·Meta-Analysis·

A Meta-analysis on the clinical efficacy and safety of optic capture in pediatric cataract surgery

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Abstract

• **AIM: To evaluate the clinical efficacy and safety of optic capture in pediatric cataract surgery.**

• **METHODS: Searches of peer-reviewed literature were conducted in PubMed, Embase and the Cochrane Library. The search terms were "optic capture" and " cataract". The retrieval period ended in December 2014. Relevant randomized controlled trials (RCTs), case-control studies and cohort studies were included. Meta-analyses were performed. Pooled weighted mean differences and risk ratios with 95% confidence intervals were estimated.**

• **RESULTS: Ten studies involving 282 eyes were included, 5 of which were RCTs involving 194 eyes. The application of optic capture significantly reduced both opacification of the visual axis (RR: 0.12; 95% CI: 0.02 to 0.85; *P*=0.03) and occurrence of geometric decentration (RR: 0.09; 95% CI: 0.02 to 0.46; *P*=0.004). But it did not significantly affect best corrected visual acuity (BCVA) (WMD: -0.01; 95% CI: -0.07 to 0.05; *P* =0.75) and influence the occurrence of posterior synechia (RR: 1.53; 95% CI: 0.84 to 2.77; *P*=0.17). Deposits in the anterior intraocular lens were significantly increased in the optic capture group early after surgery (RR: 1.40; 95% CI: 1.05 to 1.86; *P* =0.02) and at the last follow-up (RR: 2.30; 95% CI: 1.08 to 4.92; *P*=0.03). The quality of the evidence was assessed as high.**

• **CONCLUSION: The application of optic capture significantly reduces opacification of visual axis and occurrence of geometric decentration but do not significantly improve BCVA with notable safety.**

• **KEYWORDS:** optic capture; intraocular lens; pediatric cataract; secondary opacification; Meta-analysis
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INTRODUCTION

Opacification of the visual axis after pediatric cataract surgery is a serious complication. It is potentially induced by the proliferation and migration of the remaining lens epithelial cells (LEC) after surgery. Thereby blocking the visual axis and typically causing visual acuity assessed by Snellen chart to decrease by at least 2 lines [1]. The discovery of new methods to prevent the opacification of the visual axis after pediatric surgery is a subject of ongoing research. The elimination of the secondary opacification is an important indicator of the success of pediatric cataract surgery[2]. Several techniques have been applied to inhibit the phenomenon, including posterior continuous curvilinear capsulorhexis (PCCC) combined with anterior vitrectomy before or after the implantation of the intraocular lens (IOL) [2-3], PCCC alone and bag-in-the-lens implantation [4]. Kohnen *et al*[5] and Gimbel[6] invented optic capture in 1994, and the technique, which consists of PCCC and optic capture through the posterior capsulorhexis, has become popular and average. An increasing number of authors believe that this procedure helps to maintain the centration of the IOL and prevents opacification of the visual axis. After the development of this technique, numerous clinical trials were conducted, but certain debates have lingered. Some authors do not consider the application of optic capture in pediatric cataract surgery to be useful and safe. And their clinical trials are in general quality. For example, Vasavada and Trivedi[7] reported that all eyes in the optic capture group and no-optic capture group maintained a clear visual axis in a prospective study comprising 40 eyes. The study demonstrated significantly increased posterior synechia formation in the optic capture group compared with the no-optic capture group, and 1 eye in the optic-capture group developed a membrane in front of the IOL. In another study, Koch and Kohnen[8] reported that anterior vitrectomy was the only effective method for preventing or delaying secondary

cataract formation in infants and children. All optic capture cases without vitrectomy also remained clear initially; however, after 6mo, 4 out of 5 cases developed opacification. This study was performed on a small scale and was not randomized. Other studies were also small, and the numbers of enrolled eyes ranged from 13 [6] to 50 [9]. Furthermore, no technique is perfect. For example, the disadvantage of PCCC with anterior vitrectomy is vitreous incarceration in the wound, which increases the risk of retinal detachment [1-2]. Anterior vitrectomy at the time of cataract surgery also increases the risk for cystoid macular edema (CME)[3], however, the incidence of CME in children has been reported to be low[4]. These disadvantages could be avoided if a technique could serve as a substitute for anterior vitrectomy. Thus, research on relevant topics is very meaningful.

