


Efficacy of the efficacy between dexamethasone versus triamcinolone acetonide after cataract surgery

A systematic review and meta-analysis

Tianqiu Zhou, PhD^{a,*} , Mei Yang, PhD^a, Junfang Zhang, PhD^a, Guowei Zhang, PhD^a, Lihua Kang, MS^a, Huaijin Guan, MS^a

Abstract

Purpose: To evaluate the clinical effects between dexamethasone and triamcinolone acetonide (TA) after phacoemulsification and intraocular lens implantation among cataract patients.

Methods: Pubmed, Embase, and the Cochrane Library were searched for studies published up to August 2020. The primary outcome was intraocular pressure. The secondary outcomes were the logarithm of the minimum angle of resolution (logMAR), anterior chamber cell, and anterior chamber flare. The pooled effect sizes were expressed as weighted mean differences (WMDs) or standardized mean differences (SMDs) of 95% confidence intervals (95% CIs). Cochrane Collaboration risk of bias tool and Newcastle-Ottawa scale criteria were used for the quality assessment of included studies.

Results: Seven relevant studies met the inclusion criteria. For the primary outcome, there was no significant difference between TA injection and dexamethasone in comparing intraocular pressure (IOP) (SMD = 0.22, 95% confidence interval [CI] [-0.29, 0.73], $P = .408$; $I^2 = 86.9\%$) in the first day after treatment and last day of assessment. For the secondary outcomes, the logMAR (WMD = 0.01, 95% CI [-0.06, 0.08]) and the anterior chamber flare (SMD = 0.08, 95% CI [-0.01, 0.18], $P = .087$; $I^2 = 0\%$) showed no differences. However, the amount of anterior chamber cells (SMD = -0.21, 95% CI [-0.42, -0.01], $P = .044$; $I^2 = 0\%$) in the TA injection on the first day postoperative was higher than for dexamethasone. After treatment, there was no difference between the 2 groups.

Conclusions: This study supports that there were no differences in IOP, logMAR, and anterior chamber flare between TA injection and dexamethasone among cataract patients. TA injection treatment on the first day showed higher amounts of anterior chamber cells than with dexamethasone.

Abbreviations: CIs = confidence intervals, IOP = intraocular pressure, logMAR = logarithm of the minimum angle of resolution, RCT = randomized controlled trial, SMD = standardized mean difference, TA = triamcinolone acetonide, WMDs = weighted mean differences.

Keywords: dexamethasone, inflammation, phacoemulsification, triamcinolone acetonide

1. Introduction

Cataract is a type of lens abnormality characterized by decreased transparency and increased turbidity, and it is the main cause of reversible visual impairment and blindness worldwide especially in lower socioeconomic status and developing countries.^[1] Cataracts can be confirmed based on clinical evaluation of the eyes, assessment of patients' visual impairments and other symptoms, as well as accompanying eye diseases that may affect visual outcomes were performed.^[2] The main treatment

modality for cataracts is surgery.^[3,4] Phacoemulsification and ocular lens implantation are the most popular therapeutic strategies for cataract extraction. Although phacoemulsification technology has made great progress in recent years, it still involves surgical trauma, making patients prone to postoperative inflammation.^[5] Postoperative inflammation control is important, and serious complications may occur with poor control, such as including cystoid macular edema, increased IOP, adhesion formation, posterior capsule clouding and secondary glaucoma.^[5,6]

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All data generated or analyzed during this study are included in this published article [and its supplementary information files].

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^a Eye Institute, Affiliated Hospital of Nantong University, Nantong, Jiangsu, China.

* Correspondence: Tianqiu Zhou, Eye Institute, Affiliated Hospital of Nantong University, Nantong Jiangsu 226000, China (e-mail: akiraqq@163.com).

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Corticosteroids have been used to treat postoperative inflammation since the 1950s. There are several types of corticosteroid medications, and the most commonly used postoperatively administration method are injections.^[7] Among them, dexamethasone is a common and widely available ophthalmic corticosteroid as the primary anti-inflammatory therapy for patients who underwent cataract extraction.^[8] Because dexamethasone interferes with multiple steps of the inflammatory cascade and has the advantage of corticosteroids regulating 4000 genomic and non-genomic behaviors, its application after cataract surgery is an interesting option for the prevention of postoperative inflammation. Recent improvements in the administration method of this drug type, such as the delivery of dexamethasone into the vitreous cavity, have revived its potential as a substitute for new compounds.^[9] However, since commonly used dexamethasone in the water-soluble form of phosphate ester (dexamethasone phosphate) is to be administered as eye drops multiple times a day for several weeks postoperatively, patient compliance plays a crucial role in treatment.^[10,11] However, compliance with the regulated use of eye drops may be unpredictable in the elderly cataract surgery patient population.^[12] Studies have reported non-adherence to regulated eye drop therapy ranging from 5% to 80%.^[13] As a result, there is a growing interest in postoperative “drop-free” dosing regimens.^[14]

