Effect of dexamethasone intravitreal implant for refractory and treatment-naive diabetic macular edema in Taiwanese patients

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Abstract

Background: Dexamethasone (DEX) implant has been shown to improve visual and anatomic function in patients with diabetic macular edema (DME). The purpose of this study was to investigate the efficacy and safety of DEX implant between refractory and naive eyes with DME.

Methods: We retrospectively reviewed data from pseudophakic patients with center-involved DME who received DEX implant (1 + as needed retreatment) from May 2015 to May 2017. Baseline clinical characteristics, changes in best-corrected visual acuity (BCVA) and central foveal thickness (CFT) were analyzed and compared between the two groups. Adverse events were recorded.

Results: Thirty-four eyes of 31 patients refractory to anti–vascular endothelial growth factor agents and 41 eyes of 38 treatment-naive patients were reviewed. Baseline characteristics were comparable between the two groups ($p > 0.05$). In the refractory eyes, significant improvements in both BCVA and CFT were observed at 1 month post DEX implant and sustained throughout 6 months. Mean change from baseline in BCVA at 6 months was –0.17 ± 0.35 logMAR (7.29 ± 16.22 letters) and 155.44 ± 112.67 μm in CFT. Similar trends of improvement were seen in treatment-naive eyes; however, the visual improvement (–0.30 ± 0.29 logMAR [16.42 ± 14.38 letters]) was significantly better than the refractory group, with significantly less injections (1.54 ± 0.49 versus 1.82 ± 0.38, $p = 0.007$). Between-group changes in CFT were comparable. No serious ocular complications occurred, and about a quarter of the patients had elevated intraocular pressures that were manageable with topical medications.

Conclusion: To our knowledge, this was the first study comparing DEX implant between treatment-naive and refractory Asian patients with DME. Intravitreal DEX implant can effectively treat refractory and treatment-naive patients with DME. In addition, superior visual outcomes were observed in the naive group comparing to the refractory group following DEX implant treatment in Taiwanese pseudophakic eyes with DME.

Keywords: Dexamethasone; Diabetic retinopathy; Intravitreal injection; Macular edema; Refractory; Treatment-naive

1. INTRODUCTION

There are 35% of patients with diabetes worldwide with some forms of diabetic retinopathy (DR); and 7% with diabetic macular edema (DME), the most common cause of DR-induced vision loss in working-aged adults.[1] The current guidelines recommend early intensive anti–vascular endothelial growth factors (VEGFs) as the first-line therapy for center-involving DME with visual impairment, with the choice of agent based on baseline visual acuity (VA) and subsequently at fixed or individualized dosing depending on VA and optical coherence tomography (OCT) findings.[2,3]

Although many DME patients benefit from anti-VEGF therapy, refractory cases remain a clinical challenge. Data from the DRCR.net Protocol I study showed that the prevalence of chronic persistent DME through 3 years was about 40% in ranibizumab-treated eyes.[4] Additionally, nearly 40% of eyes treated with ranibizumab and prompt/deferred laser therapy had suboptimal best-corrected visual acuity (BCVA) improvements at 12 weeks, and these eyes showed poorer long-term visual outcomes.[5] In the DRCR.net Protocol T, 44% to 68% of patients treated with anti-VEGFs manifested chronic persistent DME over 2 years.[6] In real-life practice, anti-VEGF therapy resulted in poorer VA gains than those reported by interventional studies such as RESOLVE, RISE/RIDE, VIVID, VISTA, and RESTORE.[7]

Inflammatory cytokines and chemokines play a major role in the pathogenesis of DME by mechanisms that lead to breakdown of the blood-retinal barrier (BRB). Although VEGF is involved in breaking down the BRB and is targeted in DME, the suboptimal response to anti-VEGFs suggests the involvement of other inflammatory mediators.[8,9] Dexamethasone (DEX) intravitreal implant (Ozurdex®; Allergan Inc., Irvine, CA, USA) is a biodegradable