The accuracy of conclusions from many previous clinical trials remains uncertain because these trials did not adopt random methods. Furthermore, it is unclear whether the application of optic capture in pediatric cataract surgery can significantly reduce secondary opacification of the visual axis and geometric decentration due to the small sample sizes of individual studies. As we all know, the quality of multi-center clinical trial and Meta-analysis rank first in evidence based medicine. Multi-center clinical trial is time-consuming and costly. Thus, a systematic review and Meta-analysis can elucidate the benefits of optic capture.

MATERIALS AND METHODS

This review was conducted and reported according to the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) statement issued in 2010[10].

Systematic Literature Search Comprehensive searches of peer reviewed literature were conducted using PubMed (ended in Dec. 2014), Embase (ended in Dec. 2014), Cochrane Library (ended in Dec. 2014). The search terms, including MeSH words and text words, were "optic capture" and "cataract". Overall, 58 papers were obtained from PubMed, 61 from Embase, 20 from Cochrane library. All the papers had abstracts or full texts written in English.

Inclusion and Exclusion Criteria For inclusion, studies had to meet the following criteria: 1) pediatric cataracts were diagnosed, and the patients in optic capture group and no-optic capture group were comparable; 2) the study contained at least an optic capture group and a no-optic capture group, and PCCC was performed in every eye of the two groups; 3) the study was required to be a clinical trial, including cohort studies, case control studies or randomized controlled studies, with suitable methods and designs; 4) at least one of the primary outcomes [secondary opacification, best-corrected visual acuity (BCVA)] or secondary outcomes (posterior synechia, deposits in the anterior IOL, decentration of IOL) was evaluated. Studies were excluded if any of the following criteria were met: 1) the study concerned irrelevant topics or was repeatedly included in several databases; 2) the study contained no original data (reviews, comments or letters); 3) the study was a case series report; 4) a significant heterogeneity in age existed between study groups, for example the study groups were divided according to age.

Data Extraction and Quality Assessment To avoid bias in the data extraction process, two investigators independently extracted and collected data following the selection criteria described above. Any discrepancy was resolved by discussion and consensus. The following information was extracted from each trial: first author's name, publication year, type of study, the number of treated patients, duration of follow-up, patients' ages, the number of eyes with secondary opacification, BCVA, the number of occurrences of geometric decentration of IOL, the number of eyes with deposits in the anterior IOL early after surgery, the number of eyes with posterior synechia and the number of eyes with deposits in the anterior IOL at the last follow-up. Quality assessment of the evidence was performed by GRADE.

Statistical Analysis To evaluate the efficacy and safety between the optic capture group and no-optic group for the treatment of pediatric cataract, we assessed the overall effect of optic capture and no-optic capture from the data of the included studies and used the pooled weighted mean differences (WMDs) and risk ratios (RRs) with 95% confidence intervals (CIs) as the metric of choice for all the outcomes. The overall effects were evaluated using Z-statistics, and the value of P was acquired according to the value of Z. We implemented a Meta-analysis of the direct evidence for each outcome by combining pairwise comparisons between the optic capture and no-optic capture groups using Review Manager 5.2. Between-study heterogeneity was evaluated by Q-statistics and quantified by the I^2 statistic. If statistically significant heterogeneity was considered to be present (I^2>50%), we chose a random-effects model; otherwise, a fixed effects model was used. Any P-value less than 0.05 was regarded as statistically significant for all included studies. To analyze the between-study heterogeneity, we divided the subgroups or excluded one study at a time until all of the studies had been excluded once in this manner. To analyze the sensitivity of the Meta-analysis, we excluded one study at a time until all the studies had been excluded once in this manner.