Triamcinolone acetonide (TA) is a medium-strength corticosteroid with a relatively long duration of action,^[15] which can improve macular edema by local anti-allergy, inhibiting angiogenesis and cell proliferation, reducing vascular permeability, etc.^[16,17] Subconjunctival TA reservoirs provide a therapeutic approach with long-term anti-inflammatory therapeutic effects and may also reduce complications associated with non-adhesion in patients with eye drop administration.^[18] After intravitreal injection, endothelial cell proliferation and angiogenesis can be blocked to achieve the effect of treating fundus vascular diseases, so that patients can obtain the best corrected vision.^[19,20] TA has been effectively used in ocular therapies for over 50 years and showed a dramatic increase in controlling ocular inflammatory disease after phacoemulsification and intraocular lens implantation in recent years and studies have reported that it has shown significant efficacy in controlling ocular inflammatory disease following ultrasound emulsification and intraocular lens implantation.^[21,22]

Several clinical trials have been conducted on the comparative effectiveness of TA and dexamethasone in the treatment of inflammation after ultrasound emulsification and intraocular lens implantation procedures, but no relevant pooled analyses are available. A randomized controlled trial (RCT) showed that dexamethasone and TA were similarly effective in controlling inflammation after uncomplicated cataract echo-emulsification, with some studies suggesting that TA is safer and better tolerated than dexamethasone.^[23] Another RCT noted that it remains uncertain whether a single injection of TA is as effective as dexamethasone in controlling severe anterior chamber inflammation.^[24] Based on the above disputes and the potential clinical value of the 2 drugs, it is necessary to summarize the relevant published studies and pool the quantitative results through meta-analysis to provide evidence for clinical decision-making. Therefore, the aim of this meta-analysis was comparing the effectiveness of dexamethasone and TA in controlling inflammation after emulsification and intraocular lens implantation in cataract patients.

2. Methods

2.1. Literature search

According to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guideline, we aimed to perform a systematic review and meta-analysis. Two independent reviewers (Tianqiu Zhou and Mei Yang) started with searching relevant articles

through PubMed, Embase, and the Cochrane Library published up to December 2022 and using the PICOS principle, followed by screening based on the inclusion and exclusion criteria. Authors contacted for the papers excluded due to having insufficient data. The following keywords were used database search: TA, dexamethasone, cataract, surgery. Two authors independently screened the titles and abstracts of the citations identified through database search. Next, a full-text reading of potentially eligible articles was performed for final assessment for eligibility.

2.2. Inclusion and exclusion criteria

2.2.1. Study selection. The eligibility criteria were population: patients who underwent phacoemulsification and intraocular lens implantation without restriction of age; intervention: TA injection; control: dexamethasone; outcomes at postoperative first day and last day of assessment: cell (count data), flare (count data), intraocular pressure (IOP) in mm Hg, and visual acuity (converted to logarithm of the minimum angle of resolution (logMAR) for statistical purposes); no restriction of study type; language was limited to English. Exclusion criteria were as follows: reviews, conference abstracts, animal studies, case reports, data not extractable, non-English citations.

2.2.2. Data extraction and quality assessment. Study and patient characteristics (authors, year of publication, the country where the study was performed, sample size, sex, time at follow-up assessment, and mean age) were extracted for each group. The treatment parameters were the dose or density of TA and dexamethasone. The primary outcome was IOP (in mm Hg). The secondary outcomes were anterior chamber cells, anterior chamber flare, and logMAR (visual acuity). Anterior chamber cells were graded as: 0 = <5 cells; 1 = mild, 5 to 10 cells; 2 = moderate, 10 to 20 cells; 3 = marked, 21 to 50 cells; 4 = severe, >50 cells, and 5 = hypopyon.^[25] Anterior chamber was graded as: 0 = none; 1 = mild (just detectable); 2 = moderate (iris details clear); 3 = marked (iris details hazy), and 4 = severe (heavy with fibrin deposits and clots).^[25] Visual acuity was measured using the Snellen VA chart and values were converted to logMAR.^[26]

Risk of bias in all included articles was independently assessed by 2 authors (Junfang Zhang and Guowei Zhang) according to the Cochrane Collaboration risk of bias tool and Newcastle-Ottawa scale criteria. Differences in the assessment were resolved through discussion until a consensus was reached.

2.2.3. Data synthesis. Continuous data were expressed as weighted mean differences (WMDs) or standardized mean differences (SMDs) of 95% confidence intervals (95% CIs). The included studies rarely reported different statistical parameters, so the coefficient of variance was used to estimate the standard deviation of the mean IOP.^[7,10,18,27–31] We calculated correlation coefficients from reported values retrieved by Rattan et al in 2018 to estimate the baseline to time changes in IOP in other studies. The variance estimates of changes in the mean and standard deviation were used to calculate the WMDs. The WMD between the treatment and the control was provided for the continuous variables studied. The weights reflected the reciprocal of the treatment variance. Wang et al randomly divided the patients into 4 groups according to different doses. Since there is only one control group and 3 intervention groups, we divided the whole control group into 3 control groups with evenly distributed sample sizes and compared them with each intervention group to keep the sample size of the original control group unchanged.

