaucoma (POAG) is by far the most common type of glaucoma (Friedman 2004). It is usually insidious in onset, slowly progressive and painless. It is generally bilateral and often asymmetrical. Because the central vision is relatively unaffected until late in the disease, visual loss generally progresses without symptoms.

Diagnosis of POAG is based on the evidence of optic nerve damage presented as a structural abnormality of the optic disc or retinal nerve fiber layer or 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 glaucoma patients have an increase of intraocular pressure (IOP) upon repeated measurement, some may have an IOP that is within the average range (AAO 1996).

Primary angle-closure glaucoma is appositional or synechial closure of the anterior chamber angle mainly caused by relative papillary block in the absence of other causes of angle-closure. The relative pressure gradient between the posterior and anterior chambers causes a forward bowing of the peripheral iris such that the iris occludes the filtering portion of the trabecular meshwork leading to elevation of IOP. However, not all primary angle-closures occur this way. A small percentage of patients have angle-closure from the plateau iris mechanism where anteriorly positioned ciliary processes place the peripheral iris in contact with the trabecular meshwork. Another cause is a prominent last iris roll or iris crowding mechanism, with the last roll of iris becomes thicker with dilation and the iris comes in contact with the trabecular meshwork and blocks aqueous outflow (He 2006).

Patients may present with elevation of IOP acutely, when the entire circumference of the anterior chamber angle is obstructed suddenly, or intermittently, when the closure of the angle is self-limited and resolved spontaneously. Intermittent closure of the anterior chamber angle may lead to chronic angle-closure (AAO 1996).

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

Description of the intervention

Treatment options—Currently, treatments of glaucoma are directed at lowering IOP by a predetermined level (usually 20% or more) because IOP is the known risk factor that can be treated and has a beneficial effect at reducing progression of visual field loss (AGIS 2000; CNTGSG 1998; Gordon 2002; Heijl 2002).

Pharmacologic therapy—Conventional treatment of glaucoma usually begins with use of topical antiglaucoma medications. The first-line medical treatment has been either a topical beta-blocker that reduces the IOP by decreasing aqueous humor formation or a topical prostaglandin analog that increases the uveoscleral outflow of aqueous (Lee 2005; Marquis 2005; van der Valk 2005). They are used as an initial treatment because they have relatively few ocular adverse effects, generally are more effective, can be used once or twice daily, and do not affect pupil size or accommodation. The second-line drugs of choice include alpha-agonists and topical carbonic anhydrase inhibitors (Lee 2005). These

medications may cause ocular irritation, generally are less effective than the first-line drugs, and require to be used twice or three times daily. Parasympathomimetic (miotic) agents, most commonly pilocarpine, are considered third-line treatment options (Lee 2005). These agents affect pupil size or accommodation, are used two to four times daily, and reserved for those patients who do not respond to other topical antiglaucoma medications. Medical interventions for POAG are the subject of a published Cochrane systematic review (Vass 2007).

Laser therapy—An alternative or additive treatment to the use of medications is laser trabeculoplasty. This lowers IOP by using laser energy to mechanically or biologically stimulate the trabecular meshwork to reduce its resistance to the outflow of aqueous humor (Lee 2005). The degree of trabecular pigmentation may correlate with better success and the treatment effect in lowering IOP can diminish with time. A Cochrane review on laser trabeculoplasty for OAG has been published (Rolim de Moura 2007)

Incisional surgery—If the patient's IOP cannot be reduced with medications, incisional surgery should be considered (Lee 2005). Filtering surgery reduces the IOP by creating a new channel that improves the outflow of the aqueous humor. The most common type of surgical procedure used to lower the IOP is trabeculectomy. The opening is created in the anterior chamber angle by an extraocular approach and allows the aqueous humor to flow from the anterior chamber into a space beneath the conjunctiva under the surface of the eye. It is currently the standard operation in OAG. The most common problem associated with this surgery is the growth of scar tissue, which causes an obstruction in this artificial channel and blocks the aqueous humor drainage. The IOP lowering effect may decrease gradually with time. Other vision-threatening complications include but are not limited to over-filtration, hypotony, bleeding and infection.