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implant with sustained-release dexamethasone that suppresses inflammation. Clinical trials have demonstrated improved VA and reduced edema in DME following DEX implant treatment. The Macular Edema: Assessment of implantable Dexamethasone in Diabetes (MEAD) study showed a significantly higher proportion of patients with ≥15-letter improvement in BCVA treated with DEX implants than sham.[10] In the 2-year BEVORDEX study, the proportion of eyes with ≥10-letter visual gain was the same between those treated with DEX implant and bevacizumab.[11,12] Furthermore, real-world studies of DEX implant for naive and refractory DME showed seemingly better visual gains across baseline VA subgroups than interventional trials.[7] In the subgroup analyses of a large study with over 3-year follow-up, naive eyes with DME treated with DEX implant showed a significantly longer time to retreatment and a trend toward a better visual improvement compared with non-naive eyes.[13]

Few studies directly compare the efficacy of DEX implant between naive and refractory DME. The Multicenter Ozurdex assessment for diabetic macular edema (MOZART), ESCOBAR, and International Retina Group real-life multicenter study for DEXamethasone implant (IRGREL-DEX) studies all suggest that treatment-naive patients have better visual improvements with DEX implant than refractory ones.[14–16] Given the limited and scarce data in the Asian population, the purpose of this study was to investigate the efficacy and safety of DEX implant between refractory and naive eyes with DME over a 6-month follow-up in real-life practice.

2. METHODS

The content of the study was approved by the Far Eastern Memorial Hospital review board committee and conformed to the principles of the Declaration of Helsinki. From May 2015 to May 2017, consecutive pseudophakic eyes with center-involved DME were retrospectively reviewed. These treatment-naive eyes did not receive any intravitreal injections, macular laser, vitrectomy, or other ocular interventions except cataract surgery or panretinal photocoagulation at least 3 months ago. All the patients underwent baseline examinations and fulfilled the following criteria: age >18 years, glycosylated hemoglobin (HbA1c) under 10.0%, BCVA between 20/200 and 20/40 using Snellen charts, intraocular pressure (IOP) using pneumotonometer (CT-80; Topcon Inc., Tokyo, Japan) under 20 mmHg with or without topical hypotensive drugs, normal anterior segment using slit lamp, with or without DR checked by fundus biomicroscope, macular leakage on fundus fluorescein angiography (TRC-NW7SF; Topcon Inc.), and macular edema with central foveal thickness (CFT) >300 μm on spectral-domain OCT (SD-OCT, RTVue; Optovue Inc., San Francisco, CA, USA) using six radial line scans through the fovea. The types of DME consisted of macular cysts, submacular fluid, or diffuse macular thickening, but no co-existing macular traction by posterior hyaloid and epiretinal membrane. We excluded patients who are pregnant or breastfeeding, with the history of thromboembolic events within the previous 3 months, presence of anterior chamber intraocular lens or subluxated/dislocated posterior chamber intraocular lens, uncontrolled hypertension, presence of active infectious disease or intraocular inflammation, or presence of iris neovascularization/vitreous hemorrhage.

Following detailed explanation and instruction of various treatment strategies by the attending physicians (J.-K.W. and Y.-R.H.), all the patients selected their own monotherapy and signed the informed consent, including macular laser, intravitreal anti-VEGF agents (ranibizumab 0.5 mg or aflibercept 2 mg), or intravitreal DEX implant 0.7 mg. The patients undergoing macular laser or responding well to the anti-VEGF agents were excluded. The patients responding poorly to intravitreal anti-VEGF agents were defined as having paradoxical increase in CFT and/or BCVA decrease ≥1 line following at least 3 monthly anti-VEGF injections. Group 1 included the refractory cases, which received intravitreal DEX implant at least 1 month after the last anti-VEGF administration. Group 2 consisted of the treatment-naive eyes undergoing DEX implant injections intravitreally.

The 1+PRN (as needed) DEX implant injections in the study were performed in all eyes by two surgeons (Wang JK and Hsu YR). Repeated injections were allowed in at least a 4-month interval with CFT >300 μm or BCVA <20/25 according to the protocol of the BEVORDEX study. During six monthly visits, BCVA in Snellen chart (converting into logMAR for statistical comparison), IOP, SD-OCT of the macula, and anterior/posterior segments were examined. At every visit, VA was tested in the same room. The follow-up SD-OCT scans used the baseline scan results as references. Additional macular laser was not performed in all patients. If IOP elevated >20 mmHg after injection during follow-up, topical hypotensive agents were prescribed.

