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ARTICLE

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Intravitreal dexamethasone implant versus anti-vascular endothelial growth factor therapy combined with cataract surgery in patients with diabetic macular oedema: a systematic review with meta-analysis

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OBJECTIVE: To compare outcomes of cataract surgery combined with either anti-Vascular Endothelial Growth Factor (anti-VEGF) therapy or dexamethasone implant (DEX) in patients with diabetic macular oedema (DMO).

METHODS: Pubmed and Embase databases were searched for studies reporting outcomes of diabetic cataract surgery combined with either anti-VEGF or DEX, with a follow-up ≥3 months. The primary outcome was the mean change in central macular thickness (CMT). Mean change in best corrected visual acuity (BCVA) was considered as a secondary outcome. The mean difference between baseline and post-treatment values (MD) with 95%-Confidence Interval (95%CI) was calculated and meta-analyses were performed.

RESULTS: Nine-teen studies were included, 8 in the DEX group and 11 in the anti-VEGF group. A significant reduction of macular thickness was shown in the DEX group at 3 months (MD = −98.35 µm; 95% CI, −147.15/−49.54), while mean CMT change was non-significant in the anti-VEGF group (MD = −21.61 µm; 95% CI, −59.46/16.24; test of group differences, $P < 0.001$). At 3 months, no difference in visual gain was found between the two groups ($P = 0.13$).

CONCLUSIONS: In DMO patients, cataract surgery combined with DEX seems to provide better anatomical outcomes compared with cataract surgery combined with anti-VEGF therapy. However, our evidence was limited by significant heterogeneity. Randomised trials comparing these two different combined approaches are warranted.

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INTRODUCTION

Cataract surgery represents one of the most common surgical procedures worldwide [1]. About 20% of patients undergoing cataract surgery are diabetic at the time of surgery [2]. The management of diabetic cataract can be challenging because the surgery may increase diabetic retinopathy and/or maculopathy (i.e. diabetic macular oedema, DMO) [3, 4]. This becomes even more relevant as one out of four diabetic patients scheduled for cataract surgery is already affected by DMO [2].

Worsening of DMO following cataract surgery is related to post-surgical inflammation with overexpression of vasoactive and inflammatory cytokines, including vascular endothelial growth factors (VEGFs) [5–7]. Additionally, the risk of macular oedema post cataract surgery is associated with the pre-operative diabetic retinopathy grade. The risk being higher in more advanced stages, such as moderate and severe non proliferative diabetic retinopathy [5].

In this context, both intravitreal anti-VEGF agents and corticosteroids have been used in combination with cataract surgery to reduce the risk of post-surgical exacerbation of diabetic retinopathy and maculopathy [8–11].

Intravitreal anti-VEGFs combined with cataract surgery have been demonstrated to be effective as prophylactic treatment to prevent a worsening of diabetic retinopathy in patients with and without DMO [11–13].

More recently, increasing attention has been drawn to the use of the 0.7 mg dexamethasone intravitreal implant (DEX) combined with cataract surgery in patients with DMO. Anatomic and functional outcomes of this combined procedure seem promising [8, 9, 14–16].

Whether the approach of combining cataract surgery with DEX is comparable or not with cataract surgery combined with anti-VEGF agents in patients with DMO hasn't been investigated yet.

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The purpose of this systematic review is to gather available evidence on diabetic cataract surgery combined with either intravitreal anti-VEGF agents or DEX implant, conducting a meta-analysis on anatomic and visual outcomes. Comparison of pooled results could help to have useful insights in this issue, providing support to clinical practice.

MATERIALS AND METHODS

This systematic review was conducted in accordance with the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) [17] and with those of the Cochrane Handbook [18] (PRISMA Checklist available online as Supplementary Table S1).

Search method

Studies reporting outcomes of cataract surgery in diabetic patients combined with administration of either intravitreal anti-VEGF drugs or intravitreal dexamethasone implant were systematically searched. An electronic search was performed on Pubmed and Embase databases, from their inception to 28th March 2021. A detailed search strategy is available online (Supplementary Table S2 available online). Reference lists of included studies and review articles on the same topic were also screened.

Eligibility criteria

To be included, studies had to satisfy the following criteria: a) to include patients with DMO undergoing cataract surgery; b) to combine cataract surgery with intravitreal injection of either an anti-VEGF agent (such as bevacizumab, ranibizumab or aflibercept) or a 0.7 mg dexamethasone implant; c) to have a follow-up of 3 months or longer; d) to report visual and/or anatomic outcomes. Any study design apart from case report was considered. Abstracts were excluded as well as articles published in non-peer reviewed journals or in a language different from English. No restriction on publication status and date was imposed.