In addition to trabeculectomy, non-penetrating surgical procedures such as viscocanalostomy and deep sclerectomy have been developed. These avoid full-thickness penetration into the anterior chamber of the eye. Fewer complications have been reported but the effectiveness at lowering IOP may have been limited compared with trabeculectomy (Netland 2001). A Cochrane systematic review comparing medical and surgical interventions for glaucoma has been published (Burr 2004).

Glaucoma drainage devices—Tube and plate drainage devices have been developed aiming to maintain drainage of aqueous humor in spite of subconjunctival scarring (Burr 2004; Lim 1998). Surgery using glaucoma drainage devices is usually reserved for situations where trabeculectomy is unlikely to succeed and is not generally accepted as an alternative to standard filtration surgery. A Cochrane systematic review of these devices has been published (Minckler 2006).

Other procedures—Alternative microsurgical procedures on the trabecular meshwork (trabecular aspiration, gonioscurectomy, 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 2004).

Although there are many treatments, glaucoma is a chronic condition for which there is no cure. 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 which has been used for more than 2000 years in the treatment of various illnesses. In traditional Chinese medicine, the body is seen as a delicate balance of two opposing and inseparable forces: yin

and yang. Yin represents the cold, slow, or passive principle, while yang represents the hot, excited, or active principle. An imbalance of these two opposing forces is associated with blockage in the flow of Chi (vital force or energy) and 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. The points are stimulated typically by inserting needles, however, related techniques such as manual (acupressure), electrical or laser stimulation of acupuncture points are also often included under this term (Rhee 2002).

The exact mechanism or physiologic process of the effects of acupuncture is far from clearly delineated. Research efforts have been focused on explaining how acupuncture works within the framework of the Western system on medicine. Different mechanisms of action have been proposed (Cho 2006; Moffet 2006). The dominant mechanism cited by studies on acupuncture is that acupuncture stimulates the release of neurochemicals (usually endogenous opioids or serotonin). “Gate theory” or segmental effects is another proposed mechanism specifically for analgesia. In the “gate theory”, sensory input from acupuncture is thought to block or interfere with nociceptive pain signals at the spinal level. In addition, a number of studies also report the possibility of involuntary body functions being regulated by the autonomic nervous system; examples of such functions include heart rate, blood pressure, post-menopausal vasomotor symptoms, and respiration. By incorporating the results from studies on different body systems affected by acupuncture, a model termed the broad sense hypothalamus-pituitary-adrenal (BS-HPA) axis was proposed recently. The model hypothesizes that the central nervous system is essential for processing the effect of acupuncture by modulating of the autonomic nervous system, neuroimmune system and hormonal regulation. It seems likely that different mechanisms proposed so far are part of an elaborated interaction of difference systems of the body.

Ocular effects associated with acupuncture have been studied in animal models and small samples of subjects. Some studies report potentially beneficial effects of IOP reduction, improvement of central visual acuity, increase of ocular blood flow, preservation of normal waveform characteristics of multifocal electroretinogram (mfERG), alteration of visual function tested by visual evoked potential (VEP), and increase of 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 US population in 1998 indicated that the prevalence use of acupuncture among people reporting use of complementary medicine for glaucoma was 1.8% (1/54) (Rhee 2001; Rhee 2002). A comprehensive collection and summary of currently available clinical trials will provide best evidence to determine whether acupuncture is effective in treating glaucoma.

Objectives

The objective of this review was 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 planned to include all relevant randomized controlled trials and quasi-randomized controlled trials in this review.

Types of participants—We planned to include trials enrolling participants of any age and sex with any type of glaucoma, and as diagnosed in the included studies.

Types of interventions—Acupuncture was defined as the stimulation of acupuncture points by any methods, including needle insertion, acupressure, surface electrical and laser stimulation. We planned to include studies that compared acupuncture therapy with other treatments, no treatment, or placebo for treating any type of glaucoma. We also planned to include studies that compared different types of acupuncture therapy, as well as studies in which acupuncture in combination with another treatment was compared with the other treatment alone.

Types of outcome measures

Primary outcomes: The primary outcome for this review was change in visual field comparing the follow up visual field with the baseline visual field as measured by any methods defined in the methodology of the included trial.