The primary outcome measure included changes in CFT and BCVA at month 6. Injection number, BCVA, CFT, postinjection complications, and IOP were recorded and compared by using Wilcoxon signed-rank test within the group and Wilcoxon rank-sum test between groups. Fisher's exact test was used for categorical comparison between groups. A $p < 0.05$ was considered statistically significant.

3. RESULTS

Intravitreal DEX implants were injected in 34 eyes of 31 patients with DME refractory to anti-VEGF agents in group 1, and 41 eyes of 38 patients with treatment-naive DME in group 2. The mean age of the patients was 60.97 ± 8.50 and 59.80 ± 11.90 years in groups 1 and 2, respectively. More male patients than female ones were found in both the groups. The mean HbA1c values were both 8% to 9% and not statistically different between groups. There were 31 and 36 eyes with proliferative DR treated with panretinal photocoagulation; 2 and 3 eyes with moderate nonproliferative DR; 1 and 2 eyes with mild non-proliferative DR in groups 1 and 2, respectively. Baseline BCVA, CFT, and IOP were all comparable between the two groups (all $p > 0.05$, Table 1).

In group 1, the eyes initially received anti-VEGF injections, including aflibercept for 4 and ranibizumab for 30 eyes. The mean injection number for these patients was 5.38 ± 1.68 during mean 7.97 ± 4.4 months of follow-up. The mean BCVA deteriorated from 0.54 ± 0.26 to 0.68 ± 0.29 logMAR ($p < 0.0001$), and the mean CFT increased from 424.09 ± 111.71 to 469.09 ± 124.49 μm ($p < 0.0001$) following the last 3 monthly anti-VEGF treatments. These refractory cases were switched to receive intravitreal DEX implant therapy. The mean BCVA

Table 1

Comparison of baseline data between eyes with refractory and treatment-naive DME

	Refractory eyes (n = 34)	Treatment-naive eyes (n = 41)	*p*
Age, mean ± SD, y	60.97 ± 8.50	59.80 ± 11.90	0.62
Gender (male:female)	24:10	25:16	0.07
HbA1c, mean ± SD, %	8.52 ± 2.01	8.12 ± 1.95	0.24
PDR with PRP, n (%)	31 (91)	36 (88)	0.11
BCVA, logMAR	0.75 ± 0.37	0.64 ± 0.35	0.21
CFT, mean ± SD, μm	489.77 ± 134.96	471.39 ± 152.79	0.58
IOP, mean ± SD, mmHg	16.78 ± 5.22	17.22 ± 4.98	0.44

BCVA: best-corrected visual acuity; CFT = central foveal thickness; DEX = dexamethasone; DME = diabetic macular edema; HbA1c = glycosylated hemoglobin; IOP = intraocular pressure; PDR with PRP = proliferative diabetic retinopathy with panretinal photocoagulation.

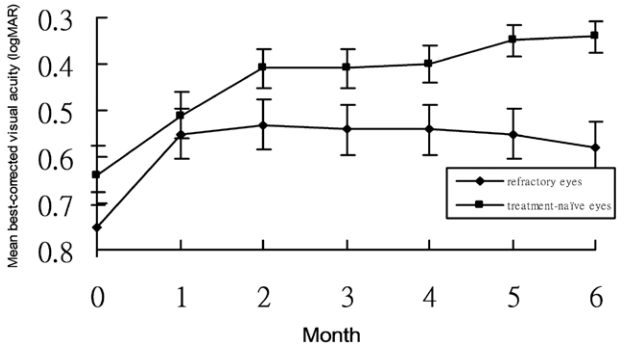

Fig. 1 Mean best-corrected visual acuity (logMAR) in refractory and treatment-naive eyes with diabetic macular edema treated with intravitreal dexamethasone implant over 6-month follow-up.