Eyes receiving cataract surgery combined with intravitreal anti-VEGF injection were included in the anti-VEGF group. Eyes receiving cataract surgery combined with intravitreal DEX implant were included in the DEX group. To be considered as a combined procedure the intravitreal injection of anti-VEGF or DEX had to be administered in combination with cataract surgery, either at the beginning or at the end of the procedure.

The primary outcome of the present meta-analysis was the mean change in optical coherence tomography (OCT) central macular thickness (CMT) at 3-months follow-up in eyes with DMO at baseline in both groups. Secondary outcomes included: (i) one-month mean CMT change; (ii) mean change in best corrected visual acuity (BCVA) at different follow-ups;(iii) mean intraocular pressure (IOP) change in the DEX group; (iv) proportion of eyes requiring IOP-lowering drops for IOP rise in the DEX group. Central macular thickness was defined as the average thickness of the 1 mm fovea-centred circle [19].

Data collection and risk of bias assessment

Eligibility of identified reports was evaluated by two investigators (P.M. and M.F.) independently. In case of discordance, a third investigator (M.R.) was involved to reach agreement. When clarifications or additional information were needed, the authors of the study were contacted. Data of each included study was analysed and extracted by the same two investigators (P.M. and M.F.) independently. For each study, the following items were extracted: first author, publication year, design, mean age, number of patients, follow-up length. For both the anti-VEGF and DEX cohorts, the following items were collected: number of patients, mean age, type of anti-VEGF agent, number of injections, follow-up length, BCVA change, CMT change, mean IOP, rate of IOP rise and rate of eyes receiving IOP-lowering drops and adverse events. If more than one article reported outcomes of the same patient cohort, the one with either better quality or longer follow-up was included in this systematic review.

Risk of bias assessment was based on the Cochrane collaboration tool for randomised clinical trials [18]. The methodological item for non-randomised studies (MINORS) scale was used to evaluate non-randomised studies [20], considering a score ≥9 as low-to-moderate risk of bias [21].

Statistical analysis

For continuous outcomes (i.e., BCVA and CMT), pooled effect size was obtained through meta-analysis and reported as the mean difference between baseline and post-treatment values (i.e., pre-post mean difference, MD) with 95% Confidence Interval (95%CI). Heterogeneity across studies was tested and measured using the Q-statistics and the I^2 index, respectively. In presence of significant heterogeneity (p value for Q-statistics < 0.1 and $I^2 > 50\%$), a random effect model with the DerSimonian-Laird method was applied. Subgroup analyses were performed to compare the effect of intravitreal anti-VEGF drugs and intravitreal dexamethasone implant. Meta-regression was applied for evaluating factors associated with each outcome and eventually for identifying methodological (i.e., study design, mean age, follow-up length, type of anti-VEGF agent and number of injections) and clinical (i.e., BCVA and CMT values at the baseline) characteristics acting as heterogeneity sources.

For outcomes related to IOP change, the meta-analyses were limited to patients treated with DEX implant. The IOP change was considered as a continuous outcome and analysed as pre-post MD. We also examined the proportion of eyes requiring IOP-lowering drops for IOP rise. Specifically, the score confidence intervals were constructed for each individual study and proportions were pooled using the random-effects model [22]. The extent of publication bias was explored by funnel plots and tested using the Egger's test. Statistical analyses were performed using STATA (version 16). All the analyses were two-tailed, with significance level $\alpha < 0.05$ if not otherwise stated.

RESULTS

The flow chart of study selection process is shown in Supplementary Fig. 1 (available online as supplementary material). A total of 1417 articles were identified following electronic search, of which 315 were duplicates. Abstracts and titles of 1102 reports were screened by applying eligibility criteria, of which 1041 were excluded. A total of 61 potentially eligible studies were full-text evaluated, of which 42 did not fully satisfy inclusion criteria and were ruled out. Nine-teen studies were included [8–10, 12, 14–16, 23–34].