Secondary outcomes: Secondary outcomes for this review were:

1. reduction of intraocular pressure;
2. change in visual acuity;
3. progression of optic disc damage or nerve fiber layer loss.

The timing of the outcome assessment was:

1. short term: outcomes up to one year;
2. long term: more than one year.

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

1. pain and bleeding due to the placement of the acupuncture needle;
2. reduction in visual acuity;
3. cataract formation;
4. infections;
5. punctured organs;
6. 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 any validated measures that were presented.

Economic data: We planned to document reported cost-benefit analyses and other data on economic outcomes in the reported studies.

Follow up: There was no restriction based on length of follow up.

Search methods for identification of studies

Electronic searches—We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (which contains the Cochrane Eyes and Vision Group Trials Register) (*The Cochrane Library* 2010, Issue 3), MEDLINE (January 1950 to March 2010), EMBASE (January 1980 to March 2010), Latin American and Caribbean Literature on Health Sciences (LILACS) (January 1982 to March 2010), ZETOC (January 1993 to March 2010), Allied and Complementary Medicine Database (AMED) (January 1985 to March 2010), the *meta*Register of Controlled Trials (*m*RCT) (www.controlled-trials.com), ClinicalTrials.gov (www.clinicaltrials.gov) and the National Center for Complementary and Alternative Medicine web site (NCCAM) (<http://nccam.nih.gov>). There were no language or date restrictions in the search for trials. The electronic databases were last searched on 23 March 2010 with the exception of NCCAM which was last searched on 14 July 2010.

See: Appendices for details of search strategies for CENTRAL (Appendix 1), MEDLINE (Appendix 2), EMBASE (Appendix 3), LILACS (Appendix 4), ZETOC (Appendix 5), AMED (Appendix 6), *m*RCT (Appendix 7), ClinicalTrials.gov (Appendix 8) and NCCAM (Appendix 9).

Although the Cumulative Index to Nursing and Allied Health Literature (CINAHL), the Chinese Acupuncture Trials Register, the Traditional Chinese Medical Literature Analysis and Retrieval System (TCMLARS), and the Chinese Biological Database (CBM) were searched for the original review, we did not search these databases for the 2010 review update.

Searching other resources—We planned to search the reference lists of the studies included. We planned to use the Science Citation Index to search for references that cited the included studies. We planned to contact the primary investigators of identified trials for details of any additional 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.

Data collection and analysis

Selection of studies—Two authors independently assessed the titles and abstracts resulting from the searches. Each report was labeled as definitely exclude, unclear or definitely include. We obtained full copies of all potentially or definitely related articles. Discrepancies were discussed between the two authors. We documented the excluded studies and reasons for exclusion (see ‘Characteristics of excluded studies’).

Since no trials were found, we did not perform quality assessment, data collection, data synthesis and sensitivity analysis. However, the following methods will be adopted for future updates of this review.

Data extraction and management—Two authors will independently extract the data for the primary and secondary outcomes onto paper data collection forms developed by the Cochrane Eyes and Vision Group. Discrepancies will be resolved by discussion. Authors of included studies will be contacted for missing data. One author will enter all data into Review Manager (RevMan 5). The second author will independently check the data entered.

Assessment of risk of bias in included studies—Two authors will independently assess the included studies for the following sources of systematic bias using forms that will be developed for this purpose. The forms will be developed according to guidelines in Chapter 8 of the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2008).

We will consider four parameters of quality:

1. Selection Bias: Were the participants selected to different treatment groups in an unbiased fashion? For randomized studies, we will assess the method of allocation and allocation concealment. Allocation concealment will be graded as yes (low risk of bias), no (high risk of bias) and unclear. We will contact authors to clarify details of any trials assessed as unclear. If the authors do not respond within a reasonable time period we will grade the trial based on available information. Approaches to allocation concealment that should be considered adequate include: centralized (e.g. allocation by a central office unaware of participant characteristics) or pharmacy-controlled randomization; pre-numbered or coded identical containers which are administered serially to participants; on-site computer system combined with allocations kept in a locked unreadable computer file that can be accessed only after the characteristics of an enrolled participant have been entered; sequentially numbered, sealed, opaque envelopes. Other approaches may include approaches similar to ones listed above, along with reassurance that the person who generated the allocation scheme did not administer it. Some schemes may be innovative and not fit any of the approaches above, but still provide adequate concealment (Higgins 2008).

