

Review Article

The influence of triamcinolone acetonide on glaucoma surgery: a meta-analysis of randomized controlled trials

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Abstract: Introduction: The impact of triamcinolone acetonide on glaucoma surgery remains controversial. We conducted a systematic review and meta-analysis to explore the influence of triamcinolone acetonide on the success rate of glaucoma surgery. Methods: We searched PubMed, Embase, Web of Science, EBSCO, and the Cochrane library databases through April 2018 for randomized controlled trials (RCTs) assessing the effect of triamcinolone acetonide on glaucoma surgery. Results: Four RCTs involving 230 patients are included in the meta-analysis. Overall, compared with the control group for glaucoma surgery, triamcinolone acetonide can significantly improve the success rate (RR=1.27; 95% CI=1.05 to 1.53; P=0.01) and reduce intraocular pressure in 6 months (MD=-0.62; 95% CI=-1.09 to -0.15; P=0.01) but shows no important impact on intraocular pressure at 1 week (MD=-3.48; 95% CI=-9.43 to 2.48; P=0.25) or 1 month (MD=-3.69; 95% CI=-9.56 to 2.19; P=0.22), antiglaucoma medications at 1 year (MD=-0.46; 95% CI=-0.93 to 0.01; P=0.05), BCVA (MD=-0.11; 95% CI=-0.34 to 0.11; P=0.33), hypotony (RR=1.48; 95% CI=0.72 to 3.07; P=0.29), and choroidal detachment (RR=1.45; 95% CI=0.41 to 5.10; P=0.56). Conclusions: Triamcinolone acetonide is associated with a significantly improved success rate and intraocular pressure control for glaucoma surgery.

Keywords: Triamcinolone acetonide, glaucoma surgery, success rate, randomized controlled trials, meta-analysis

Introduction

The prevention of wound healing is very crucial for the success of glaucoma surgery [1-3]. The process of wound healing involves the replacement and regeneration by collagen lay-down from fibroblasts [4, 5]. The failure of glaucoma-filtering surgery can result in fibroblastic proliferation and cellular inflammation [6-8]. Intraoperative antimetabolites are associated with an increase in the success of glaucoma filtering surgery and the benefits of anti-inflammatory medications in postoperative management [9, 10].

Topical corticosteroid is reported to reduce postoperative intraocular pressure and improve thin, cystic bleb formation after trabeculectomy surgery [11]. Few studies explore the role of intraoperative corticosteroid use during glaucoma surgery [12, 13]. Triamcinolone acetonide is known as a sterile, non-preserved injectable corticosteroid ophthalmic suspension. The use of triamcinolone acetonide in ocular sur-

gery is well established in the form of intravitreal and sub-tenon injections. The intracameral injection of triamcinolone acetonide shows safe and positive results in the pediatric population during cataract surgery, with no significant postoperative intraocular pressure elevation [14-17].

The efficacy of triamcinolone acetonide on glaucoma surgery has not been well established. Recently, several studies on the topic have been published, and the results have been conflicting [13, 18, 19]. With accumulating evidence, we therefore performed a systematic review and meta-analysis of RCTs to investigate the influence of triamcinolone acetonide injection on glaucoma surgery.

Materials and methods

Ethical approval and patient consent are not required because this is a systematic review and meta-analysis of previously published studies. The systematic review and meta-analysis

were conducted and reported in adherence to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) [20].

Search strategy and study selection

Two investigators independently searched the following databases (inception to April 2018): PubMed, Embase, Web of Science, EBSCO, and the Cochrane library databases. The electronic search strategy was conducted using the following keywords: triamcinolone acetonide and glaucoma. We also checked the reference lists of the screened full-text studies to identify other potentially eligible trials.

The inclusive selection criteria were as follows: (i) population: patients with glaucoma surgery; (ii) intervention: triamcinolone acetonide; (iii) comparison: placebo; (iv) study design: RCT.

Data extraction and outcome measures

We extracted the following information: author, number of patients, age, male, intraocular pressure, and detail methods in each group etc. The data were extracted independently by two investigators, and any discrepancies were resolved by consensus. We also contacted the corresponding authors to obtain the data when necessary. No simplifications or assumptions were made.