Characteristics of included studies

Of the 19 included studies, 8 reported on DEX combined with cataract surgery [8–10, 14–16, 23, 24] and 11 reported on anti-VEGF drugs combined with cataract surgery [12, 25–34]. Publication year ranged from 2009 to 2021. In all cases cataract surgery involved phacoemulsification technique with intraocular lens implant. A total of 216 eyes were included in the DEX group. Characteristics of studies included in the DEX group are shown in Supplementary Table S3 (available online as supplementary material). All studies but one [10] provided data on visual outcome and macular thickness at 1 month postoperatively: Agarwal et al. [10] reported 6-week outcomes, which, however, were included in our 1-month analysis. All studies but one [14] provided data on 3-month outcomes: Corbelli et al. [14] reported 4-month outcomes, which, however, were included in our 3-month analysis. Information on IOP rise after DEX implant is shown in Supplementary Table S3 (available online as supplementary material). High IOP cases were managed in all cases with IOP-lowering drops and no surgery was required. No cases of endophthalmitis were recorded amongst the DEX studies. A total of 301 eyes were included in the anti-VEGF group. Characteristics of studies included in the anti-VEGF group are shown in Supplementary Table S4 (available online as supplementary material). The intravitreal anti-VEGF agent combined with cataract surgery was bevacizumab in 9 trials and [12, 25–32] ranibizumab in 2 [33, 34]. In all studies except one [28], no additional intravitreal anti-VEGF injection were administered throughout the study period; in Kandasamy's trial a mean of 1.42 injections of bevacizumab were given during a 6-month follow-up [28]. Yumusak and Ornek [33] included in their study three different groups: eyes receiving an intravitreal ranibizumab injection 2 weeks before cataract surgery; eyes receiving an intravitreal ranibizumab injection at the same time of cataract surgery; eyes receiving an intravitral ranibizumab injections 2 weeks after

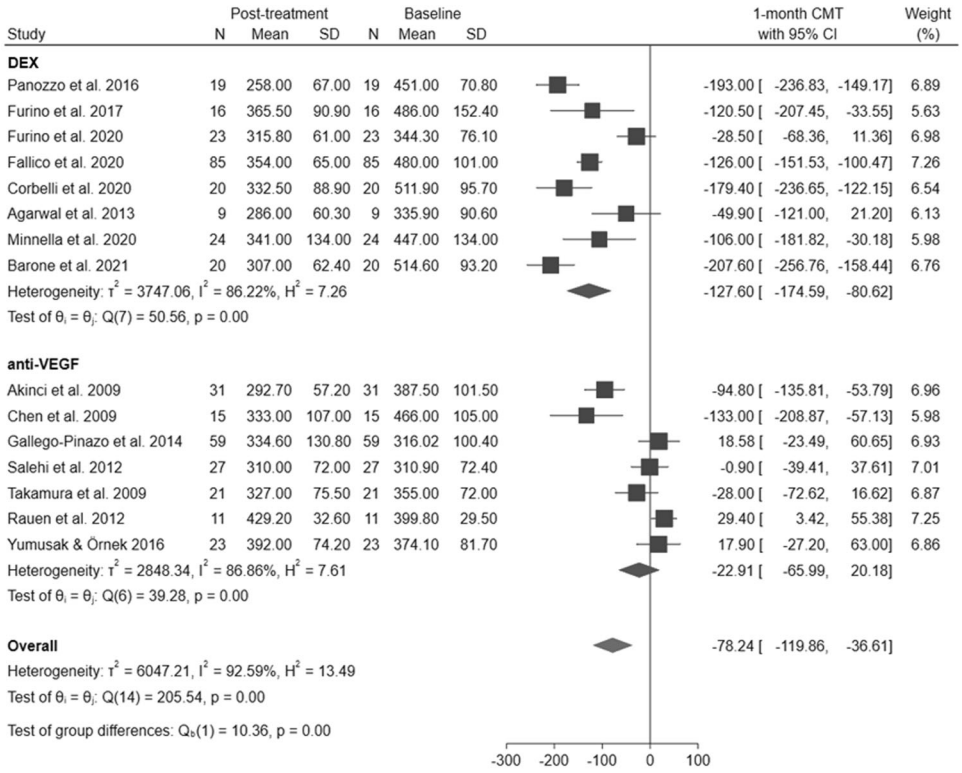

Fig. 1 One-month central macular thickness (CMT) change. Comparison of central macular thickness (CMT) change at one month after cataract surgery combined with dexamethasone implant (DEX) or anti-vascular endothelial growth factor (anti-VEGF) in patients with diabetic macular oedema.

cataract surgery. Only the cohort receiving an intravitreal ranibizumab injection in combination with cataract surgery was included in the present systematic review. Complications recorded in the studies included in the anti-VEGF group are shown in Supplementary Table S4 (available online as supplementary material). No cases of endophthalmitis were reported.

Quality assessment and risk of bias

Risk of bias assessment for RCTs is shown in Supplementary Figs. 2 and 3 (available online as supplementary material). Random sequence generation was judged as low risk in 4 trials [10, 15, 27, 28] and unclear risk in 3 trials [12, 29, 30]. Allocation concealment was evaluated as unclear risk for bias in all included RCTs [10, 12, 15, 27–30]. Performance bias was at low risk in 2 studies [28, 30], unclear risk in 4 studies [10, 12, 27, 29], high risk in one [15]. Detection bias was considered as low risk and unclear risk in 5 [10, 27–30] and 2 trials [12, 15], respectively. Risk for attrition bias was low in 3 trials [27, 28, 30] and unclear in the other 4 ones [10, 12, 15, 29]. Reporting bias was judged as low risk in one study [28] and unclear risk in 5 studies [10, 15, 27, 29, 30]. Cheema's trial [12] was considered as high risk for reporting bias because no data on baseline CMT were provided. Risk for other bias was low in 3 studies [27, 28, 30] and unclear in 3 studies [10, 12, 15]. Salehi's trial [29] was considered as high risk for other bias because of a discrepancy in reporting baseline CMT values between main text and tables. According to MINORS scale, all non-randomised studies were given a score ≥12 (Supplementary Table S5, available online). Funnel plots for 3-month CMT and BCVA outcomes are shown in Supplementary Figs. 4 and 5 (available online as supplementary material).