Approaches to allocation concealment that should be considered clearly inadequate include: alternation; the use of case record numbers, dates of birth or day of the week, and any procedure that is entirely transparent before allocation, such as an open list of random numbers (Higgins 2008).

When studies do not report any concealment approach, adequacy should be considered unclear. Examples include merely stating that a list or table was used; only specifying that sealed envelopes were used and reporting an apparently adequate concealment scheme in combination with other information that leads the author to be suspicious (Higgins 2008).

2. Performance Bias: Performance bias refers to systematic differences in the care provided to the participants in the comparison groups other than the intervention under investigation (Higgins 2008). We will examine masking of outcome assessment in which persons responsible for assessing outcomes were unaware of the assigned intervention. Masking of participants and care providers is not feasible in these trials and hence not used as a measure of quality.

3. Attrition bias: Attrition bias refers to systematic differences between the comparison groups in the loss of participants from the study (Higgins 2008). We will assess the follow-up times and losses to follow up in each group. We will also examine reasons for losses to follow up (for example, withdrawals, dropouts, protocol deviations) and how losses of participants are handled. Randomized studies will also be assessed for analysis on an intention-to-treat basis; whether participants were analyzed in the group to which they were randomized.

4. Detection bias: Detection bias refers to systematic differences between the comparison groups in outcome assessment. We will examine masking of outcome assessment, standardization, pre-specification of methods used to assess the outcome and adherence to pre-specified measurement protocol for the outcomes to identify any detection bias.

Data synthesis—Data analysis will follow the guidelines in Chapter 9 of the Cochrane Handbook for Systematic Reviews of Interventions (Deeks 2008). For dichotomous outcomes we will calculate a summary risk ratio. For continuous outcomes we will calculate the mean difference. Before combining the data we will assess heterogeneity by examining the characteristics of each study. We will use the forest plots of results of the studies, the results of the Chi² test for statistical heterogeneity and the value of I² which estimates the amount of heterogeneity between trials. If no substantial (I² value more than 50%) statistical heterogeneity is detected and if there is no clinical heterogeneity within the trials we will combine the results in a meta-analysis using a random-effects model. A fixed-effects model will be used if the number of trials is three or less. If substantial statistical or clinical heterogeneity is present we will not combine study results but will present them in a tabulated summary.

Sensitivity analysis—We will conduct sensitivity analyses to determine the impact of exclusion of studies with lower methodological quality, unpublished data, and industry-funded studies.

Results

Description of studies

Results of the search—The initial electronic searches revealed 25 distinct titles and abstracts of which two appeared to be relevant and underwent review of the full articles. Thirteen reports were identified through manual searching, none of which met the inclusion criteria. An updated search was done in July 2007 which yielded a further three abstracts. The Trials Search Co-ordinator scanned the search results but none were relevant to the scope of the review. The updated search in March 2010 yielded 15 abstracts and two clinical trials. None were relevant to the scope of the review.

Risk of bias in included studies

We did not assess methodological quality as no randomized controlled trials were included.

Effects of interventions

In the existing literature the term acupuncture embraces a variety of stimulation techniques including different types of acupuncture needles used, electric or laser stimulation with or without needle acupuncture, application of moxibustion with acupuncture, and acupressure without needling. In addition, different acupuncture points or groups of points, different intensity, duration, and frequency or repetition rate of stimulation were studied under the same category of acupuncture. These clinical heterogeneity made comparisons or analyses on studies on acupuncture almost impossible.

We did not conduct a meta-analysis for this review since we did not find any randomized or quasi-randomized clinical trials and data from a few case series of small sample size were not adequate. We felt it is inappropriate to summarize the results from these case series too because the search strategy employed was not designed for identifying non-randomized studies. In addition, the methodological limitations, including the non-standardized acupuncture practice procedure, the heterogeneity in outcome assessment, the small scale and short follow-up nature of all studies, and the lack of adjustment for potential confounders, make it impossible to quantify the magnitude of the effect.

