

Research Article

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A meta-analysis of neuroprotective effect for traditional Chinese medicine (TCM) in the treatment of glaucoma

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Abstract: Background. The aim of this study was to evaluate the neuroprotective effect of surgery combined with traditional Chinese medicine (TCM) in the treatment of glaucoma by meta-analysis based on clinical controlled trial.

Methods. All the prospective randomized controlled trials of surgery combined with TCM in the treatment of glaucoma were searched in the databases of Medline (1960~2015.1), CENTRAL (the Cochrane central register of controlled trials 1989~2015.1, EMBASE (1980~2015.1) and CNKI (1979~2015.1). Two reviewers independently assessed the quality of the included studies, extracted the relevant data and performed a cross-check. The pooled relative risk (RR) or standard mean difference (SMD) of surgery combined with TCM versus western medicine or surgery alone were calculated as the effect size by meta-analysis method. All the data was analyzed by stata11.0 software (<http://www.stata.com>; Stata Corporation, College Station, TX).

Results. Finally, eleven clinical controlled trials with 843 subjects were included in this meta-analysis. The pooled results indicated that the surgery combined with TCM treatment procedure can significantly improve the vision recovery rate compared to control group (RR=1.22, 95% CI:1.06~1.40, P=0.005); And after treatment, the visual field in combined group was significantly improved

compared to control group (SMD=0.26~95% CI:0.09~0.43, P=0.003).

Conclusion. Surgery combined with TCM can improve the vision recovery rate and the visual field in the treatment of glaucoma compared to surgery or western medicine alone.

Keywords: Glaucoma; surgery; traditional Chinese medicine; clinical controlled trial; meta-analysis

1 Introduction

Glaucoma is a term for a group of eye disorders which result in damage to the optic nerve [1]. Most of the damage to the optic nerve is related to elevated intraocular pressure (IOP) [2]. Glaucoma is the most commonly diagnosed eye disease, considered as the leading cause of blindness world-wide [3]. The exact pathogenesis for glaucoma is still not clear. Epidemiological data indicates that glaucoma may be associated with genetic susceptibility, mood swings, fatigue and other factors [4]. The goals of glaucoma management are to avoid nerve damage and preserve visual field and total quality of life for patients with minimal side effects. At present, laser surgery, conventional surgery and medicine are used to treat glaucoma. Recently, several clinical studies reported that clinical efficacy can be improved by surgery combined with traditional Chinese medicine (TCM) in the treatment of glaucoma [5, 6]. However, the effectiveness of the combined treatment varied considerably among the published studies with small sample sizes. Accordingly, we performed a meta-analysis on the basis of published clinical trials in order to identify whether the combined treatment was superior to surgery alone.

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2 Materials and methods

2.1 Studies identification

Clinical controlled trials comparing surgery plus TCM vs. surgery or surgery plus western medicine for the treatment of glaucoma, published before January 2015, were identified through an electronic sensitive search of Medline, the Cochrane central register of controlled trials, EMBSE and CNKI databases. The searching term was glaucoma [MeSH]/glaucoma [text]; Chinese medical[MeSH]/Chinese medical[test]; Chinese medicine [MeSH]/Chinese medicine[test]. And the corresponding free text words were also used as the searching term. The title and abstract of identified studies were firstly evaluated to assess whether it was appropriate to the inclusion criteria or not. Following this, all of the potentially relevant trials were evaluated in full-text paper and all references of included articles were further scanned for additional analysis.

2.2 Inclusion Criteria

The patient inclusion criteria, treatment methods and outcomes for each individual study were extracted and checked by (LC) as described by the Cochrane Handbook formeta-analysis of randomized controlled trials [7]. The inclusion for this meta-analysis was as follows: (1) The patients included in each individual study were diagnosed of glaucoma with no restriction of age and gender. (2) The treatment was surgery+TMC in the experiment group and surgery alone or surgery+western medicine in the control group. (3) The outcomes were vision recovery rate and visual field improvement. The study design was prospective clinical trials without restriction of randomization.

2.3 Data Extraction

All the data for each individual study was extracted by two reviewers independently. If disagreement was found, the third investigator was consulted for consensus. The general information (name of the first author, year of publication, number of patients, treatment methods), for each included study was extracted. The outcome data of vision recovery and visual field were recorded for each individual studies.