Central macular thickness change

Data from 15 studies, 8 In the DEX group and 7 in the anti-VEGF group, were pooled together for mean CMT change at 1 month (Fig. 1). A total of 216 eyes and 187 eyes were included in the DEX group and anti-VEGF group, respectively. At 1 month, mean CMT significantly decreased in the DEX group, with a mean difference of −127.60 µm (95% CI = −174.59–−80.62), while mean CMT change was non-significant in the anti-VEGF group (MD = −22.91 µm, 95% CI = −65.99–20.18). Test of group differences revealed a greater reduction of macular thickness in the DEX group compared with the anti-VEGF group ($P < 0.001$). A significant heterogeneity was found in both groups (DEX group, $I^2 = 86\%$, $P < 0.001$; anti-VEGF group, $I^2 = 87\%$, $P < 0.001$).

Data from 16 studies, 7 In the DEX group and 9 in the anti-VEGF group, were pooled together for mean CMT change at 3 months (Fig. 2). A total of 192 eyes and 228 eyes were included in the DEX group and anti-VEGF group, respectively. Three-month analysis revealed a significant reduction of macular thickness in the DEX group (MD = −98.35 µm; 95% CI, −147.15–−49.54), while mean CMT change was non-significant in the anti-VEGF group (MD = −21.61 µm; 95% CI, −59.46–16.24). Test of group differences showed a greater reduction in the DEX group compared with the anti-VEGF group (test of group differences, $P < 0.001$). Heterogeneity was significant in both groups (DEX group, I^2 87%, $P < 0.001$; anti-VEGF group, I^2 86%, $P < 0.001$). Results from the meta-regression did not reveal associations of other methodological and clinical characteristics with CMT change (P values > 0.05).

Visual outcome

Data from 16 studies, 8 for each group, were pooled together for mean BCVA change at 1 month. A total of 216 eyes and 201 eyes were included in the DEX group and anti-VEGF group, respectively (Fig. 3). Visual improvement was significant in both groups. A mean gain of 14.93 letters (95% CI, 12.66–17.21) was shown in the DEX group. A better visual improvement was found in the anti-VEGF group, with a mean gain of 23.46 letters (95% CI, 17.91–29.00; test of group differences, $P = 0.01$). Heterogeneity