Discussion

Acupuncture originated in China more than 2,000 years ago, making it 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 other Western countries. It was estimated that 8.2 million U.S. adults had used acupuncture, and that 2.1 million had used it in the previous year according to the 2002 National Health Interview Survey (Barnes 2002).

Following this trend, some glaucoma patients may seek acupuncture as a supplement or an alternative to their traditional glaucoma management. The limited information from a few case series highlights the gap in the existing evidence. At this point, the effectiveness of acupuncture as a therapeutic modality for glaucoma could not be established. The lack of evidence from this topic could be related to publication bias, but it could also reflect a lack of investigation.

Authors' conclusions

Implications for practice

At this time, it is impossible to draw reliable conclusions from the available data to support the use of acupuncture for the treatment of glaucoma. Since most glaucoma patients currently cared for by ophthalmologists do not use non-traditional therapy, the clinical practice decisions will have to be based on physician judgement and patients' value given this lack of data in the literature.

Implications for research

Because of ethics considerations, randomized clinical trials comparing acupuncture alone with standard glaucoma treatment or placebo are unlikely to be justified in the near future in countries where 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 will be of interest. It would be valuable for researchers and clinicians who are experience in acupuncture to agree on certain basic standards in administration of acupuncture in clinical trials. Adequate data on intraocular pressure, central visual acuity, contrast sensitivity, visual field changes, optic nerve and retinal nerve fiber layer analysis, ocular blood flow, pattern electroretinography (PERG), multifocal ERG, visual evoked potential (VEP), multifocal visual evoked potential (mfVEP), potential harms, visual-related quality of life and economic outcomes will help in evaluating effectiveness and safety of acupuncture appropriately. When these trials are not available, a systematic review of well-designed observational studies may be considered.

Acknowledgments

We thank the CEVG Trials Search Co-ordinators for devising and running the electronic searches. We thank Dr. Yuanbo Liang and his colleagues for conducting manual searches. We thank Anupa Shah, Managing Editor for CEVG for her assistance and Doug Rhee, Swaroop Vedula, Catey Bunce, Zbys Fedorowicz and Suzanne Brodney-Folse for their comments on the protocol of this review. We thank the external peer reviewer and Roberta Scherer for their comments on the review.

Appendices

1 CENTRAL search strategy

#1 MeSH descriptor Glaucoma

#2 MeSH descriptor Ocular Hypertension

- #3 MeSH descriptor Intraocular Pressure
- #4 (pressure near ocular) and (increas* or elevat* or high*)
- #5 glaucoma*
- #6 MeSH descriptor Acupuncture
- #7 acupuncture therapy
- #8 acupuncture or acupressure
- #9 (electro next stimulat*) or (electro next acupuncture)
- #10 (#1 OR #2 OR #3 OR #4 OR #5)
- #11 (#6 OR #7 OR #8 OR #9)
- #12 (#10 AND #11)

2 MEDLINE (OVID) search strategy

1. randomized controlled trial.pt.
2. (randomized or randomised).ab,ti.
3. dt.fs.
4. randomly.ab,ti.
5. trial.ab,ti.
6. groups.ab,ti.
7. or/1-7 1155275
8. exp animals/
9. exp humans/
10. 9 not (9 and 10)
11. 8 not 11 999260
12. exp glaucoma/
13. exp ocular hypertension/
14. exp intraocular pressure/
15. ((increas\$ or elevat\$ or high\$) adj3 ocular adj3 pressure).tw.
16. glaucoma\$.tw.
17. or/13-17
18. exp acupuncture/
19. exp acupuncture therapy/
20. (acupuncture or acupressure).tw.
21. (((electro adj1 stimulat\$) or electro) adj1 acupuncture).tw.
22. or/19-22
23. 18 and 23]
24. 12 and 24