RESULTS

Literature Search and Study Characteristics We identified 139 potentially relevant studies from the initial search, and 97 studies were excluded after a preliminary review. The remaining 42 studies were identified for detailed

Table 1 Characteristics of included studies

Study	Type/rank	Sources	Database	Eyes	Age	Follow-up
Kohnen *et al*[5]	Case control/Ⅲ	Cullen Eye Institute, USA	PubMed	16	1.5-12a	>6mo
Gimble[6]	Case control/Ⅲ	Gimbel Eye Centre, Canada	PubMed	13	2-12a	8-28mo
Vasavada and Trivedi[7]	RCT/Ⅱ	Iladevi Cataract & IOL Research Center, India	PubMed	40	4-55mo	5-24mo
Koch and Kohnen[8]	Case control/Ⅲ	Cullen Eye Institute, USA	PubMed	20	1.5-2a	1-4.5a
Müllner-Eidenböck *et al*[9]	RCT/Ⅱ	University of Vienna, Austria	PubMed	50	2-16a	8-41mo
Raina *et al*[11]	RCT/Ⅱ	Guru Nanak Eye Centre, India	PubMed	34	1.5-12a	8-28mo
Vasavada and Desai[12]	Cohort/Ⅲ	Iladevi Cataract & IOL Research Center, India	PubMed	18	3mo-5a	Average 13.3mo
Raina *et al*[13]	RCT/Ⅱ	Guru Nanak Eye Centre, India.	PubMed	42	36-144mo	6-18mo
Faramarzi and Javadi[14]	RCT/Ⅱ	Labbafinejad Medical Center, Iran	PubMed	28	2.5-8.0a	13-35mo
Shiratani *et al*[15]	Case control/Ⅲ	Kitasato University, Japan	Embase	21	6mo-15a	1-50mo

RCT: Randomized controlled trials.

Table 2 Secondary opacification in each included study when posterior continuous curvilinear capsulorhexis was noted

Study	Anterior vitrectomy group (secondary opacification eyes/total eyes)		No-anterior vitrectomy group (secondary opacification eyes/total eyes)	
	Capture	No capture	Capture	No capture
Kohnen *et al*[5]	0/2	0/3	0/2	4/4
Gimble[6]	-	-	0/13	2/5
Vasavada and Trivedi[7]	0/14	0/26	-	-
Koch and Kohnen[8]	0/3	0/3	4/5	4/4
Müllner-Eidenböck *et al*[9]	0/8	1/12	0/7	0/8
Raina *et al*[11]	-	-	0/16	8/18
Vasavada and Desai[12]	0/5	0/5	3/3	2/5
Raina *et al*[13]	-	0/4	0/6	0/7
Faramarzi and Javadi[14]	0/14	0/14	-	-
Shiratani *et al*[15]	-	-	0/17	0/2

-: No available data.

assessment. Finally, 5 RCTs and 5 chart series met the inclusion criteria. The selection process and reasons for exclusion are summarized in Figure 1[5-9,11-15].

The baseline characteristics of the participants and the design of the studies are summarized in Table 1. Tables 2-4 present the main results from each included study.

Secondary Posterior Capsular Opacification Figure 2 presents the forest plot of 5 RCTs involving 150 eyes that assessed the effect of preventing posterior capsular opacification (PCO) by comparing optic capture with no-optic capture. A fixed effects model was adopted because the I^2 was less than 50%. The incidence rates of PCO between the two groups were significantly different (RR: 0.12; 95% CI: 0.02 to 0.85; P=0.03) with no evidence of heterogeneity (I^2=0%, P=0.36). We studied 1 cohort and 4 case control studies together with 5 RCTs. The incidence rates of PCO between the two groups were significantly different (RR: 0.44; 95% CI: 0.22 to 0.88; P=0.02) with no evidence of heterogeneity (I^2=37%, P=0.16). No significant difference between subgroups was found (I^2=63.2%, P=0.10).