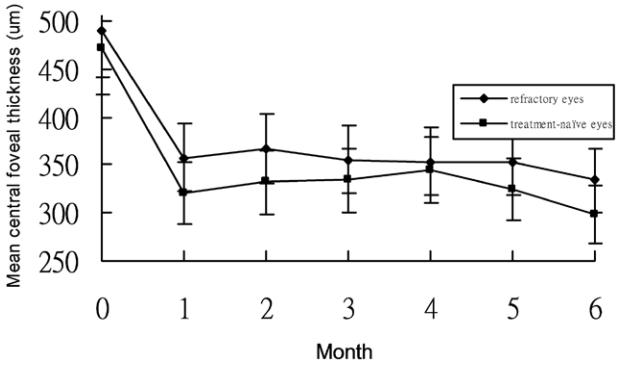

Fig. 2 Mean central foveal thickness (μm) in refractory and treatment-naive eyes with diabetic macular edema treated with intravitreal dexamethasone implant over 6-month follow-up.

significantly improved at month 1 (0.55 ± 0.23 logMAR, $p < 0.0001$), month 2 (0.53 ± 0.23 logMAR, $p = 0.0001$), month 3 (0.54 ± 0.22 logMAR, $p = 0.0002$), month 4 (0.55 ± 0.21 logMAR, $p = 0.0009$), month 5 (0.55 ± 0.21 logMAR, $p = 0.0004$), and month 6 (0.58 ± 0.34 logMAR, $p = 0.009$) after DEX intravitreal implant treatment compared with baseline BCVA (0.75 ± 0.37 logMAR) (Fig. 1). The mean change from baseline to final BCVA was –0.17 ± 0.35 logMAR (equal to 7.29 ± 16.22 letters, Table 2). There were nine eyes (26%) having a final BCVA ≥ 20/40. More than or equal to 3-line gains were found in five eyes (15%) after 6-month intravitreal DEX implant. There were seven eyes (21%) with BCVA loss ≥1 line, which was associated with decreased but persistent intraretinal cyst and/or submacular fluid in three eyes and ellipsoid zone/external limiting membrane disruption on SD-OCT in four eyes after DEX implant injections (Table 2). The average CFT significantly reduced at month 1 (357.44 ± 86.55 μm, $p < 0.0001$), month 2 (366.71 ± 93.42 μm, $p < 0.0001$), month 3 (355.74 ± 86.91 μm, $p < 0.0001$), month 4 (353.65 ± 101.09 μm, $p < 0.0001$), month 5 (353.56 ± 62.86 μm, $p < 0.0001$), and month 6 (334.32 ± 95.66 μm, $p < 0.0001$) after DEX intravitreal implant therapy compared with baseline (489.77 ± 134.966 μm) (Fig. 2). The mean decrease from baseline to final CFT was 155.44 ± 112.67 μm (Table 2).

Group 2 consisted of treatment-naive patients who underwent intravitreal DEX implant. The mean BCVA significantly improved at month 1 (0.51 ± 0.31 logMAR, $p = 0.018$), month 2 (0.42 ± 0.24 logMAR, $p = 0.0001$), month 3 (0.42 ± 0.26 logMAR, $p < 0.0001$), month 4 (0.41 ± 0.22 logMAR, $p < 0.0001$), month 5 (0.35 ± 0.19 logMAR, $p < 0.0001$), and month 6 (0.34 ± 0.26 logMAR, $p < 0.0001$) after DEX intravitreal implant treatment compared with baseline BCVA (0.64 ± 0.35 logMAR) (Fig. 1). The mean change from baseline to final BCVA was –0.30 ± 0.29 logMAR (equal to 16.42 ± 14.38 letters, Table 2). There were 23 eyes (56%) having a final BCVA ≥ 20/40. More than or equal to 3-line gains were found in 19 eyes (46%) after 6-month intravitreal DEX implant. There was 1 eye (2%) with BCVA loss ≥1 line, which was caused by ellipsoid zone disruption without macular edema on SD-OCT after injections (Table 2). The average CFT significantly reduced at month 1 (321.44 ± 64.17 μm, $p < 0.0001$), month 2 (332.27 ± 81.51 μm, $p < 0.0001$), month 3 (333.95 ± 96.11 μm, $p < 0.0001$), month 4 (345.09 ± 72.41 μm, $p < 0.0001$), month 5 (324.07 ± 66.19 μm, $p < 0.0001$), and month 6 (298.98 ± 118.43 μm, $p < 0.0001$) after DEX intravitreal implant therapy compared to baseline (471.39 ± 152.79 μm) (Fig. 2). The mean decrease from baseline to final CFT was 172.42 ± 133.79 μm (Table 2).