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

3 EMBASE (OVID) search strategy

1. exp randomized controlled trial/
2. exp randomization/
3. exp double blind procedure/
4. exp single blind procedure/
5. random\$.tw.
6. or/1-5
7. (animal or animal experiment).sh.
8. human.sh.
9. 7 and 8
10. 7 not 9
11. 6 not 10
12. exp clinical trial/
13. (clin\$ adj3 trial\$).tw.
14. ((singl\$ or doubl\$ or trebl\$ or tripl\$) adj3 (blind\$ or mask\$)).tw.
15. exp placebo/
16. placebo\$.tw.
17. random\$.tw.
18. exp experimental design/
19. exp crossover procedure/
20. exp control group/
21. exp latin square design/
22. or/12-21
23. 22 not 10
24. 23 not 11
25. exp comparative study/
26. exp evaluation/
27. exp prospective study/
28. (control\$ or prospectiv\$ or volunteer\$).tw.
29. or/25-28
30. 29 not 10
31. 30 not (11 or 23)
32. 11 or 24 or 31

33. exp glaucoma/
34. exp intraocular hypertension/
35. exp intraocular pressure/
36. ((increas\$ or elevat\$ or high\$) adj3 ocular adj3 pressure).tw.
37. glaucoma\$.tw.
38. or/33-37
39. exp acupuncture/
40. (acupuncture or acupressure).tw.
41. (((electro adj1 stimulat\$) or electro) adj1 acupuncture).tw.
42. or/39-41
43. 38 and 42
44. 32 and 43

4 LILACS search strategy

acupuncture and glaucoma

5 ZETOC search strategy

acupuncture and glaucoma

6 AMED search strategy

1. glaucoma/
2. ocular hypertension/
3. ((increas\$ or elevat\$ or high\$) adj3 ocular adj3 pressure).tw.
4. glaucoma\$.tw.
5. or/1-4
6. acupuncture/
7. exp Traditional medicine chinese/
8. (acupuncture or acupressure).tw.
9. (((electro adj1 stimulat\$) or electro) adj1 acupuncture).tw.
10. or/6-9

7 metaRegister of Controlled Trials search strategy

acupuncture and glaucoma

8 ClinicalTrials.gov search strategy

acupuncture AND glaucoma

9 National Center for Complementary and Alternative Medicine website search strategy

acupuncture and glaucoma

References to studies

Included studies

Excluded studies

Kumar BS, Nesterov AP. The effect of noninvasive electrostimulation of the optic nerve and retina on visual functions in patients with primary open-angle glaucoma. *Vestnik Oftalmologii*. 1994; 110(2): 5–7. [PubMed: 8073582]

Nesterov AP, Khadikova EV. Effect of ciliary muscle electrical stimulation on ocular hydrodynamics and visual function in patients with glaucoma. *Vestnik Oftalmologii*. 1997; 113(4):12–4. [PubMed: 9381633] Studies awaiting classification Ongoing studies

Other references

Additional references

American Academy of Ophthalmology (AAO). Preferred Practice Pattern. American Academy of Ophthalmology (AAO); San Francisco (CA): 1996. Primary open-angle glaucoma.

American Academy of Ophthalmology (AAO). Preferred Practice Pattern. American Academy of Ophthalmology (AAO); San Francisco (CA): 2000. Primary open-angle glaucoma.

The AGIS Investigators. The advanced glaucoma intervention study (AGIS): 7. The relationship between control of intraocular pressure and visual field deterioration. *American Journal of Ophthalmology*. 2000; 130(4):429–40. [PubMed: 11024415]

Barnes PM, Powell-Griner E, McFann K, Nahin RL. Complementary and alternative medicine use among adults: United States, 2002. *CDC Advance Data Report #343*. 2004

Burr J, Azuara-Blanco A, Avenell A. Medical versus surgical interventions for open-angle glaucoma. *Cochrane Database of Systematic Reviews*. 2004; (Issue 2) Art. No.: CD004399 DOI: 10.1002/14651858.CD004399.pub2.

Chan HH, Leung MC, So KF. Electroacupuncture provides a new approach to neuroprotection in rats with induced glaucoma. *Journal of Alternative and Complementary Medicine*. 2005; 11(2):315–22.