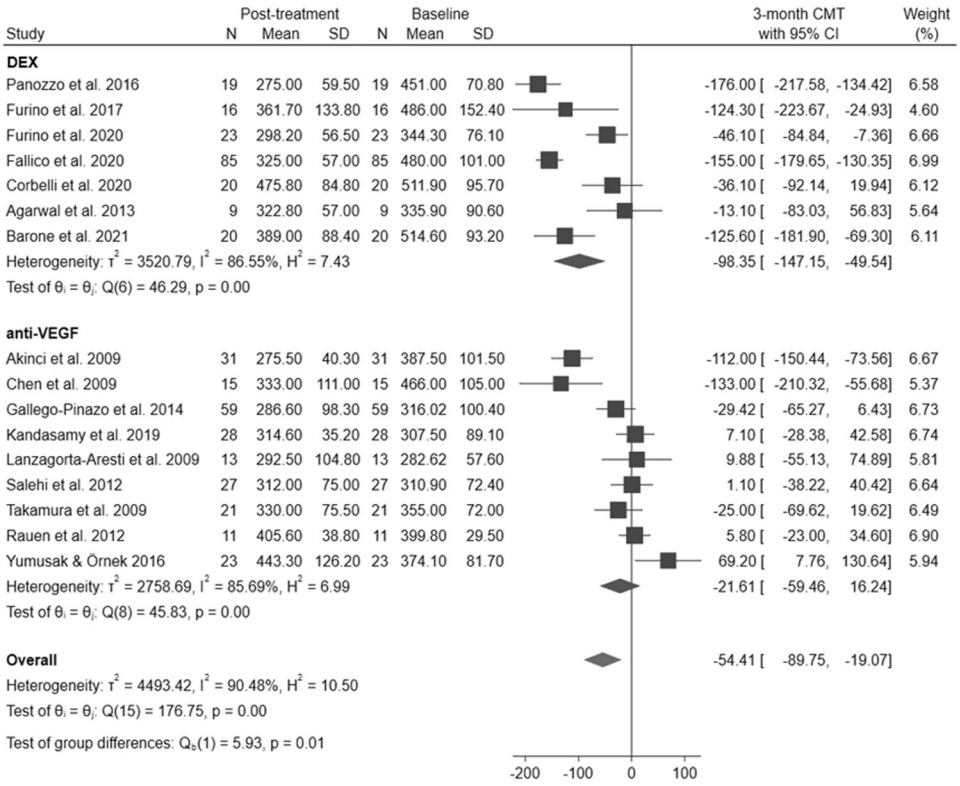

Fig. 2 Three-month central macular thickness (CMT) change. Comparison of central macular thickness (CMT) change at 3 months after cataract surgery combined with dexamethasone implant (DEX) or anti-vascular endothelial growth factor (anti-VEGF) in patients with diabetic macular oedema.

was low in the DEX group (I^2 12%, $P = 0.52$), while this was significant in the anti-VEGF group (I^2 91%, $P < 0.001$).

Data from 19 studies, 8 in the DEX group and 11 in the anti-VEGF group, were pooled together for mean BCVA change at 3 months (Fig. 4). A total of 216 eyes and 301 eyes were included in the DEX group and anti-VEGF group, respectively. Visual improvement was significant in both groups and no difference was found between them (test of group differences, $P = 0.13$), with a mean gain of 16.36 letters (95% CI, 13.84–18.89) and 21.32 letters (95% CI, 15.51–27.14) in the DEX group and anti-VEGF group, respectively. Heterogeneity was low in the DEX group (I^2 32%, $P = 0.26$), while this was significant in the anti-VEGF group (I^2 92%, $P < 0.001$). Results from the meta-regression did not reveal associations of other methodological and clinical characteristics with BCVA change (P values > 0.05).

IOP change

Intraocular pressure change and pooled proportion of eyes with high IOP were analysed in the DEX group. For IOP change, data from 4 studies (68 eyes) and 6 studies (172 eyes) were pooled together at 1 month and 3 months, respectively (Supplementary Figs. 6 and 7, available online). A mean increase of 0.54 mmHg (95% CI, −1.11–2.18, $P = 0.52$) and 1.20 mmHg (95% CI, 0.27−2.12, $P = 0.01$) was demonstrated at 1 month and 3 months, respectively. High heterogeneity was found at both 1-month and 3-month follow-ups (1 month, I^2 78%, $P < 0.001$; 3 months, I^2 65%, $P = 0.01$). Pooled proportion of eyes with high IOP was 9.4% (95% CI, 5.4–14.2%) (Table 1).

DISCUSSION

The present study sought to explore the efficacy of either intravitreal anti-VEGF drugs or DEX implant administered at the time of cataract surgery in eyes with DMO, comparing these two different combined treatments. Cataract surgery combined with DEX implant provided better anatomical outcomes compared with anti-VEGF drugs, while no difference in terms of visual outcome was found at 3 months post-operatively.

The issue as how to deal with cataract surgery in diabetic patients has gained increasing attention in the era of intravitreal therapy. On the one hand, DMO has been demonstrated to get worse following uneventful cataract surgery. Macular thickness was shown to increase by 11% to 30% in 22–25% of diabetic patients following cataract surgery [4, 35]. A large real-world study including almost 5000 diabetic eyes reported an increase in the rate of treatment-requiring DMO following cataract surgery, from 2.9% in the year before surgery to 5.3% in the year after surgery [5]. On the other hand, diabetic patients without DMO are at higher risk of cystoid macular oedema following cataract surgery [36]. These events have been related to the postsurgical inflammatory state that contributes to the breakdown of an already impaired blood retinal barrier.

In this scenario, physicians strived to develop new strategies aimed at reducing the risk of DMO worsening after phacoemulsification surgery. In particular, combining cataract surgery with the administration of intravitreal drugs that are used for DMO treatment, such as anti-VEGF agents or DEX, has shown positive functional and anatomical outcomes. Such a combined procedure has become fairly common in clinical practice when approaching cataract surgery in patients with DMO.

Anti-VEGF agents have been used in combination with cataract surgery in diabetic patients for many years [11–13, 25, 26, 28, 37]. The rationale for anti-VEGF use is related to a VEGF overexpression in diabetic patients after cataract surgery [3, 38]. Ocular VEGF levels have been reported to peak postoperatively on day one, settling down to normal levels at 1 month [3]. This timing would make reasonable a combined administration of intravitreal anti-VEGF with cataract surgery [11].