Best Corrected Visual Acuity Figure 3 illustrates a forest plot of 3 RCTs involving 75 eyes showing the effect of mean BCVA after surgery between the two groups. Because the outcome of the heterogeneity test was not significant (I^2=0%, P=0.63), a fixed effects model was adopted. The pooled result indicates that the mean BCVAs were not significantly different between the two groups (WMD: -0.01; 95% CI: -0.07 to 0.05; P=0.75). Furthermore, mean BCVAs of patients whose ages are less than 4 or equal to 4 were not significantly different between the two groups (I=0.708; P=0.489).

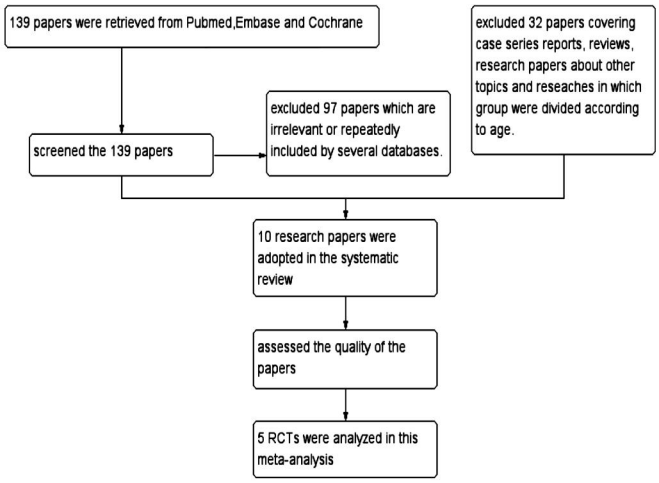

Figure 1 PRISMA flow chart of the literature search and study selection.

Table 3 Best corrected visual acuity before and after surgery as well as available spherical equivalent after surgery in included randomized controlled trials

Study	Capture group			No capture group		
	Before surgery (logMar)	After surgery (logMar)	Spherical equivalent (D)	Before surgery (logMar)	After surgery (logMar)	Spherical equivalent (D)
[1]Raina *et al* [11]	-	0.23±0.15	-	-	0.21±0.15	-
[2]Raina *et al* [13]	-	0.19±0.11	-0.250	-	0.19± 0.10	-0.264
Faramarzi and Javadi[14]	0.99±0.18	0.27±0.14	0.75±1.37	0.97±0.23	0.32±0.14	0.82±0.92

[1]The data for this reference were extracted from their tables and calculated according to the principles of data processing, and entries labeled CNBA (could not be assessed) were excluded; [2]The data for this reference were from B group and D group; -: No available data.

Table 4 Main complications of the included randomized controlled trials

Study	Capture (evented eyes/total eyes)			No capture (evented eyes/total eyes)		
	Synechia	Deposits	Decentration	Synechia	Deposits	Decentration
Vasavada and Trivedi[7]	10/14	14/14	0/14	9/26	16/26	19/26
Müllner-Eidenböck *et al*[9]	-	2/8	0/8	-	0/12	2/12
Raina *et al*[11]	-	9/16	-	-	10/18	-
Raina *et al*[13]	0/6	5/6	-	1/7	4/7	-
Faramarzi and Javadi[14]	0/14	3/14	0/14	1/14	3/14	3/14

-:No available data.