For eyes with treatment-naive DME (group 2), there were greater visual improvement, more eyes with BCVA gains ≥3 lines and final BCVA ≥ 20/40, and fewer eyes with BCVA loss ≥1 line, compared with the group of refractory eyes (group 1) (all $p < 0.05$, Table 2). The mean BCVA was comparable between the two groups at month 1 ($p = 0.54$), but it was inferior in group 1 at month 2 ($p = 0.04$), month 3 ($p = 0.02$), month 4 ($p = 0.008$), month 5 ($p < 0.0001$), and month 6 ($p = 0.001$) compared with those in group 2. The mean CFT was not significantly different

Table 2

Comparison of clinical data between refractory and treatment-naive eyes with DME after 6-month treatment of intravitreal DEX implant

	Refractory eyes (n = 34)	Treatment-naive eyes (n = 41)	*p*
Changes in BCVA, mean ± SD, ETDRS letters	7.29 ± 16.22	16.42 ± 14.38	0.0008*
Changes in BCVA, mean ± SD, logMAR	–0.17 ± 0.35	–0.30 ± 0.29	0.0002*
Eyes with BCVA gain ≥3 lines, n (%)	5 (15%)	19 (46)	0.008*
Eyes with BCVA loss ≥1 line, n (%)	7 (21)	1 (2)	0.002*
Final BCVA, mean ± SD, logMAR	0.58 ± 0.34	0.34 ± 0.26	0.001*
Eyes with final BCVA ≥20/40, n (%)	9 (26)	23 (56)	0.01*
Changes in CFT, mean ± SD, μm	–155.44 ± 112.67	–172.42 ± 133.79	0.27
Final CFT, mean ± SD, μm	334.32 ± 95.66	298.98 ± 118.43	0.16
Final IOP, mean ± SD, mmHg	17.87 ± 4.94	18.52 ± 3.43	0.57
IOP elevation >20 mmHg, n (%)	9 (26)	11 (27)	0.29
Injection number, mean ± SD	1.82 ± 0.38	1.54 ± 0.49	0.007*

BCVA = best-corrected visual acuity; CFT = central foveal thickness; DEX = dexamethasone; DME = diabetic macular edema; ETDRS = Early Treatment Diabetic Retinopathy Study; IOP = intraocular pressure.
*$p < 0.05$.

between groups at month 1 (p = 0.05), month 2 (p = 0.10), month 3 (p = 0.31), month 4 (p = 0.68), month 5 (p = 0.05), and month 6 (p = 0.16). Comparable changes in CFT were observed after 6 months of DEX intravitreal implant between the two groups (p = 0.27, Table 2). Within group 1, 28 eyes (82%) required two injections and 6 eyes (18%) required one injection. In group 2, 22 eyes (54%) were injected twice and 19 eyes (46%) were injected once. Group 1 needed significantly more injections (1.82 ± 0.38) than group 2 (1.54 ± 0.49) (p = 0.007, Table 2).

The injections were well tolerated in all patients. No serious ocular complications were observed, such as retinal detachment, infectious endophthalmitis, anterior chamber migration of DEX implant, or intractable IOP elevation requiring glaucoma incisional surgery. The incidence of temporary IOP elevation >20 mmHg was found in approximately one fourth of the participants after DEX implant administration in both group, and all can be controlled under 20 mmHg by topical hypotensive agents (Table 2). In group 1, 9 of 34 eyes (26%) with postinjection increased IOP had a mean IOP of 27.34 ± 6.23 mmHg (range, 21-38 mmHg) between 1 and 3 months after injection. In 11 of the 41 (27%) eyes in group 2 with postinjection increased IOP, the mean IOP was 25.89 ± 5.77 mmHg (ranged 21-32 mmHg) between 1 and 3 months after injection. Final IOP and the rate of IOP elevation were comparable between groups (p > 0.05, Table 2). Other common side effects were local hyperemia and subconjunctival hemorrhage at the site of injection.