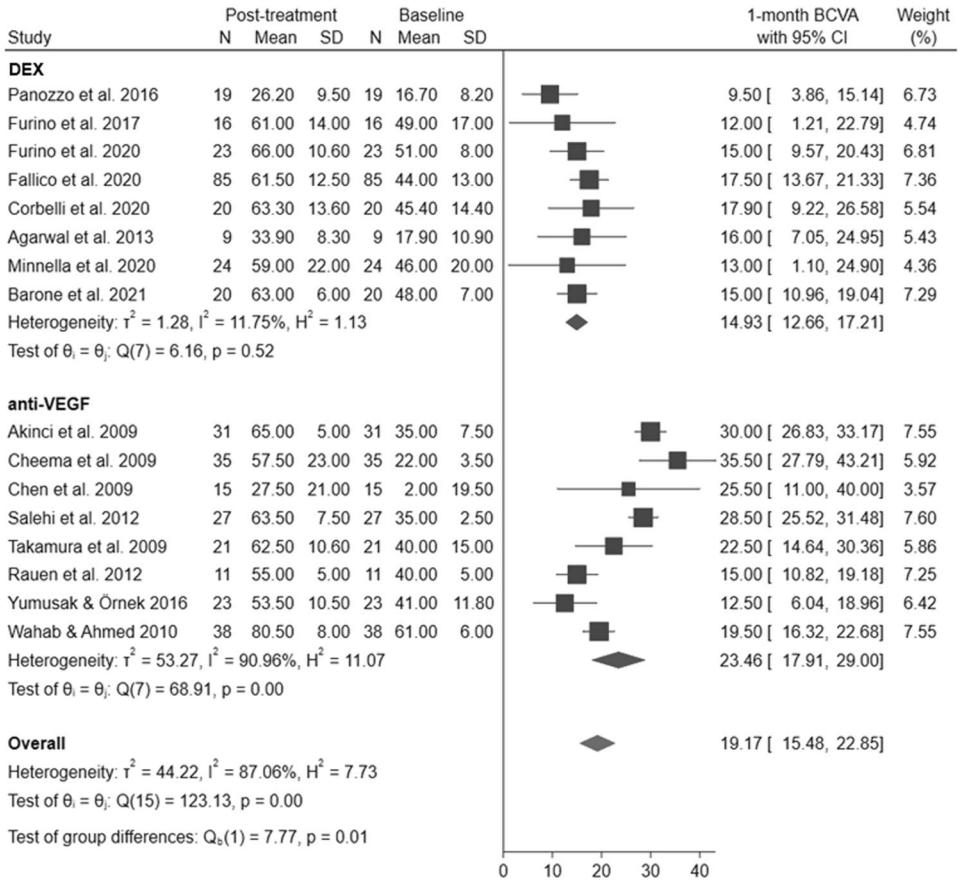

Fig. 3 One-month best corrected visual acuity (BCVA) change. Comparison of best corrected visual acuity (BCVA) gain at one month after cataract surgery combined with dexamethasone implant (DEX) or anti-vascular endothelial growth factor (anti-VEGF) in patients with diabetic macular oedema.

More recently, DEX has been combined with cataract surgery in patients with DMO [9, 14–16, 23, 24]. Both its long-lasting effect and its anti-inflammatory properties make this implant suitable for combining its use with cataract surgery [9, 39]. The purpose is to reduce postsurgical inflammation, which represents the trigger for DMO worsening [9]. The slow-release formulation of the implant allows it to have its effect for 4 months [39], covering the 12-week postoperative period at risk of DMO worsening [9]. For these characteristics, DEX has been also used in combination with other types of intraocular surgery to prevent macular oedema and postoperative inflammation [40–43]. In term of timing, most commonly DEX is given in combination with cataract surgery. A few studies described its use in eyes with DMO one month before cataract surgery [9, 44], but clinical outcomes seem better when given in combination with cataract surgery [9].

To the best of our knowledge, no study has compared outcomes of cataract surgery combined with anti-VEGF agents versus DEX implant in diabetic patients. Feng et al. conducted a meta-analysis of 6 studies on the use of intravitreal bevacizumab in combination with cataract surgery in diabetic patients [11]. Their analyses showed favourable anatomical and functional outcomes following bevacizumab administration at the time of cataract surgery. However, the authors pooled together eyes with DMO and eyes without DMO [11]. This could be a relevant limitation of their work. Additionally, they analysed a preoperative-postoperative change of a single cohort with no control group.

In the present systematic review, only eyes with DMO were included. Our findings showed a greater reduction of macular thickness in the DEX group compared with the anti-VEGF group, both at 1 and 3 months postoperatively. Importantly, in the anti-VEGF group, macular thickness reduction was not significant at both 1 and 3 months (Figs. 1 and 2). This would suggest that anti-VEGF drugs help to prevent macular thickening rather than providing a significant CMT reduction.