2.2.4. Statistical analysis. All analyses were performed using STATA SE 14.0 (StataCorp, College Station, TX). The CI method was used to compare the results. The statistical

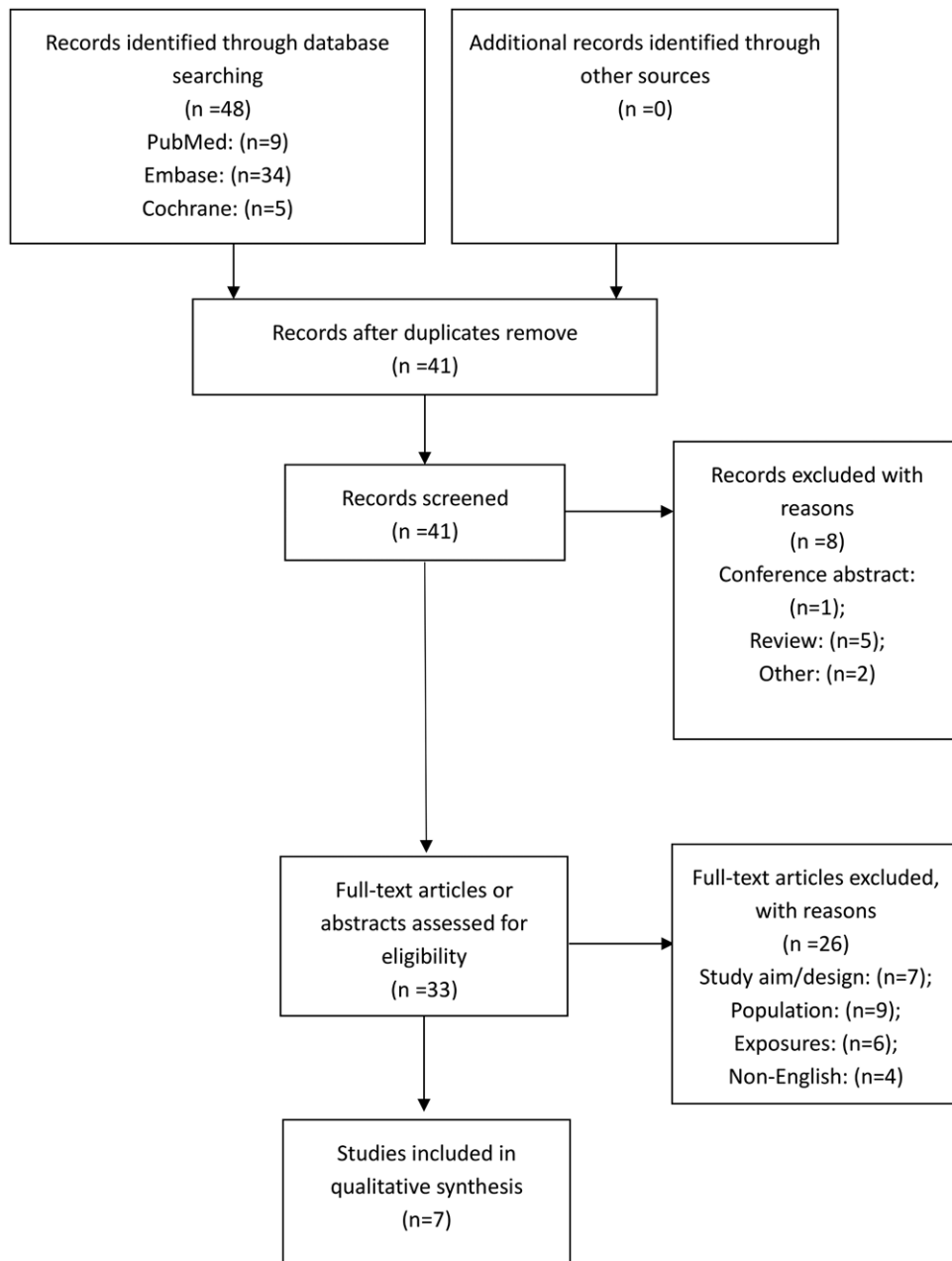


Figure 1. Flow diagram of the study selection.

heterogeneity was calculated by Cochran Q-test and I^2 index. We speculated that there might be a high degree of heterogeneity due to the differences in dose and the median follow-up for each study. Therefore, the random-effects model was used to analyze regardless of the results of the Cochran Q-test and I^2 index. Four sensitivity analyses were carried out. We did not assess potential publication bias was evaluated graphically by funnel plot and Egger test because the number of studies included in this meta-analysis was <10. In this case, the funnel plot and Egger test might produce misleading results and are not recommended. A P value < .05 was considered statistically significant.

3. Results

3.1. Search process

The electronic search ended with 41 articles. After careful reading, 33 papers met the preliminary standard. In the

further screening, 26 articles were excluded because of improper research type and insufficient data and article type. We eventually included 7 studies^[7,18,27-31] in this meta-analysis. Figure 1 shows the flowchart of identification, inclusion, and exclusion, reflecting the search process and the reasons for exclusion.