4. DISCUSSION

In this single-center retrospective study, we sought out to investigate the efficacy and safety of DEX implant between refractory and naive eyes over a 6-month follow-up in Taiwanese patients with DME. Regardless of treatment experience, intravitreal DEX implant significantly improved visual/anatomic functions of the patients. However, comparing the outcomes between the two groups, greater visual improvement was found in treatment-naive than in refractory eyes. Both groups had similar decrease in CFT over the study period, although the refractory eyes received significantly more injections. Treatment with DEX implant was generally well tolerated. A little over a quarter of patients had IOP elevations that were manageable with topical hypotensive agents, and no serious ocular complication was observed.

Various inflammatory mediators and VEGF can initiate processes of leukostasis, alterations in endothelial tight junction proteins or even neurodegeneration that involves in the breakdown of the BRB can also lead to microvascular leakage and the onset of DME.[8,17,18] Intravitreal DEX implant can slowly release corticosteroid, which reduce both intraocular VEGF and inflammatory cytokines such as tumor necrosis factor alpha, intercellular adhesion molecule, monocyte chemotactic protein 1, interleukin-1β, and reactive oxygen species following intravitreal injections.[19] Of treatment-naive pseudophakic patients with DEX implant-treated DME in prior two randomized studies, 23.3% of cases had BCVA gains ≥3 lines in the MEAD study,[10] and the mean BCVA improved 10.4 letters in the BEVORDEX study.[11] A previous report consisting of 31 real-life studies found that treatment-naive eyes gained about 12 letters of BCVA after DEX implant therapy for DME.[7] In our study, approximately half of the treatment-naive pseudophakic eyes had BCVA gains ≥3 lines, and mean visual gains of 16.42 letters. The present study showed comparable, if not better, outcomes with previous studies.

The presence of intraocular cytokines other than VEGF or the occurrence of neutralizing antibody to anti-VEGF may cause anti-VEGF resistance in DME.[19,20] Elevated aqueous interleukin-8 was discovered in patients with DME refractory to bevacizumab.[21] Suppression of numerous intraocular cytokines using DEX implant therapy was proven to be effective for DME eyes resistant to anti-VEGF agents.[22–24] A prior randomized controlled trial reported switching to DEX implant achieved a significantly greater reduction of macular thickness than continuing bevacizumab in DME patients who were recalcitrant to bevacizumab.[22] A multicenter study demonstrated changing to DEX implant had superior visual gain (mean +6.1 letters) than persistent injections of anti-VEGFs (mean –0.4 letters) in diabetic patients with macular edema refractory to anti-VEGFs.[23] A meta-analysis favored switching to DEX implant in cases intractable to anti-VEGF agents rather than continuing anti-VEGF therapy for DME.[24] We also observed similar findings in our study. In the group of eyes resistant to anti-VEGF agents, a significant increase in BCVA of 7.29 letters was noted after switching to DEX implant treatment. Five eyes (15%) of patients with refractory DME had BCVA gains ≥3 lines. Despite variation in the definitions of refractory DME, BCVA gains ≥3 lines was reported in 15% to 22% of the patients receiving DEX implant from several studies.[10,11,22,25] Decrease in CFT in our study was also comparable to these studies, ranging 122 to 187 μm.[10,11,22,25]

There were several reports concerning DEX implant treatment for treatment-naive or non-naive patients with DME. Kodjikian et al observed that naive eyes had a mean visual gain of 12 letters, which was better than non-naive eyes (8.6 letters), following DEX implant injections in real-life studies.[7] The Reldex study showed that naive eyes improved 6.6 letters, which is superior than the 3.5-letter gain in the non-naive eyes treated by DEX implant.[13] The multicenter MOZART study and a recent single-institute study revealed that DEX implant led to greater visual gains and superior final BCVA in treatment-naive patients than those cases previously treated with other regimens for DME.[14,26] The authors also concluded that macular thickness reduction in naive eyes was larger or equal to that in non-naive eyes.[14,26] These findings demonstrated that DEX implant can treat DME better in naive eyes than in non-naive eyes. Intravitreal DEX implant can be the first-line management for DME.