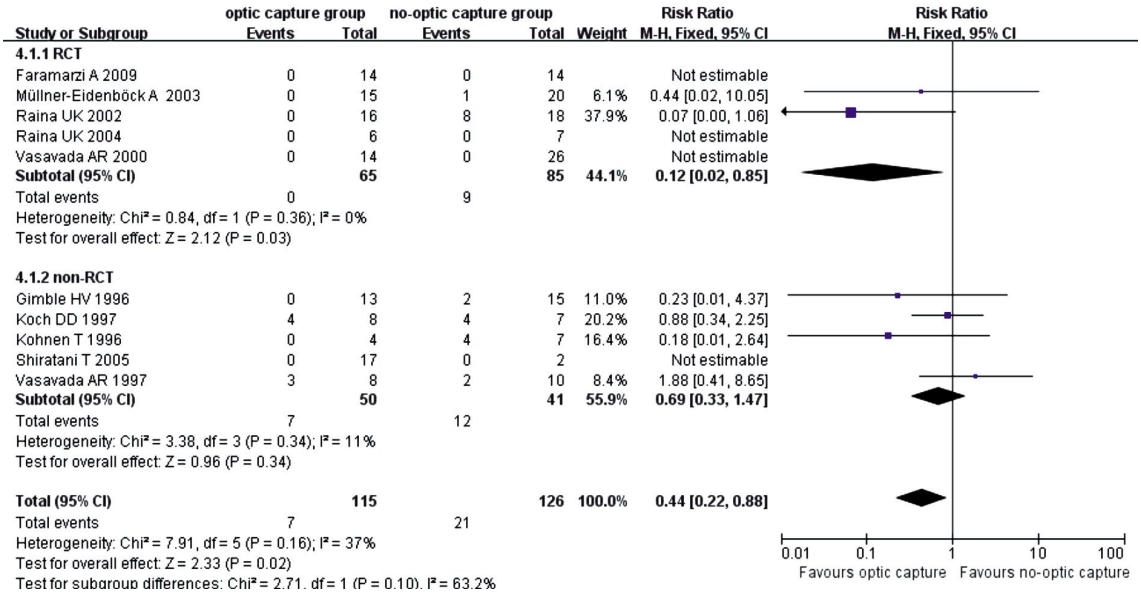

Figure 2 Forest plots for RRs of posterior capsular opacification comparing optic capture to no-optic capture.

Geometric Decentration of IOL Figure 4 presents a forest plot of 3 RCTs involving 88 eyes assessing the effect of preventing geometric decentration after surgery between the two groups. Because the outcome of the heterogeneity test was not significant (I^2=0%, P=0.62), a fixed effects model was adopted. The pooled result indicates that the incidence rates of geometric decentration were significantly different between the two groups (RR: 0.09; 95% CI: 0.02 to 0.46; P=0.004).

Adverse Events The main adverse events after pediatric cataracts in the two groups were PCO, geometric decentration, posterior synechia and deposits on the anterior IOL. Other rare adverse events include proliferating cells on the posterior capsulorhexis margin, glistening on the IOL and suture granuloma [14]. The available data regarding posterior synechia, deposits in the anterior IOL and geometric decentration in RCTs are presented in Table 4.

We analyzed 3 RCTs involving 81 eyes assessing the incidence rates of posterior synechia after surgery for the two groups. Because the outcome of the heterogeneity test was not significant (I^2=25%, P=0.27), a fixed effects model was adopted. The pooled result indicates that the incidence rates of posterior synechia were not significantly different between the two groups (RR: 1.53; 95% CI: 0.84 to 2.77; P=0.17).

Figure 5 presents forest plots of 5 RCTs involving 135 eyes assessing the incidence rates of deposits on the anterior IOL surface early after the surgery and at the last follow-up between the two groups. Because the outcome of the heterogeneity test was not significant (I^2=0%, P=0.53; Figure 5A), a fixed effects model was adopted. The overall results from 5 RCTs indicate that the incidence rate of

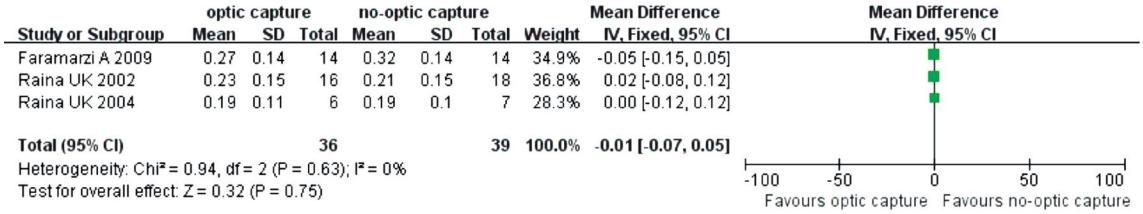

Figure 3 Forest plot for WMD of mean BCVA comparing optic capture to no-optic capture.