2.4 Statistical analysis

STATA/SE 11.0 (Stata Corp LP, <http://www.stata.com>) was used to perform the statistical analysis. Dichotomous data is calculated as the risk ratio (RR) with a95% confidence interval (CI). Measurement data was demonstrated by mean with its standard difference and pooled by standard mean difference (SMD). Statistical heterogeneity of the results across the included studies was evaluated by Chi-square (χ^2) test [8], and the inconsistency was calculated by I2 [9]. If heterogeneity was found (χ^2 , $p < 0.05$ or $I^2 > 50\%$), the random-effect method (Dersimonian-Laird method) was used to pool the data. Otherwise, without significant heterogeneity, fixed-effect method was used. The Egger's tests were performed to evaluate publication bias as described by Egger [10].

3 Results

3.1 General characteristic of included studies

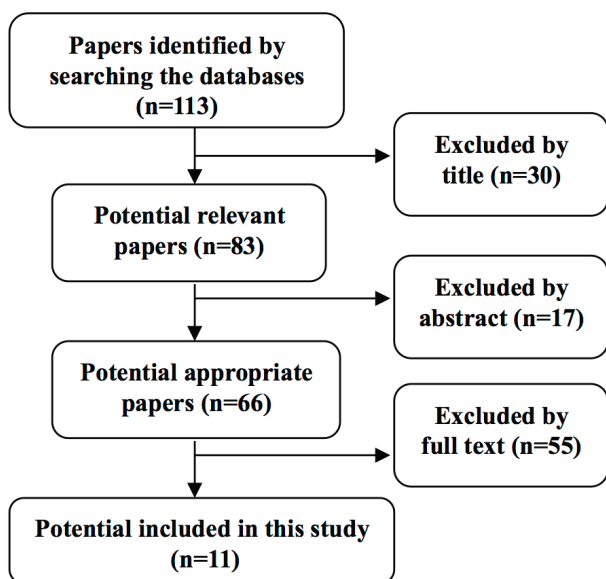
Through searching the electronic databases of Medline (1960~2015.1), CENTRAL (the Cochrane central register of controlled trials 1989~2015.1), EMBASE (1980~2015.1) and CNKI (1979~2015.1), a total of 113 articles were initially identified. Of these, 66 potential applicable studies, published from2004 and 2014, were reviewed in full-text paper. Finally, 11 clinical studies [5, 6, 11-19] with 457 cases in the surgery+TCM and 386 subjects in the control group were included in this meta-analysis (Figure 1). The general information for the included studies was demonstrated in Table 1.

3.2 Heterogeneity assess

Significant heterogeneity was not found in the effect size of RR ($I^2=0.00\%$, $P=0.647$), which indicated the pooled RR was calculated by fixed effect model. For SMD, no statistical heterogeneity existed in this meta-analysis ($I^2=39.6\%$, $P=0.142$) which indicated the SMD was pooled by fixed effect model.

Table 1: The general characteristics of included studies

First author	Year	Surgery+TCM		Surgery		Treatment (month)
		n	Treatment	n	Treatment	
Liu An	2006	33	Surgery+TCM	31	Surgery+medicine	3
Tao Rongsan	2010	40	Surgery+TCM	38	Surgery	3
Lin Xiaodong	2005	30	Surgery+TCM	30	Surgery	3
Wang Yan	2010	53	Surgery+TCM	48	Surgery	3
He Yuhong	2008	29	Surgery+TCM	23	Surgery	4
LiXiang	2010	95	Surgery+TCM	100	Surgery	3
Pang Youhui	2009	82	Surgery+TCM	28	Surgery	3
Li Jinshan	2009	34	Surgery+TCM	28	Surgery	2
Ye Changhua	2003	23	Surgery+TCM	22	Surgery+Placebo	6
Liu Dongjing	2004	18	Surgery+TCM	18	Surgery+Placebo	6
Xiang Minhong	2006	20	Surgery+TCM	20	Surgery+Placebo	6

**Figure 1:** The searching flow chart of this meta-analysis

3.3 Vision recovery

Nine studies reported the vision recovery rate. The pooled results indicated that the surgery combined with traditional Chinese medicine treatment procedure can significantly improve the vision recovery rate compared to control group (RR=1.22, 95% CI:1.06~1.40, $P=0.005$), Figure 2.

3.4 Visual field

Six papers reported the data of visual field improvement. The pooled results indicated that the visual field in

combined group was significantly improved compared to control group (SMD=0.26, 95% CI:0.09~0.43, $P=0.003$), Figure 3.