The primary outcome is the success rate. Secondary outcomes include intraocular pressure at 1 week, 1 month and 6 months, antiglaucoma medications in 1 year, best-corrected visual acuity (BCVA), hypotony, and choroidal detachment. Success was defined as the absence of: intraocular pressure above 21 mm Hg on 2 consecutive measurements or IOP lower than 6 mm Hg and no light perception, glaucoma surgery, or serious complications [18].

Quality assessment in individual studies

The methodological quality of the included studies was independently evaluated using the modified Jadad scale [21]. There are 3 items in the Jadad scale: randomization (0-2 points), blinding (0-2 points), dropouts and withdrawals (0-1 points). The Jadad Scale score varies from 0 to 5 points. An article with a Jadad score ≤ 2 is considered to be of low quality. If the Jadad

score ≥ 3 , the study is thought to be of high quality [22].

Statistical analysis

We estimated the mean difference (MD) with a 95% confidence interval (CI) for continuous outcomes (intraocular pressure at 1 week, 1 month and 6 months, antiglaucoma medications at 1 year, and BCVA) and risk ratios (RRs) with 95% CIs for dichotomous outcomes (success rate, hypotony, and choroidal detachment). Heterogeneity was tested using the Cochran Q statistic ($P < 0.1$) and quantified with the I^2 statistic, which describes the variation of effect size that is attributable to heterogeneity across studies. An I^2 value greater than 50% indicates significant heterogeneity. The value of the I^2 statistic is used to select the appropriate pooling method: fixed-effects models are used for $I^2 < 50\%$ and random-effects models for $I^2 > 50\%$. Whenever significant heterogeneity is present, we search for potential sources of heterogeneity via omitting one study in turn for the meta-analysis or performing a subgroup analysis. Publication bias is not evaluated because of the limited number (< 10) of included studies. All statistical analyses are performed using Review Manager Version 5.3 (The Cochrane Collaboration, Software Update, Oxford, UK).

Results

Literature search, study characteristics and quality assessment

A detailed flowchart of the search and selection results is shown in **Figure 1**. 467 potentially relevant articles were identified initially. Finally, four RCTs that meet our inclusion criteria were included in the meta-analysis [13, 18, 19, 23].

The baseline characteristics of the four eligible RCTs in the meta-analysis are summarized in **Table 1**. The four studies were published between 1994 and 2014, and the sample sizes ranged from 49 to 77, for a total of 230. Among the four studies included here, three studies report a success rate [18, 19, 23], two studies report intraocular pressure at 1 week and 1 month [13, 18], three studies report 6 months [13, 18, 23], two studies report antiglaucoma medications at 1 year [13, 18], two studies report BCVA [13, 23], and two studies report hypotony and choroidal detachment [13, 18].

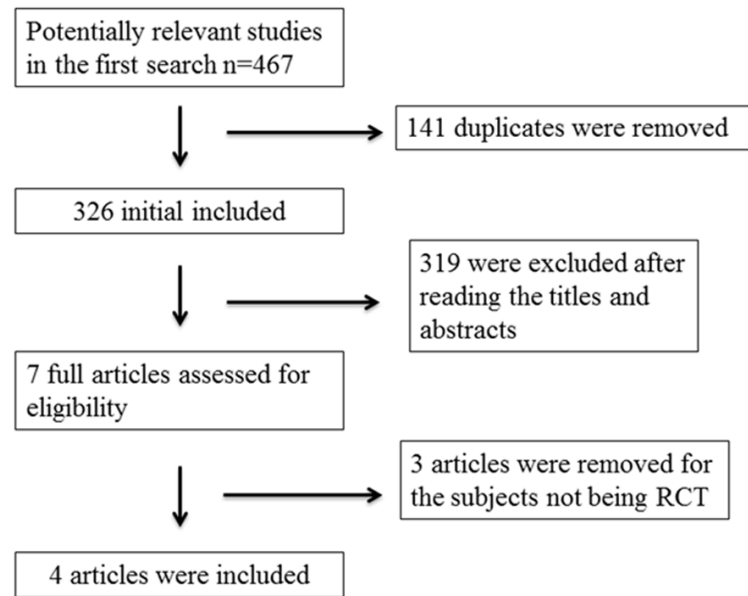


Figure 1. Flow diagram of the study searching and selection process.