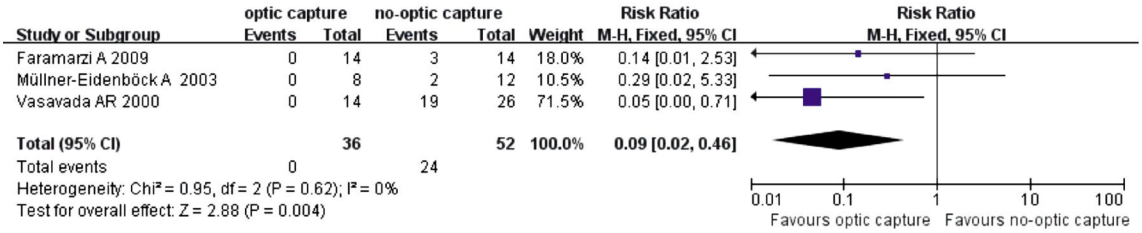

Figure 4 Forest plot for RR of geometric decentration comparing optic capture to no-optic capture.

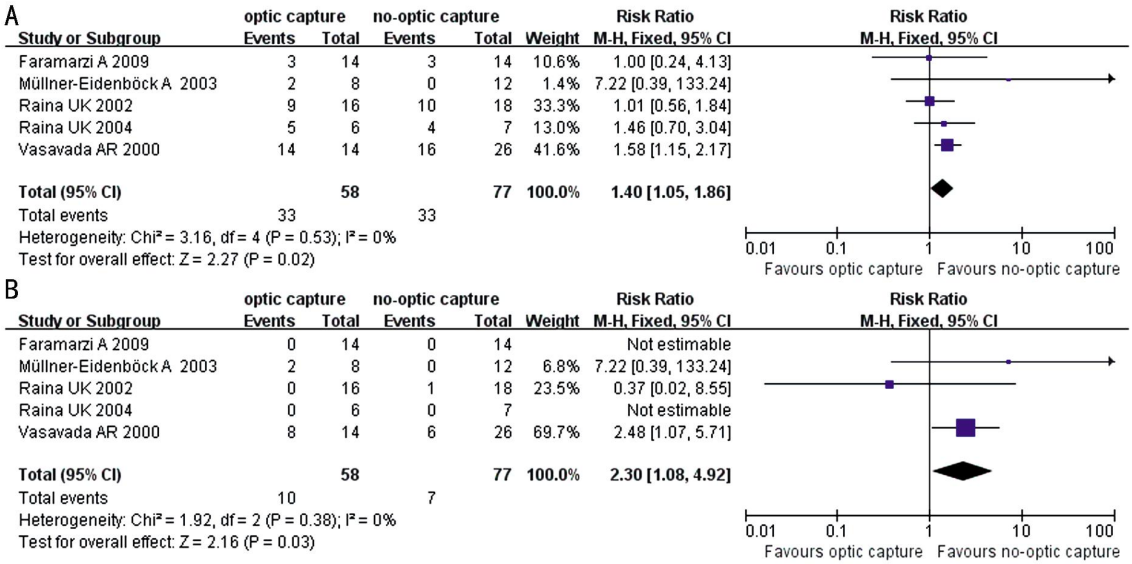

Figure 5 Forest plots for RRs of deposits in anterior IOL comparing optic capture to no-optic capture A: Deposits in the anterior IOL early after surgery; B: Deposits in the anterior IOL at the last follow-up.

deposits in the anterior IOL of the optic capture group was significantly higher compared with the no-optic capture group early after the surgery (RR: 1.40; 95% CI: 1.05 to 1.86; P=0.02; Figure 5A). Because the outcome of the heterogeneity test was not significant (I^2=0%, P=0.38; Figure 5B), a fixed effects model was adopted. The overall results from 5 RCTs indicate that the incidence rate of deposits on the anterior IOL in the optic capture group remained significantly higher compared with the no-optic capture group at the last follow-up (RR: 2.30; 95% CI: 1.08 to 4.92; P=0.03; Figure 5B).