3.2. Characteristics of included studies

All included studies were published from 2010 to 2020. A total of 1535 patients were included in this meta-analysis. The 9 datasets of the 7 studies included 5 RCTs and 2 retrospective studies. The detailed characteristics of the included studies are described in Table 1. Wang et al divided their patients into 3 intervention groups with TA at 0.5 mg, 1.0 mg, and 2.0 mg, respectively, and one control group without TA. All treatment groups received TA injections with different doses. For the control groups, Wang et al used dexamethasone ointment, and Gungor et al performed dexamethasone injection,

Table 1**Literature search and study characteristic.**

Author, yr	Country	Study design	Treatment	Control	N	Age case/control (yr)	Sex, male/ female	Median follow-up	Outcomes
Gungor, 2014 ^[7]	Turkey	RCT	2 mg/0.05 mL injection of TA	0.4 mg/0.1 mL injection of dexamethasone	60	69.8 ± 10.5/71.4 ± 9.4	24/36	D 1, 7, 30	Cell, flare, IOP, logMAR
Khan, 2016 ^[30]	Pakistan	RCT	40 mg/mL injection of TA	0.1% dexamethasone eye drops	108	57.77 ± 8.93/58.87 ± 9.69	72/36	D 1, 14, 42	IOP, Grade cell, flare
Shaheen, 2020 ^[31]	Pakistan	RCT	1 mg intracameral injection of TA	0.1% dexamethasone eye drops	80	50 ± 5/51 ± 4	51/29	D 1, 7, 28	Cell, flare, IOP
Simaroi, 2011 ^[29]	Thailand	RCT	2 mg/0.1 mL injection of TA	0.1% dexamethasone eye drops	60	66.77 ± 8.29/65.37 ± 7.97	24/36	D 1, 7, 30	Grade cell, IOP, logMAR
Wang, 2013a	China	RCT	0.5 mg injection of TA	0.1% dexamethasone ointment	43	63.69 ± 9.66/65.39 ± 6.08	19/24	D 1, 7, 14, 28	IOP, Grade cell, flare
Wang, 2013b	China	RCT	1 mg injection of TA	0.2% dexamethasone ointment	42	62.90 ± 8.74/65.39 ± 6.08	21/21	D 1, 7, 14, 28	IOP, Grade cell, flare
Wang, 2013c	China	RCT	2 mg injection of TA	0.3% dexamethasone ointment	41	64.33 ± 8.27/65.39 ± 6.08	21/20	D 1, 7, 14, 28	IOP, Grade cell, flare
Lindholm, 2019	Finland	Prospective trial	20 mg injection of TA	1 mg/mL dexamethasone eye drops	101	74.7 ± 6.7/74.5 ± 6.5	33/68	D 7, 28, 90	IOP, logMAR
Rattan, 2018	Iraq	Prospective	4 mg/0.4 mL injection of TA	0.1% dexamethasone eye drops	1000	59.7 ± 8.84/59.4 ± 9.04	380/620	D 90	IOP

IOP = intraocular pressure, logMAR = logarithm of the minimum angle of resolution, RCT = randomized controlled trial, TA = triamcinolone acetonide.

while Khan et al, Shaheen et al, Simaroi et al, Lindholm et al, and Rattan et al used dexamethasone eye drops.

3.3. Quality assessment

Five randomized controlled trials and 2 prospective cohort studies were included (Table S1A and S1B, <http://links.lww.com/MD/M825>). The quality of included studies was rated as moderate to high. The intervention in each group cannot be blinded, thus the 5 RCTs were of high risk of performance bias. The study of Shaheen et al might have other biases because the authors did not explain whether the outcome measures were measured by the same investigator.

3.4. Primary outcome

3.4.1. IOP between TA injection and dexamethasone. As shown in Table 2, 6 studies with 8 datasets involved the first day posttreatment, and there was no significant difference between TA injection and dexamethasone (SMD = 0.22, 95% CI [-0.29, 0.73], $P = .408$; $I^2 = 86.9\%$, Fig. 2). Nine studies involved the last follow-up, and there was also no significant difference between TA injection and dexamethasone (SMD = 0.04, 95% CI [-0.18, 0.26], $P = .737$; $I^2 = 58.1\%$, Fig. 2). The result showed that IOP in the 2 groups had no difference on the first day and last follow-up after surgery (Table 2).

3.5. The secondary outcomes

3.5.1. LogMAR. One study reported visual acuity on the first day posttreatment (WMD = 0.01, 95% CI [-0.06, 0.08], Fig. 3). On the last follow-up visual acuity analysis, there was also no difference between the 2 treatments (WMD = 0.01, 95% CI [-0.04, 0.06], $P = .789$; $I^2 = 0\%$). The results showed that there was no significant difference between TA injection and dexamethasone both on the first day posttreatment and the last follow-up.

3.5.2. Anterior chamber cells. Two articles were included in the analysis.^[7,31] The results showed that there is no difference in the amount of anterior chamber cells between the TA injection and dexamethasone groups in the last follow-up (SMD = 0.03,

Table 2**Postoperative outcomes in both groups.**

	N	Effects (95% CI)	P	I-square	P (heterogeneity)
IOP					
First day	8	0.216 (-0.295, 0.726)	.408	86.9	<.001
Last day	9	0.037 (-0.181, 0.256)	.737	58.1	.014
LogMAR					
First day	2	0.005 (-0.052, 0.062)	.861	0.0	.768
Last day	3	0.007 (-0.042, 0.055)	.789	0.0	.607
Flare					
First day	2	0.082 (-0.012, 0.176)	.087	0.0	.678
Last day	1	-0.020 (-0.108, 0.068)	.656		
Cell					
First day	2	-0.210 (-0.415, -0.005)	.044	0.0	.891
Last day	1	0.030 (-0.064, 0.124)	.534		

CI = confidence interval, IOP = intraocular pressure, logMAR = logarithm of the minimum angle of resolution.