The clinical outcomes of anti-VEGF refractory DME cases were poorer than those of naive ones after DEX implant therapy. Another 6-month prospective study, conducted by Escobar-Barranco et al, used DEX implant to treat 36 naive eyes and 40 eyes that did not respond to two or more of the following regimens for DME: intravitreal injections, vitrectomy, or macular and peripheral photocoagulation.[15] The authors found better visual improvements in naive (11.5 letters) compared to refractory patients (7.7 letter) treated with similar number of DEX implants.[15] In the multicenter international retrospective study (IRGREL-DEX), the investigators included one group without any treatment experience, and another group that were resistant to at least 3 monthly anti-VEGF injections (bevacizumab, ranibizumab, or aflibercept). There were significantly higher visual gains (11.3 letters) in naive eyes than in anti-VEGF resistant eyes (7.3 letters) over 24 months, with 3.9 and 3.1 DEX implants (both range 1-4), respectively.[16] Macular thickness was significantly higher in refractory eyes than in naive eyes during the treatment. In the current study, we also demonstrated a 7.3-letter visual improvement in the resistant eyes, which was inferior to that (16.4 letters) in the naive eyes, with significantly more injections over a 6-month period. However, the changes and final values of macular thickness were not different between the two groups. Poor response to DEX implant and photoreceptor impairment by edema from anti-VEGF resistance can explain the inferior visual outcomes in the refractory DME group. Visual loss ≥1 line was detected even after switch to DEX implant in seven eyes recalcitrant to prior anti-VEGF therapy. In the refractory group, irreversible damage of photoreceptor structure was found in four eyes without edema. Another

three refractory eyes had insufficient reduction of edema after intravitreal DEX implant, which may be possible that some intraocular cytokines responsible for DME remained elevated or were decreased but not low enough following DEX implant administration. Together, these findings support the argument of the first-line or earlier DEX implant for DME. Data regarding the difference in injection number between naive and refractory remain inconclusive, although subgroup analysis from the Reldex study has found a significantly longer time to retreatment in naive than in non-naive eyes.[13] Treatment-naive patients significantly required less DEX implant injections than refractory ones in our study. Whether naive patient may require less injection of DEX implant warrants further investigation.

The risks of cataract, ocular hypertension, and ocular infection were the major concern for using intravitreal injection of corticosteroids. Only one endophthalmitis (0.03%) was reported using DEX implant to treat DME among 2897 injections in 31 articles.[7] Elevation of IOP requiring topical IOP-lower medication after DEX implant injections was reported in 14% to 41.5% of participants with DME in several large-scale studies.[7,10–13,16] Merely 0.6% of the patients with medically uncontrolled ocular hypertension underwent incisional glaucoma drainage surgery in the MEAD trial.[10] In our study, topical hypotensive agents were required in 26.6% of all eyes for ocular hypertension after DEX implant, comparable to the incidence reported previously. No additional procedures (laser or surgery) were needed to normalize IOP. No infectious endophthalmitis or other serious ocular complications were discovered.

Some of the limitations of our study included the single-center and retrospective nature of the study design, the short duration of follow-up, and the small patient cohort. Future prospective studies with a larger population and longer follow-up would be helpful to support the early use of DEX implant in the treatment of DME. To our knowledge, this was the first study concerning treatment response of DEX implant between treatment-naive and refractory Asian patients with DME.

In conclusion, our study showed that in pseudophakic eyes of Taiwanese patients with DME, intravitreal DEX implant could provide substantial visual and anatomic improvements in both treatment-naive and refractory patients during the 6-month period. In addition, the visual gain was greater in naive eyes than in refractory eyes. The findings may have implications for the treatment of DME in that early DEX implant could provide better visual benefit for pseudophakic patients.

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