3.5 Publication bias evaluation

A Begg's funnel plot and Egger's test were used to evaluate the publication bias [13]. For the effect size of RR, the Begg's funnel plot showed a small amount of asymmetry at the bottom (Figure 4). But the Egger's test demonstrated no significant publication bias ($t=0.78, P=0.44$). For effects size of SMD, no significant publication bias was found by Egger's test ($t=1.82, P=0.143$).

4 Discussion

Glaucoma, the leading cause of blindness in the world-wide for people more than forty years old, is generally clinically divided into open-angle glaucoma and closed angle glaucoma. Regardless of open-angle or closed angle glaucoma, the major pathophysiology is that the intraocular pressure was increased, which can finally damage the optic nerve even leading to loss of vision.

In clinical management, the general treatment modality was to avoid or reduce nerve damage, and preserve visual field, with minimal side effects [20, 21]. At present, laser surgery, conventional surgery and medicine are commonly used to treat glaucoma. The effectiveness of these therapies is either limited or associated with significant side effects.

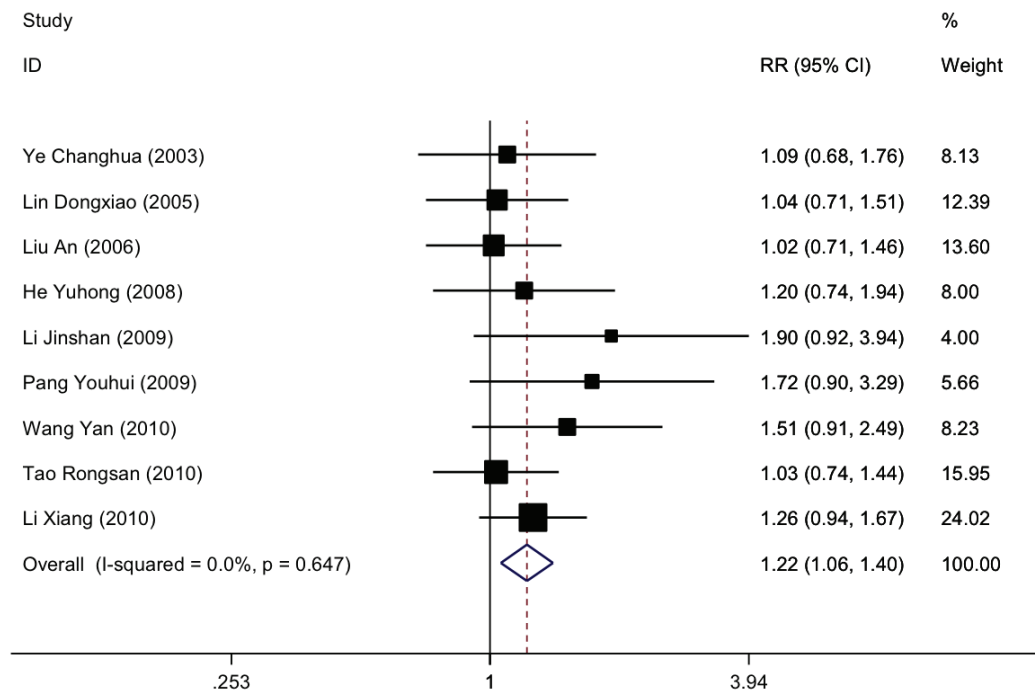


Figure 2: The forest plot of vision recovery treated by surgery+TCM versus surgery or western medicine alone