95% CI [-0.06, 0.12], $P = .534$; $I^2 = 0\%$, Fig. 4), while there was a difference in the first day posttreatment (SMD = -0.21, 95% CI [-0.42, -0.01], $P = .044$; $I^2 = 0\%$). It indicated that the number of anterior chamber cells in the TA injection group was higher than in the dexamethasone group before treatment. After treatment, there was no difference between the 2 groups.

3.5.3. Anterior chamber flare. Two articles were included in the analysis.^[7,31] The results showed that there was no difference in the amount of anterior chamber flare between the TA injection and dexamethasone groups in the first day posttreatment (SMD = 0.08, 95% CI [-0.01, 0.18], $P = .087$; $I^2 = 0\%$, Fig. 5) and last follow-up (SMD = -0.02, 95% CI [-0.11, 0.07], $P = .656$; $I^2 = 0\%$).

3.6. Sensitivity analysis and publication bias

As shown in Supplementary Figure S1, <http://links.lww.com/MD/M824>, the heterogeneity of IOP and visual acuity might be attributed to the different results of each study. Supplementary Figure S1, <http://links.lww.com/MD/M824> indicated that the result in this article was robust after eliminating included study one after another. We did not assess potential publication bias

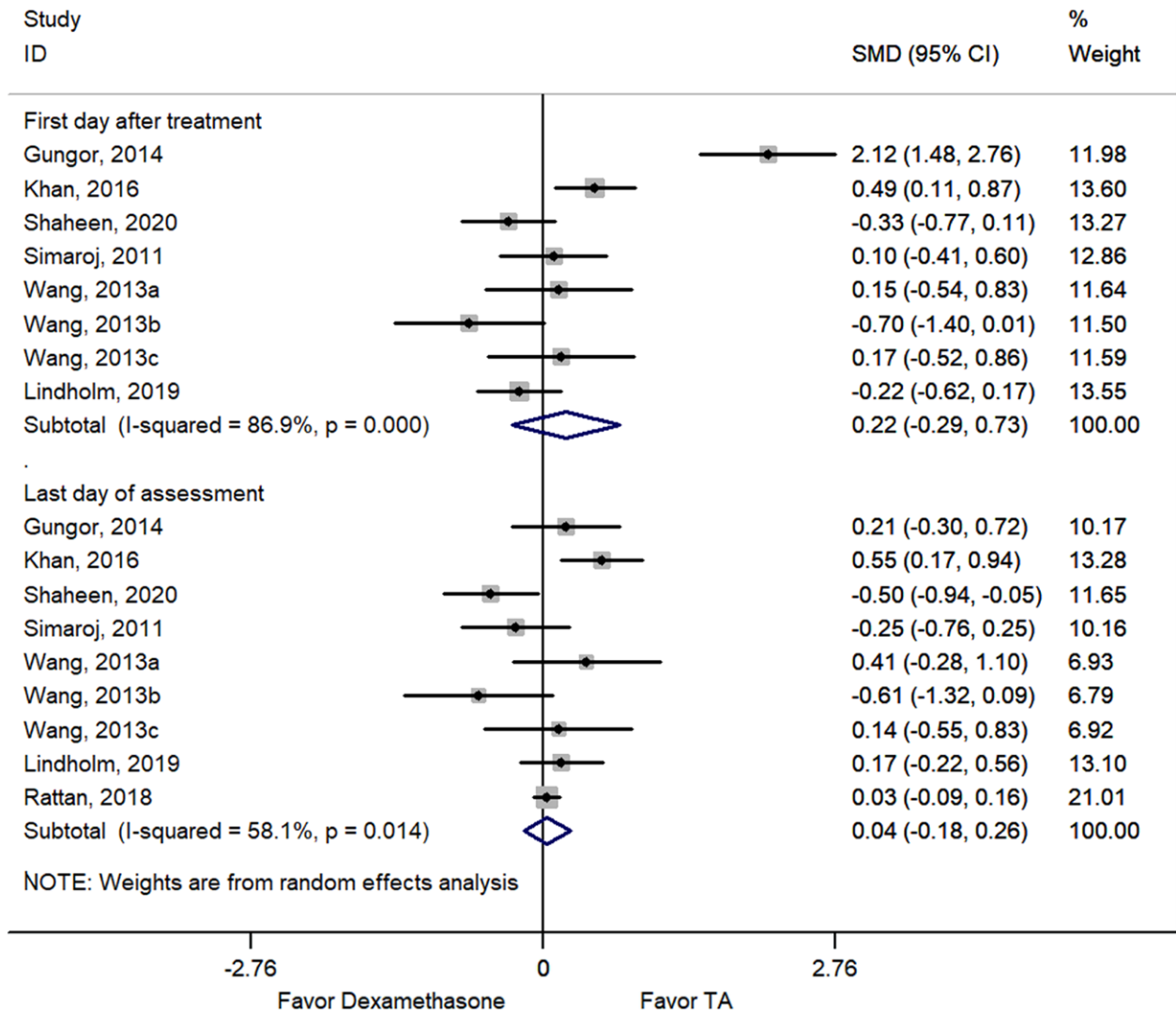


Figure 2. Forest plots of intraocular pressure between triamcinolone acetonide injection and dexamethasone.

by funnel plot and Egger test because the number of studies included in this meta-analysis was <10. In this case, the funnel plot and Egger test might produce misleading results and are not recommended.