The Jadad scores of the four included studies vary from 3 to 5, and all four studies are considered to be high-quality ones according to the quality assessment.

Primary outcome: success rate

This outcome data is analyzed with the fixed-effects model, and the pooled estimate of the three included RCTs suggested that compared to the control group for glaucoma surgery, triamcinolone acetonide can significantly improve the success rate (RR=1.27; 95% CI=1.05 to 1.53; P=0.01), with low heterogeneity among the studies ($I^2=26\%$, heterogeneity P=0.26) (Figure 2).

Sensitivity analysis

Low heterogeneity is observed among the included studies for the primary outcome, so we did not perform a sensitivity analysis by omitting one study in turn to detect the heterogeneity.

Secondary outcomes

Compared to the control group for glaucoma surgery, triamcinolone acetonide shows no substantial influence on intraocular pressure at 1 week (MD=-3.48; 95% CI=-9.43 to 2.48; P=0.25; Figure 3), and 1 month (MD=-3.69; 95% CI=-9.56 to 2.19; P=0.22; Figure 4).

Triamcinolone acetonide is associated with significantly reduced intraocular pressure at 6 months in patients with glaucoma surgery (MD=-0.62; 95% CI=-1.09 to -0.15; P=0.01; Figure 5), but has no important impact on antiglaucoma medications at 1 year (MD=-0.46; 95% CI=-0.93 to 0.01; P=0.05; Figure 6), BCVA (MD=-0.11; 95% CI=-0.34 to 0.11; P=0.33; Figure 7), hypotony (RR=1.48; 95% CI=0.72 to 3.07; P=0.29; Figure 8), and choroidal detachment (RR=1.45; 95% CI=0.41 to 5.10; P=0.56; Figure 9).

Discussion

The success of glaucoma filtering surgery is achieved through the inhibition of wound healing [24]. The initial steps in wound healing are inflammation and coagulation composed of biological events including cellular, hormonal, and growth factor release which finally lead to scar tissue formation [2, 13]. Mitomycin C is widely used to inhibit fibroblast proliferation in trabeculectomy and promote the formation of relatively avascular filtration blebs with less fibrovascular scarring and an increased success rate [25, 26]. Corticosteroids are found to reduce and regulate wound healing and inflammation through the inhibition of macrophage functions, the release of enzymes like collagenase, plasminogen activators, and growth factors, as well as vascular permeability and fibroblast proliferation [25].

Topical corticosteroids are reported to significantly increase the success of trabeculectomy by inhibiting wound healing because of their suppression of inflammation and fibroblast proliferation [11]. Sub-tenon injection of triamcinolone acetonide is widely accepted for treating uveitis, diabetic macular edema, macular edema post-branch, and central retinal vein occlusion [27-29]. Direct injection of triamcinolone acetonide into the sub-tenon area may inhibit wound healing and increase the success rate of glaucoma surgery through high-dose corticosteroid delivery [30]. Our meta-analysis suggests that triamcinolone acetonide injection

Triamcinolone acetonide and glaucoma surgery

Table 1. Characteristics of the included studies

NO.	Author	Triamcinolone acetonide group					Control group					Jada scores
		Number	Age (years)	Male (n)	Intraocular pressure (mm Hg)	Methods	Number	Age (years)	Male (n)	Intraocular pressure (mm Hg)	Methods	
1	Koval 2014	37	68 (47-88), median (range)	17	24.5 (13-40), median (range)	Intracameral triamcinolone acetonide 0.1cc	40	69 (42-88), median (range)	23	23.8 (8.5-56), median (range)	Matched placebo	3
2	Teixeira 2012	22	62.91±7.26	16	-	0.1 mL of triamcinolone acetonide (40 mg/mL) was injected into the vitreous cavity	27	57.48±15.32	15	-	Matched placebo	5
3	Yuki 2009	26	61.8±14.3	22	31.34±4.68	Trabeculectomy with intraoperative sub-tenon injection of triamcinolone acetonide	27	59.1±13.9	19	34.30±10.94	Matched placebo	4
4	Wang 1994	22	30.4±12.56	16	29.96±6.45	Subconjunctival injection of triamcinolone acetonide 12 mg	29	29.0±12.0	22	29.72±6.10	Matched placebo	4