In response to anti-inflammation treatments, the deposits on the anterior IOL early after surgery can gradually disappear [11,13-14]. Among the studies, 2 studies specified the use of steroids[11,13].

Publication Bias To analyze the publication bias, we created funnel plots. For the available data, no publication bias existed in any of the previously mentioned Meta-analyses.

Heterogeneity and Sensitivity Analysis The Meta-analyses of the effects of optic capture on the incidence rates of PCO, BCVA after surgery, posterior synechia, geometric decentration and deposits in the anterior IOL early after surgery and at the last follow-up exhibited no heterogeneity given that the I^2 values in these Meta-analyses were all less than 50%.

A sensitivity analysis for the Meta-analysis of the effect of optic capture on preventing PCO after surgery was accomplished as follows. After excluding the study of Raina *et al* [11], the outcome of the Meta-analysis significantly altered. We further studied the data of the paper. In optic capture group, study has 4 patients operated at ≤4y. Follow-up of these 4 patients varies from 8 to 14.5mo. In no-optic capture group, 6 patients are ≤4 years old. Follow-up of these 6 patients ranges from 12 to 26mo and 5/6 required PCO surgery, and the interval between surgery and PCO ≥2+ formation ranges from 6 to 12mo. Thus the

two sets of data are consistent, and the sensitivity could be merely due to the fact that the study [11] accounted for 37.9% of the weight. The outcome of the sensitivity analysis for the Meta-analysis of the effect of optic capture on the incidence rate of deposits in anterior IOL early after surgery found that 2 studies [7,9] significantly affected the outcome of the Meta-analysis. The outcome of the sensitivity analysis of the Meta-analysis of the effect of optic capture on the incidence rate of geometric decentration found that 1 study [7] significantly affected the outcome of the Meta-analysis. No sensitivity existed in the other Meta-analyses.

Risk of Bias and Quality Assessment We created a risk of bias table for the 5 included RCTs, and no high risk of bias was found. One study [11] specified that the postoperative outcome was assessed by a third party doctor. With regard to the use of random methods, 1 study [11] employed a random digits table, and 1 study [7] adopted the envelope method. Furthermore, 4 studies [9,11,13-14] specified that the operator was a single person. With regard to the method of blinding, we can not get any details.

The quality of evidence from each Meta-analysis was assessed to be high using GRADE recommended by Word Health Organization.

DISCUSSION

This analysis indicates that the application of optic capture in pediatric cataract surgery significantly reduced PCO (P= 0.02) and geometric decentration after surgery (P=0.004) but did not significantly affect BCVA after surgery (P=0.75). The application of optic capture in pediatric cataract surgery did not significantly affect the incidence rate of posterior synechia after surgery (P=0.17) and significantly increased the incidence rates of deposits in the anterior IOL early after surgery (P=0.02) and at the last follow-up (P=0.03). Though the incidence rate of deposits in the anterior IOL early after surgery was significantly higher in the optic capture group compared with the no-optic capture group, the application of optic capture did not seriously increase the incidence rate (RR: 1.40). And several studies [11,13-14,16] have indicated that the incidence rate of deposits in the anterior IOL dramatically decreased at the last follow-up after anti-inflammatory therapy. In the included studies, the total incidence rates of deposits in the anterior IOL decreased from 33/58 to 10/58 in the optic capture group and from 33/77 to 7/77 in the no-optic capture group. Based on the available data, this analysis found that optic capture is a helpful surgical method in preventing PCO and geometric decentration after pediatric cataract surgery with robust efficacy and a high degree of safety.