4. Discussion

This meta-analysis aimed to compare the anti-inflammatory efficacy of dexamethasone and TA after cataract surgery. Previous single studies focused on and reported short-term clinical outcomes.^[7,18,27-31] Accordingly, the primary outcome in this meta-analysis was IOP and secondary outcomes included the number of anterior chamber cells, anterior chamber flare, and visual acuity. This meta-analysis showed that comparing TA injections with dexamethasone showed no difference in IOP, visual acuity, and the anterior chamber flare. The number of anterior chamber cells was higher in the TA injection group than in the dexamethasone group on the first day posttreatment, while there was no difference between the 2 groups at the last follow-up after treatment.

The study by Zerener et al also supported that dexamethasone and TA had similar clinical effects in reducing edema, pain, and trismus for cataract patients undergoing surgery.^[15] Lindholm et al study demonstrated insignificant differences between dexamethasone and TA in IOP and visual

acuity at the last day of follow-up.^[18] In the study by Gungor et al, results showed no statistically significant differences in visual acuity, the amount of anterior cells and flare between the dexamethasone and TA groups.^[7] The reason for these insignificant differences be that small amount of dexamethasone and TA was used, and patients with known family history of glaucoma or any early ocular hypertension response to systemic or local corticosteroids were excluded from several original included studies. Another reason may be that the follow-up duration of most was short (28 days) in included, Lindholm et al study demonstrated that aqueous flare reached its peak value at 7 days in TA and dexamethasone groups and then returned gradually to baseline level by 90 days in the TA group but remained elevated in the dexamethasone group, which suggest that TA has a more sustainable anti-inflammatory effect.^[18]

In addition, it is noteworthy that different drug delivery routes have been adopted to manage eye diseases based on the location of the disease.^[32] Drugs with high corneal permeability and drug products with extended pre corneal retention can help improve the bioavailability of the ocular surface and anterior segment.^[33] Local administration is generally the most suitable for targeting drug effects and minimizing systemic adverse events to anterior eye diseases.^[34] Previous studies reported that direct injection of TA into the anterior chamber can safely and effectively control

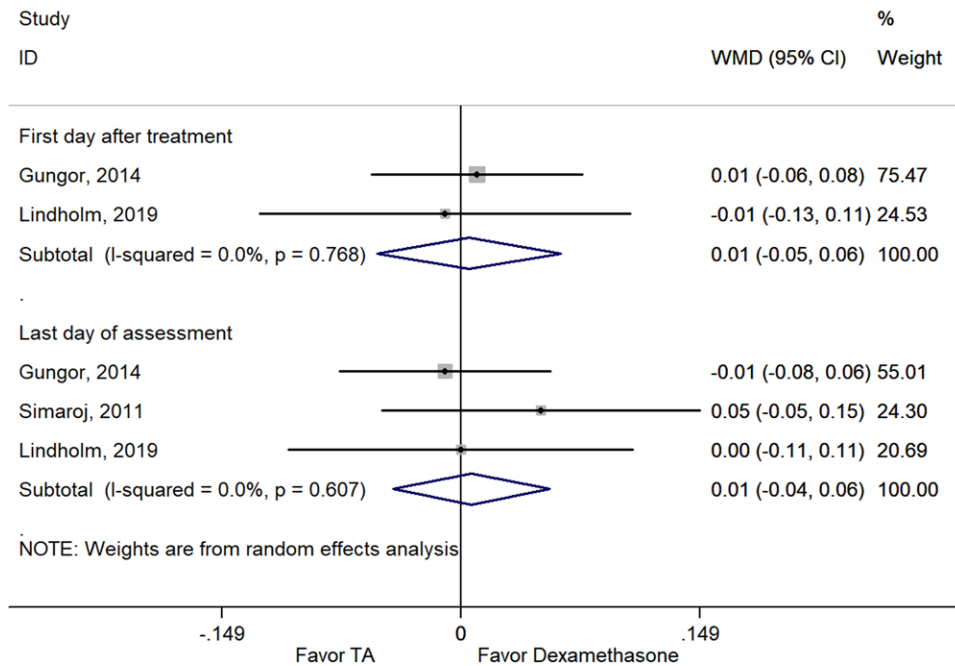


Figure 3. Forest plot of visual acuity (logMAR) between triamcinolone acetonide injection and dexamethasone.