A significant visual gain was shown in both the DEX group and the anti-VEGF group at 1 month and 3 months postoperatively (Figs. 3 and 4). When comparing the two combined approaches, no difference in visual improvement was found at 3 months (Fig. 4), while a better visual outcome was demonstrated in the anti-VEGF group at one month (Fig. 3). Thus, eyes undergoing cataract surgery in combination with anti-VEGF drug had no significant change in postoperative macular thickness, whilst 1-month visual gain was greater compared with the DEX group.

This discrepancy between anatomical and functional outcomes at 1-month follow-up is not surprising and needs to be interpreted cautiously. Visual outcome is likely to be affected by many variables. Long standing DMO is likely to be associated with a damage to macular microstructure. Therefore, DMO duration should be taken into account. A more advanced diabetic retinopathy stage as well as the presence of macular ischaemia are other clinical variables that can lead to a poorer visual prognosis. Data provided by included studies did not allow to conduct stratified analyses aimed at testing these confounding factors. Additionally, cataract surgery itself has a great influence on visual outcome, yielding a relevant visual gain. In this context, macular thickness change is supposed to be a more reliable indicator of intravitreal treatment effectiveness compared with visual outcome. For such a reason, we decided to consider the 3-month macular thickness change as a primary outcome

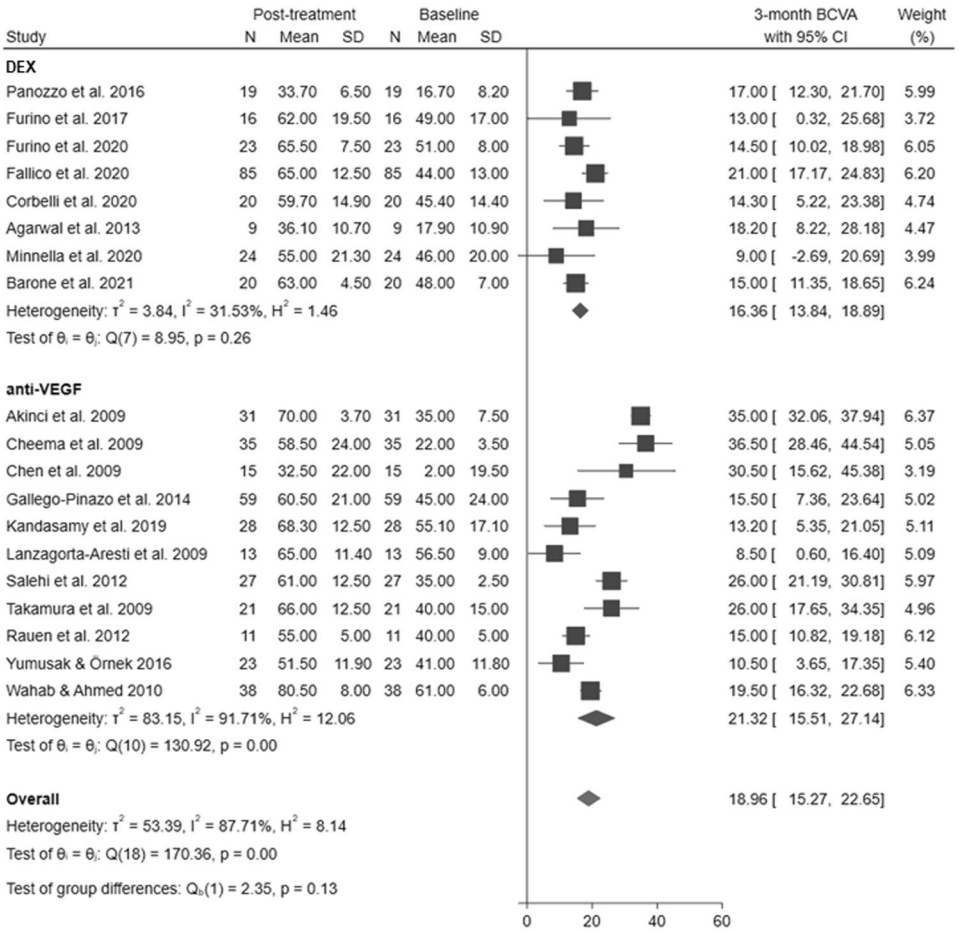

Fig. 4 Three-month best corrected visual acuity (BCVA) change. Comparison of best corrected visual acuity (BCVA) gain at 3 months after cataract surgery combined with dexamethasone implant (DEX) or anti-vascular endothelial growth factor (anti-VEGF) in patients with diabetic macular oedema.

Table 1. Proportion of events of high intraocular pressure (IOP) after treatment with dexamethasone implant combined with cataract surgery.