As the anterior vitrectomy increases the incidence rate of vitreous incarceration in the wound as well as the risk for retinal detachment[1-2] and CME[3]. Some authors attempted to identify a substitute for anterior vitrectomy. Koch and Kohnen [8] in a case control study which was conducted on a small scale and did not adopt random methods found that anterior vitrectomy was the only effective method for preventing or delaying secondary cataract formation in infants and children, but in fact optic capture does not contradict anterior vitrectomy. Optic capture plus anterior vitrectomy should be a preferable surgical method based on all the findings. Nowadays IOL with 4 haptics is popular; however, IOL with 4 haptics is not suitable for pediatric surgery in certain situations. For example, a C-loop IOL may serve as a better choice than an IOL with 4 haptics in a capsular which is too small or is partly fibrotic. Optic capture is especially suitable for C-loop IOL, thus optic capture is helpful in the aforementioned situation. Some special IOLs, for example the bag-in-the-lens which contains a circular concavity on its edge that permits the margins of the posterior capsular hole to be embedded in it, can facilitate the application of optic capture[4]. In addition, optic capture is the method of choice in cases of tear formation in anterior continuous curvilinear capsularhexis (ACCC) [17]. Optic capture is easy to perform, as many authors have shown.

Optic capture of the IOL through the PCCC hole provides a complete fusion of the anterior capsule leaflets, posterior capsule leaflets and the IOL surface. Thus, the capsular space is closed, and the migration of LEC to the center of visual axis is more difficult. The pediatric capsular space is smaller than the adult eye. Implantation of an adult-sized IOL in an infant capsular bag causes ovalization of the PCCC hole and stretches the capsular bag [18]. These effects result in posterior capsule folds and striae. The LEC can migrate toward the center through the capsular folds, leading to PCO. Optic capture closes the capsular space, thereby preventing capsule stretching and PCO. Faramarzi and Javadi [14] found that the incidence rate of geometric decentration in the optic capture group was less than that in the no-optic capture group, although the difference was not significant. Vasavada and Trivedi [7] and Müllner-Eidenböck *et al* [9] reported similar findings. These 3 RCTs are small in scale but were well designed. A Meta-analysis of these 3 RCTs leads to the clear conclusion that optic capture significantly reduces the incidence rate of geometric decentration. Continuous capsular margins lock the IOL optic and potentially prevent it from decentering, whereas in-the-bag implantation may cause IOL decentration given asymmetric contraction of the capsular space [17]. Optic capture could prevent asymmetric contraction, thus preventing the IOL optic from decentering. Although Vasavada and Trivedi [7] reported that posterior synechia formation was significantly increased in the optic capture group, 2 additional RCTs [13-14] found that the posterior synechia was reduced in the optic capture group compared

with the no-optic capture group. This study found that the incidence rate of posterior synechia was reduced in the optic capture group compared with the no-optic capture group; however, the difference was not significant. Thus, whether optic capture increases or decreases the incidence rate of posterior synechia remains controversial. On one hand, optic capture alters the anatomical structure of the posterior capsule. Thus, optic capture may reduce the inflammation, thereby increasing the incidence rate of posterior synechia and deposits on the anterior IOL surface. On the other hand, the optic was captured through the PCCC hole, and thus, optic capture may reduce chaffing and rubbing on the posterior surface of the iris. The IOL implantation site may be another factor that affects the incidence rates of posterior synechia and deposits in the anterior IOL. When the IOL is placed in the sulcus, postsurgical inflammation may be more serious than when the IOL is placed in the bag.

This research only included studies with data available in English abstract or full text; therefore, some language bias may exist. As we only aimed to study the effects of the procedure of optic capture, we did not divide the data into subgroups according to the performance of anterior vitrectomy. Although no heterogeneity existed on all the meta-analyses, the included studies have some heterogeneity in terms of study location, population, basal condition and surgical techniques. Though Doctor of Statistics solved difficult data problems, relevant data were relatively complex. A delay between the literature search and publication was inevitable.

Large-scale, multicenter, randomized controlled clinical trials aimed at studying infants less than 1.5y in age should have additional effects. Specific IOLs for pediatric cataract should be developed to work with optic capture. All of these will induce resurgent studies on optic capture and improve the outcome of pediatric cataract surgery.

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