Cho ZH, Hwang SC, Wong EK, Son YD, Kang CK, Park TS, et al. Neural substrates, experimental evidences and functional hypothesis of acupuncture mechanisms. *Acta Neurologica Scandinavica*. 2006; 113(6):370–7. [PubMed: 16674603]

Chu TC, Potter DE. Ocular hypotension induced by electroacupuncture. *Journal of Ocular Pharmacology and Therapeutics*. 2002; 18(4):293–305. [PubMed: 12222760]

Collaborative Normal-Tension Glaucoma Study Group. Comparison of glaucomatous progression between untreated patients with normal-tension glaucoma and patients with therapeutically reduced intraocular pressures. *American Journal of Ophthalmology*. 1998; 126(4):487–98. [PubMed: 9780093]

Deeks, JJ.; Higgins, JPT.; Altman, DG.; Higgins, JPT.; Green, S., editors. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.0.1*. The Cochrane Collaboration; 2008. Chapter 9: Analysing data and undertaking meta-analyses. Available from www.cochrane-handbook.org. [updated September 2008]

Friedman DS, Wolfs RC, O'Colmain BJ, Klein BE, Taylor HR, West S, et al. Prevalence of open-angle glaucoma among adults in the United States. *Archives of Ophthalmology*. 2004; 122(4): 532–8. [PubMed: 15078671]

Glanville JM, Lefebvre C, Miles JN, Camosso-Stefinovic J. How to identify randomized controlled trials in MEDLINE: ten years on. *Journal of the Medical Library Association*. 2006; 94(2):130–6. [PubMed: 16636704]

- Gordon MO, Beiser JA, Brandt JD, Heuer DK, Higginbotham EJ, Johnson CA, et al. The Ocular Hypertension Treatment Study: baseline factors that predict the onset of primary open-angle glaucoma. *Archives of Ophthalmology*. 2002; 120(6):714–20. [PubMed: 12049575]
- He M, Foster PJ, Johnson GJ, Khaw PT. Angle-closure glaucoma in East Asian and European people. Different diseases? *Eye*. 2006; 20(1):3–12.
- Heijl A, Leske MC, Bengtsson B, Hyman L, Bengtsson B, Hussein M. Reduction of intraocular pressure and glaucoma progression: results from the Early Manifest Glaucoma Trial. *Archives of Ophthalmology*. 2002; 120(10):1268–79. [PubMed: 12365904]
- Higgins, JPT.; Altman, DG.; Higgins, JPT.; Green, S., editors. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.0.1*. The Cochrane Collaboration; 2008. Chapter 8: Assessing risk of bias in included studies. Available from www.cochrane-handbook.org [updated September 2008]
- Lee OA, Higginbotham EJ. Glaucoma and its treatment: A review. *American Journal of Health System Pharmacy*. 2005; 62(7):691–9. [PubMed: 15790795]
- Lim KS, Allan BD, Lloyd AW, Muir A, Khaw PT. Glaucoma drainage devices; past, present, and future. *British Journal of Ophthalmology*. 1998; 82(9):1083–9. [PubMed: 9893602]
- Marquis RE, Whitson JT. Management of glaucoma: focus on pharmacological therapy. *Drugs Aging*. 2005; 22(1):1–21. [PubMed: 15663346]
- Martin MJ, Sommer A, Gold EB, Diamond EL. Race and primary open-angle glaucoma. *American Journal of Ophthalmology*. 1985; 99(4):383–7. [PubMed: 3985075]
- Minckler DS, Vedula SS, Li TJ, Mathew MC, Ayyala RS, Francis BA. Aqueous shunts for glaucoma. *Cochrane Database of Systematic Reviews*. 2006; (Issue 2) Art. No.: CD004918. DOI: 10.1002/14651858.CD004918.pub2.
- Moffet HH. How might acupuncture work? A systematic review of physiologic rationales from clinical trials. *BMC Complementary and Alternative Medicine*. 2006; 6:25. [PubMed: 16824230]
- Naruse S, Mori K, Kurihara M, Nakajima N, Matsumoto Y, Kinoshita S, et al. Chorioretinal blood flow changes following acupuncture between thumb and forefinger. *Nippon Ganka Gakkai Zasshi*. 2000; 104(10):717–23. [PubMed: 11081307]
- National Center for Complementary and Alternative Medicine, National Institute of Health. [Access date: July 23, 2007] Acupuncture: How might acupuncture work?. <http://nccam.nih.gov/health/acupuncture/>
- Netland PA. Nonpenetrating glaucoma surgery. *Ophthalmology*. 2001; 108(2):416–21. [PubMed: 11158823]
- Pagani L, Manni L, Aloe L. Effects of electroacupuncture on retinal nerve growth factor and brain-derived neurotrophic factor expression in a rat model of retinitis pigmentosa. *Brain Research*. 2006; 1092(1):198–206. [PubMed: 16696953]
- Quigley HA, Vitale S. Models of open-angle glaucoma prevalence and incidence in the United States. *Investigative Ophthalmology & Visual Science*. 1997; 38(1):83–91.
- Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020. *British Journal of Ophthalmology*. 2006; 90(3):262–7. [PubMed: 16488940]
- Rhee DJ, Katz LJ, Spaeth GL, Myers JS. Complementary and alternative medicine for glaucoma. *Survey of Ophthalmology*. 2001; 46(1):43–55. [PubMed: 11525790]
- Rhee DJ, Spaeth GL, Myers JS, Steinmann WC, Augsburger JJ, Shatz LJ, et al. Prevalence of the use of complementary and alternative medicine for glaucoma. *Ophthalmology*. 2002; 109(3):438–43. [PubMed: 11874744]
- Rolim, de Moura C.; Paranhos, A, Jr. Trabeculectomy for open angle glaucoma. *Cochrane Database of Systematic Reviews*. 2007; (Issue 4) Art. No.: CD003919. DOI: 10.1002/14651858.CD003919.
- Sagara Y, Fuse N, Seimiva M, Yokokura S, Watanabe K, Nakazawa T, et al. Visual function with acupuncture tested by visual evoked potential. *The Tohoku Journal of Experimental Medicine*. 2006; 209(3):235–41. [PubMed: 16778370]
- Tsai JC, Kanner EM. Current and emerging medical therapies for glaucoma. *Expert Opinion on Emerging Drugs*. 2005