Triamcinolone acetonide and glaucoma surgery

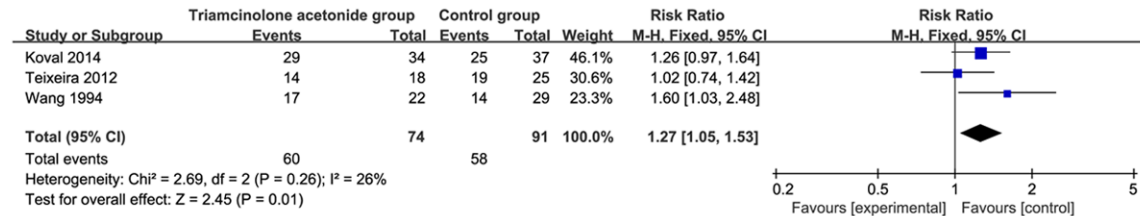


Figure 2. Forest plot for the meta-analysis of the success rate.

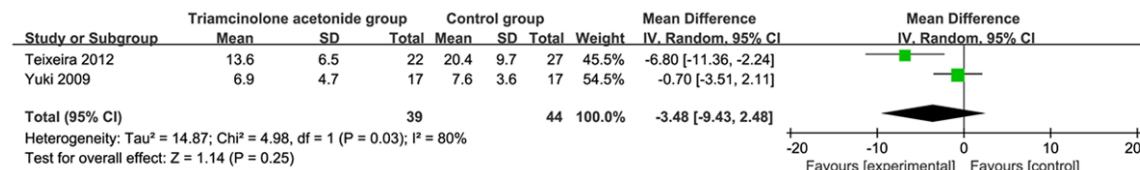


Figure 3. Forest plot for the meta-analysis of intraocular pressure at 1 week (mm Hg).

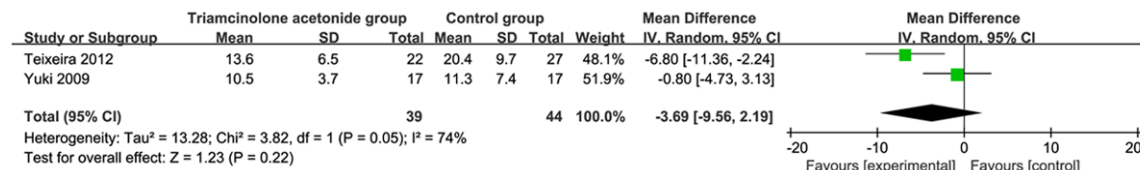


Figure 4. Forest plot for the meta-analysis of intraocular pressure at 1 month (mm Hg).

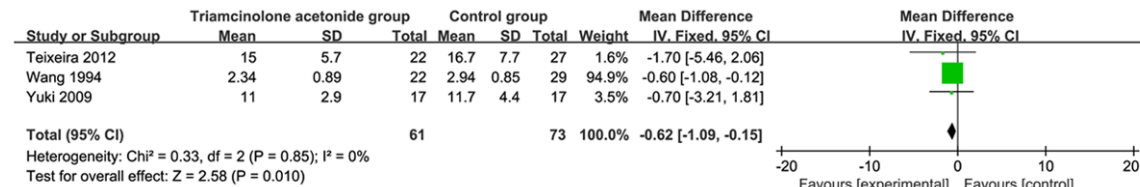


Figure 5. Forest plot for the meta-analysis of intraocular pressure at 6 months (mm Hg).

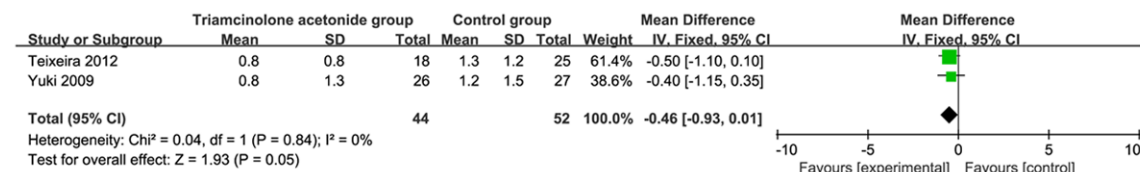


Figure 6. Forest plot for the meta-analysis of antiglaucoma medications at 1 year.