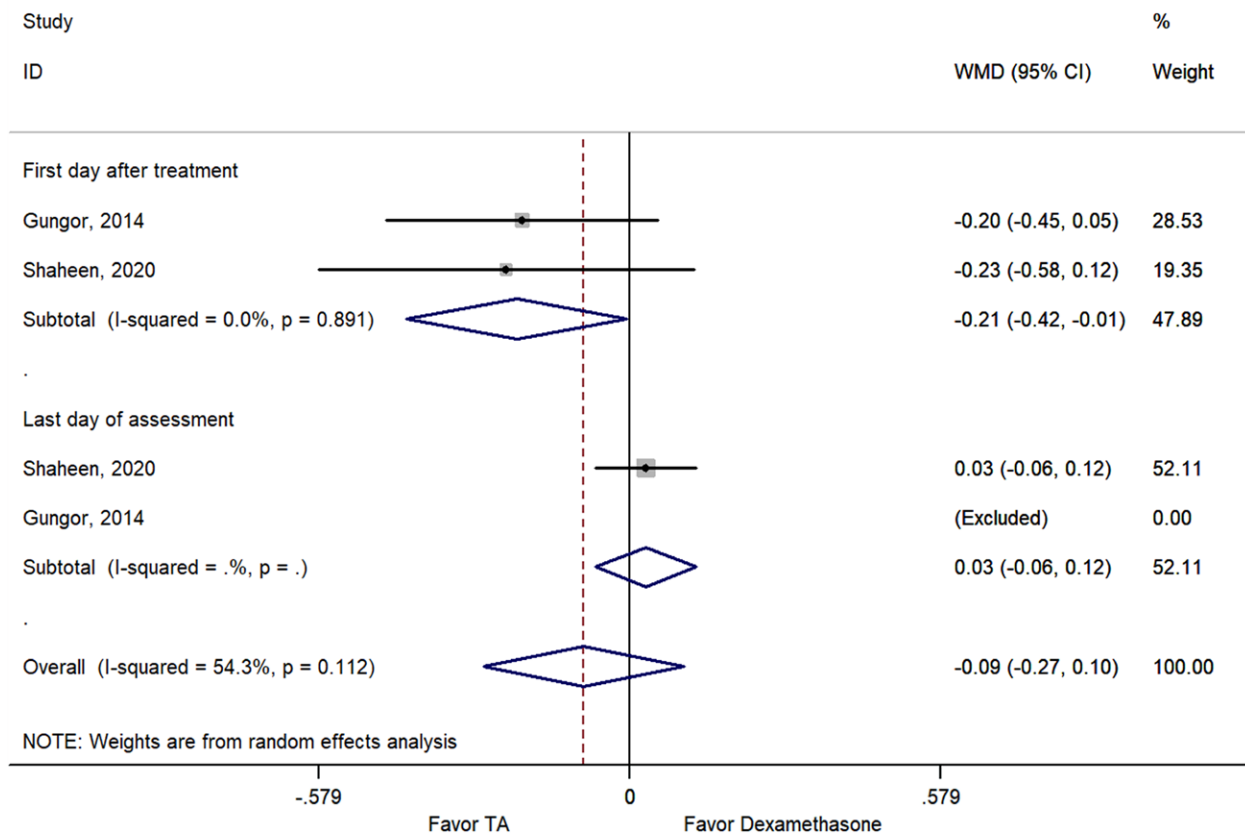


Figure 4. Forest plots of the amount of anterior chamber cell between triamcinolone acetonide injection and dexamethasone.

inflammation after cataract surgery.^[35-38] Nevertheless, intraocular injection of TA is a non-labeled use and extra caution should be exercised.^[27]

Interestingly, findings of this meta-analysis revealed that there is no difference in the amount of anterior chamber cells

between the TA injection and dexamethasone groups in the last follow-up, however, patients treated with TA had significantly fewer anterior chamber cells than those treated with dexamethasone 1 day after surgery. This finding indicated that postoperative inflammation decreased significantly with TA treatment