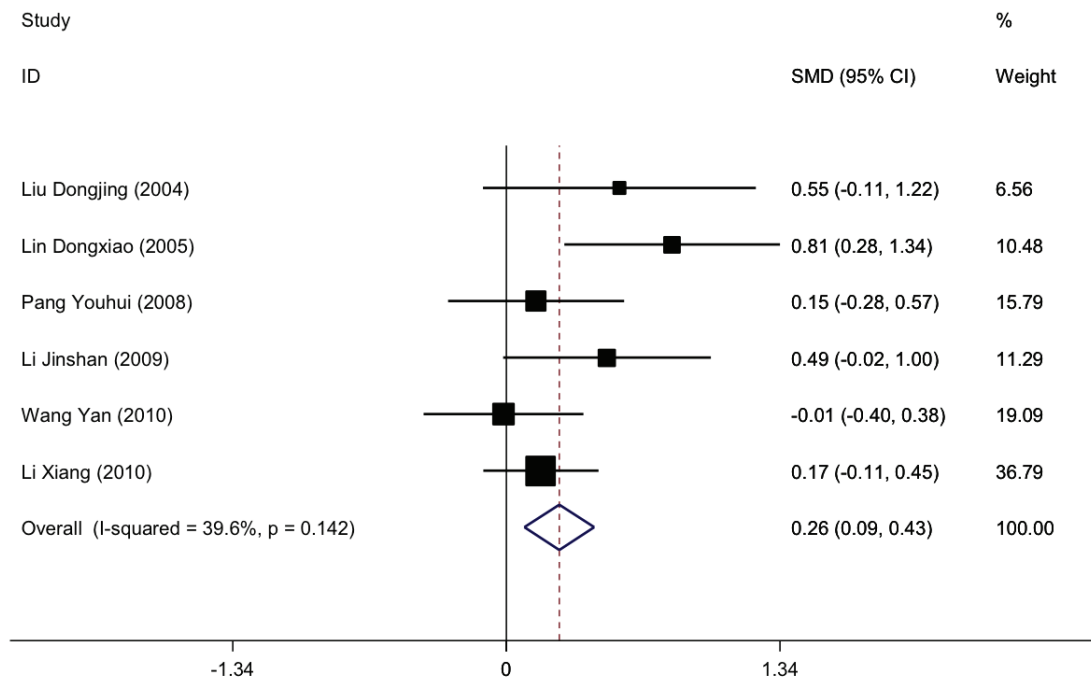


Figure 3: The forest plot of vision field improvement treated by surgery+TCM versus surgery or western medicine alone

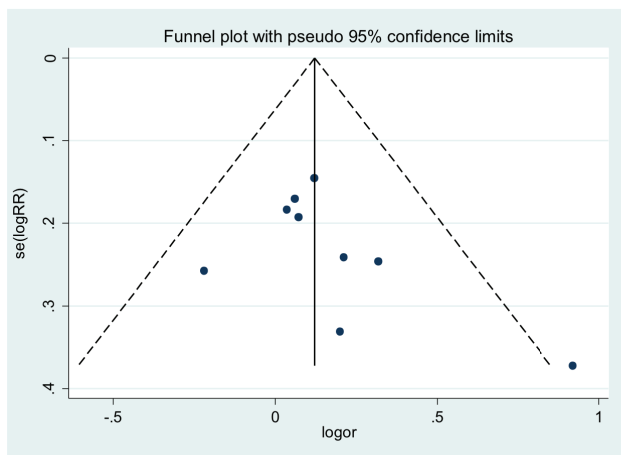


Figure 4: The Begg's funnel plot in evaluation of publication bias for effect size of RR

Traditional Chinese medicine has a unique advantage in the treatment of chronic diseases, such as nervous system diseases. TCM believes that “the wind for glaucoma cataract” stasis caused by water, which caused the disease. The treatment should be based on supplementing Qi and nourishing Yin [22]. Several clinical studies have reported that it was effective for surgery combined with traditional Chinese medicine in the treatment of glaucoma [11-14]. But the effectiveness of the combined treatment ranged a lot among the published studies with small sample size. Thus, we searched all the published clinical studies reporting the neuroprotective effects of surgery combined with traditional Chinese medicine (TCM) in the treatment of glaucoma. We then pooled the data by meta-analysis method. The pooled results showed that surgery combined with traditional Chinese medicine

treatment procedure can significantly improve the vision recovery rate compared to control group (RR=1.33, 95% CI:1.09-1.62, $p=0.005$). This means that the combined treatment modality was superior to surgery alone for vision recovery. Meta-analysis also found that the visual field in combined group was significantly improved compared to control group (SMD=0.26, 95% CI:0.09-0.43, $p=0.003$). Therefore, the combined treatment had more advantages in the aspect of neuroprotective effect for patients with glaucoma.

Although this meta-analysis found that surgery combined with traditional Chinese medicine can improve the vision recovery rate and the visual field in the treatment of glaucoma compared to surgery or western medicine alone, several limitations are found in this study. Firstly, all of the 11 included studies come from China with patient ethnicity “Han”, which could lead to patient selective bias. Secondly, the patient number for each included studies was relative small. Thirdly, the results were pooled by extracted data of the published paper not the individual patient data, which may lead to information bias. Fourth, the treatment period ranged from 2 months to 6 months which can lead to clinical heterogeneity. In view of the above facts, multi-center prospective randomized controlled trials are needed for further evaluation of the neuroprotective effect of surgery combined with traditional Chinese medicine (TCM) in the treatment of glaucoma.

Conflict of interest statement: Authors state no conflict of interest

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