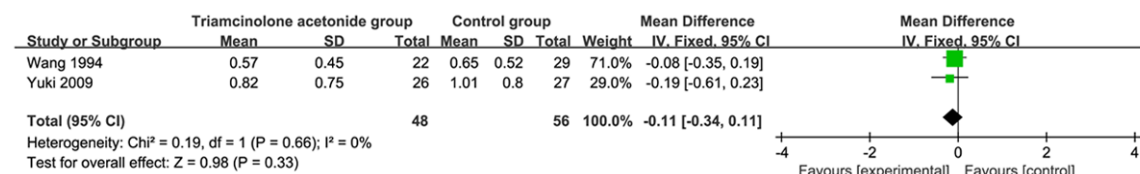


Figure 7. Forest plot for the meta-analysis of best-corrected visual acuity (BCVA).

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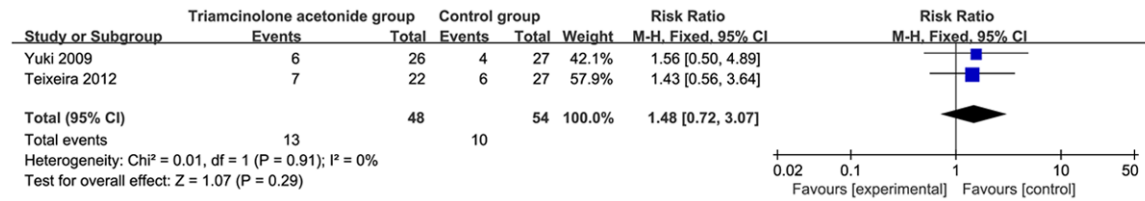


Figure 8. Forest plot for the meta-analysis of hypotony.

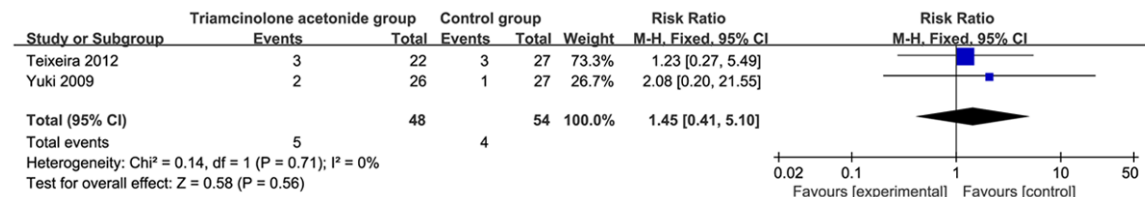


Figure 9. Forest plot for the meta-analysis of choroidal detachment.

tion can substantially improve the success rate in patients with glaucoma surgery.

Good intraocular pressure control is achieved after injecting triamcinolone acetonide (1.2 mg) into filtration blebs at the conclusion of trabeculectomy such as trabeculectomy, phacotrabeculectomy, and needling [12]. Triamcinolone acetonide (4 mg) injection subconjunctivally before a trabeculectomy benefits through diffuse microcystic filtration blebs and the control of intraocular pressure [31]. Better control of intraocular pressure at 3 months is revealed by triamcinolone acetonide injection for glaucoma surgery based on the results of our meta-analysis, but there is no significant influence of intraocular pressure at 1 week and 6 months after triamcinolone acetonide injection and these intraocular pressures in 1 week and 6 months are both at normal levels. Some complications associated with the injection of triamcinolone acetonide have been previously reported and include ptosis, orbital fat prolapse, conjunctival ulceration, retinal and choroidal vascular occlusion, and cutaneous hypopigmentation etc. [32-34]. Our meta-analysis finds no increase in complications including after triamcinolone acetonide application for glaucoma surgery.

This meta-analysis has several potential limitations that should be taken into account. Firstly, our analysis is based on only four RCTs, and all of them have a relatively small sample size ($n < 100$). More RCTs with large samples should

be conducted to confirm our findings. Next, different methods of triamcinolone acetonide injection in the included RCTs are different, which may have an influence on the pooling results. Finally, some unpublished and missing data may lead to bias to the pooled effect.

Conclusions

Triamcinolone acetonide can improve the success rate of glaucoma surgery.

Disclosure of conflict of interest

None.

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