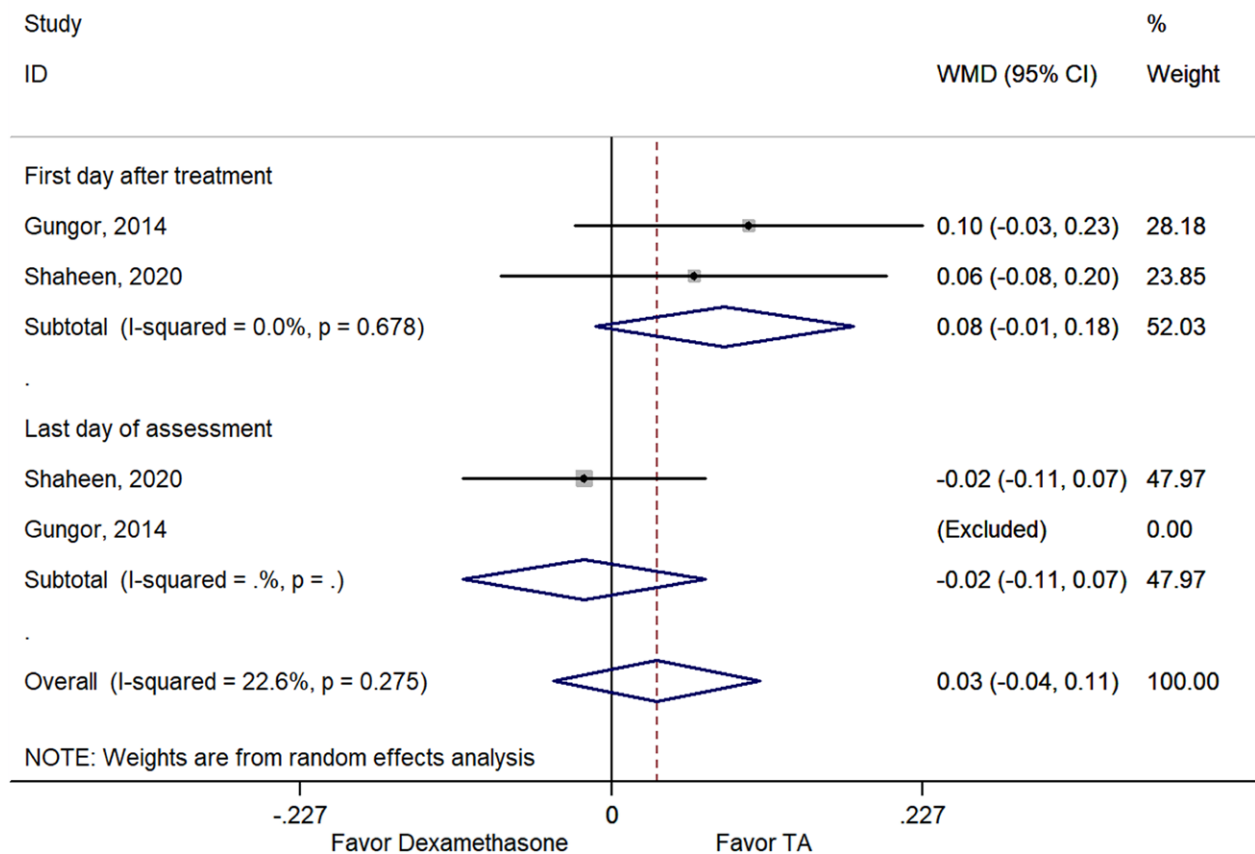


Figure 5. Forest plots of the amount of anterior chamber flare between triamcinolone acetonide injection and dexamethasone.

compared with the decrease in the dexamethasone group as TA can enhance the aqueous reaction reduction.^[27] The underlying mechanisms need to be furtherly investigated in the future. Due to limited number of included studies, subgroup analyses based on the route of administration were not performed, more well-designed trials are warranted to comprehensively investigate the impact of different routes on the clinical outcomes of TA and dexamethasone after cataract surgery. Results of this meta-analysis may provide hints for practitioners in the decision-making for the utility of TA and dexamethasone in both clinical and research settings.

Different surgeons have preferences in the way they administer medication. Some choose to use injections within 24 hours of surgery, and some surgeons opt for topical application.^[39,40] Topical eye drops have been the mainstay of postoperative prophylaxis and treatment, but due to ocular surface toxicity, high cost, unpredictable delivery of effective doses, poor compliance, and the administration of topical eye drops, there is a preference for “drop-free” delivery.^[41] As a result, traditional drug delivery methods need to change. Several studies have reported proposing intravitreal injections, and a systematic analysis confirmed that this method is effective in controlling inflammation in the perioperative period.^[42] Another study reported the same efficacy with intravitreal injections and drops.^[41]

This meta-analysis revealed significant heterogeneity in the primary outcome analysis. This heterogeneity is to be expected as the included studies used different doses and routes of administration. In addition, the pharmacokinetics of dexamethasone as a topical cream, eye drops and intravitreal injections are completely different and may have influenced the efficacy results.

Besides, there were some limitations in this study. The interpretation of the findings in this study should be with caution.

Firstly, the 7 included studies used different dosage and administration methods of dexamethasone and different methods of TA injection, probably influencing the results, more relevant studies are warranted to address these issues. Secondly, corticosteroid treatment may have raised the IOP in patients with glaucoma or ocular hypertension. Thirdly, one study used pupil expansion, which is likely to cause more inflammation and macular changes postoperatively. Future studies should include more studies on the outcomes of the number of anterior chamber cells and flare. The present study demonstrated no differences between the 2 treatments in these outcome indicators, and subsequent studies could conduct pharmacoeconomic analysis with respect to the convenience and cost of treatment. Finally, 12 out of 101 patients were patients with glaucoma in the study of Lindholm et, al, however, due to limited data extracted, subgroup analysis based on glaucoma or non-glaucoma populations cannot be performed.

This study supports that there were no differences in IOP, logMAR, and the anterior chamber flare between TA injection and dexamethasone among cataract patients. The number of anterior chamber cells was higher with TA injection on the first day postoperative than with dexamethasone. Larger studies are needed to confirm the results.

Author contributions

Conceptualization: Tianqiu Zhou.

Data curation: Tianqiu Zhou, Mei Yang, Junfang Zhang, Guowei Zhang, Lihua Kang.

Formal analysis: Tianqiu Zhou, Mei Yang, Junfang Zhang, Guowei Zhang, Lihua Kang.

Writing – original draft: Tianqiu Zhou.

Writing – review & editing: Huaijin Guan.

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