Study	High IOP (95% CI)	Weight
Panozzo et al. 2016	15.8% (3.4–39.6)	9.3%
Furino et al. 2017	6.3% (0.2–30.2)	7.8%
Furino et al. 2020	4.4% (0.1–22.0)	11.2%
Fallico et al. 2020	11.8% (5.8–20.6)	40.6%
Corbelli et al. 2020	5.0% (0.1–24.9)	9.7%
Minnella et al. 2020	16.7% (4.7–37.4)	11.6%
Barone et al. 2021	5.0% (0.1–24.9)	9.7%
Pooled proportion	9.4% (5.4-14.2)	100%

IOP intraocular pressure, *CI* confidence intervals.

measure, while visual change was explored as a secondary outcome.

Both intravitreal anti-VEGF drugs and DEX have a good safety profile [39, 45]. Endophthalmitis represents the most severe complications of intravitreal therapy, but it is a rare event [46]. No case of endophthalmitis has been reported in the studies included in the present review. Some concern has been raised about a theoretical risk of cardiovascular accidents and increased mortality in diabetic patients receiving an intense intravitreal anti-VEGF treatment on long term [47]. No relevant systemic adverse events have been recorded in the included studies. The two main adverse event related to DEX administration are cataract development and intraocular pressure rise [39]. In case of DEX use in combination with cataract surgery, our pooled analysis yielded a 9.5% rate of postoperative high IOP. This figure is lower compared with the 30% rate of ocular hypertension reported in clinical practice following traditional DEX use [48]. Our meta-analysis revealed that mean IOP increased by 0.5 mmHg and 1.2 mmHg at one month and at 3 months, respectively. Even if the 3-month change was statistically significant, this could be considered of low interest from a clinical viewpoint given the 95% confidence interval of 0.3–1.20 mmHg. Additionally, a high IOP was managed in all cases with IOP-lowering drops.

The following limitations characterised the present meta-analysis. First, significant heterogeneity was found among included studies for almost all explored outcomes. Only the 1-month and 3-month visual outcomes in the DEX group was not affected by heterogeneity. A possible explanation for the high heterogeneity could be related to the influence of different clinical variables on study outcomes. For instance, a few studies included patients naïve with regard to intravitreal therapy, while most studies enroled both naïve and chronic DMO eyes. Another clinical variable that could have had an influence on the heterogeneity for visual outcome is the cataract grading: no information on it was provided. It is highly likely this was not homogenous among included studies. A high heterogeneity could be secondary to clinical differences. Moreover, methodological issues can affect heterogeneity as well. Included studies featured different study

designs contributing to an increase in heterogeneity level. Included studies did not provide individual data. Consequently, stratified analyses aimed at ruling out possible confounders could not be conducted.

We tried to address this issue by applying meta-regressions of methodological and clinical characteristics on CMT and BCVA changes. Yet, none of the variables seemed associated with these outcomes. Another possible limitation is the relatively small number of studies included. This limitation may also partially explain non-significant results obtained through meta-regressions. However, more than 400 eyes were included for the primary outcome analyses, which is a reasonable sample size. Additionally, meta-analyses are more powerful compared with a single report, presenting more accurate confidence intervals [49, 50].

In conclusion, our findings demonstrated, even if with limited evidence, that cataract surgery combined with DEX implant seems to provide better anatomical outcomes in patients with DMO compared with cataract surgery combined with intravitreal anti-VEGF therapy. Indeed, use of a DEX implant reduced macular thickness, while anti-VEGF therapy prevented DMO from worsening. Further randomised trials that would directly compare these two different combined approaches are warranted to corroborate these results.

Summary

What was known before

- Management of cataract surgery in patients with diabetic macular oedema (DMO) is challenging because of possibility of DMO worsening.
- Intravitreal anti-vascular endothelial growth factor (anti-VEGF) agents and dexamethasone implant have been combined with cataract surgery to prevent DMO worsening.

What this study adds

- Our analyses showed that intravitreal dexamethasone implant administered in combination with cataract surgery in patients with DMO provides better anatomical outcomes over a 3-month period compared with intravitreal anti-vascular endothelial growth factors.

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AUTHOR CONTRIBUTIONS

Conceptualization, MR, MF, AA, ALotery; methodology, AM, EB, MB, GF, ALongo; investigation, MF, PM, ALongo, TA; data curation: MF, PM, AM, GF, MB, GP, AR, VB; writing—original draft preparation, VB, AR, CF, GC, EB; writing—review and editing, all authors; supervision, TA, ALotery, MR, AA. All authors have read and agreed to the published version of the manuscript.

COMPETING INTERESTS

AL has consulted for Novartis Pharmaceuticals, Allergan, Janssen and Gyroscope Therapeutics. Other authors declare no competing interests.

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