- van der Valk R, Webers CA, Schouten JS, Zeegers MP, Hendrikse F, Prins MH. Intraocular pressure-lowering effects of all commonly used glaucoma drugs: a meta-analysis of randomized clinical trials. *Ophthalmology*. 2005; 112(7):1177–85. [PubMed: 15921747]
- Vass C, Hirn C, Sycha T, Findl O, Bauer P, Schmetterer L. Medical interventions for primary open-angle glaucoma and ocular hypertension. *Cochrane Database of Systematic Reviews*. 2007; (Issue 4) Art. No.: CD003167 DOI: 10.1002/14651858.CD003167.pub2.

Plain language summary

Acupuncture as a treatment modality for patients with glaucoma

Glaucoma is a leading cause of blindness worldwide. Although there are many existing treatments, including the use of eye drops, laser treatment, and a variety of surgical procedures, some patients may seek complementary or alternative medicine such as acupuncture to supplement their regular treatment. This review aimed to evaluate available evidence of the effectiveness and safety of acupuncture in treating patients with glaucoma. We did not find any randomized clinical trials on the subject. The limited information from a few case series highlights the gap in the existing evidence. At this point, the effectiveness of acupuncture as a therapeutic modality for glaucoma could not be established.

Differences between protocol and review

Published notes

Characteristics of studies

Characteristics of included studies

Footnotes

Characteristics of excluded studies

Kumar 1994

Reason for exclusion	Non-randomized comparative study; acupuncture as defined in this review was not used.
----------------------	---

Nesterov 1997

Reason for exclusion	Non-randomized comparative study; acupuncture as defined in this review was not used.
----------------------	---

Footnotes

Characteristics of studies awaiting classification

Footnotes

Characteristics of ongoing studies

Footnotes

Summary of findings tables

Additional tables

Other published versions of this review

Classification pending references

Data and analyses

Figures

Sources of support

Internal sources

- No sources of support provided

External sources

- Contract N-01-EY-2-1003, National Eye Institute, National Institutes of Health, USA

Feedback