Editorial

Dealing with co-existent cataract and diabetic macular oedema: an increasingly common conundrum now solved?

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Visually significant cataracts combined with diabetic macular oedema (DMO) is a common and difficult clinical scenario affecting up to a quarter of all patients undergoing cataract surgery.[1] Diabetes itself leads to the earlier development of cataracts, compounding the issue.[2] Furthermore, the prevalence of diabetes has been projected to increase from 463 million in 2019 to 700 million in 2045, ensuring that cataracts and DMO will continue to be a common clinical scenario for the foreseeable future.[3]

Historically, cataract surgery performed on eyes with concurrent DMO have had a poor visual prognosis. Some studies have reported that up to 50% of eyes have a visual acuity of 6/30 or worse after surgery.[4, 5] The underlying cause of this is the disturbance in the balance of angiogenic and antiangiogenic growth factors created during cataract surgery which exacerbates the impaired blood-retinal barrier of diabetic retinopathy.[2, 6] A large real-world study has shown that "treatment requiring DMO" peaks at 3 to 6 months postoperatively as evidenced by the increased use of macular laser or intravitreal injections of anti-vascular endothelial growth factor (VEGF) agents, suggesting that this is when DMO tends to worsen post-operatively.[7]

Although, there have been advances in the treatment of DMO, the most efficacious treatment regime in the perioperative setting is still yet to be determined. Reports of the use of intravitreal anti-VEGF agents either at the time of surgery or in the weeks preceding surgery generally show it to be an effective treatment in stabilizing or improving central subfoveal thickness (CST) and visual acuity (VA).[8-10] Similarly, intravitreal corticosteroids have been shown to be effective in this clinical scenario.[11, 12] To date, there has been only one report directly comparing intravitreal anti-VEGF agents against intravitreal corticosteroids at the time of cataract surgery.[13] In this study, there was a trend for better visual acuity in those receiving intravitreal corticosteroids, and also a statistically significant difference in macular thickness in

favour of corticosteroids at 6 months postoperatively.[11] Additionally, the number of intravitreal injections required was significantly lower in the corticosteroid arm which is particularly important in resource stretched clinics.

The often artificial constructs of a clinical trial, with its strict inclusion/exclusion criteria and tight follow up, can often make it difficult to apply to the patient in front of you. Real-world data can help bridge this gap by providing more realistic results, however, real-world data on the outcomes of cataract surgery with coexistent DMO is currently lacking.

The study published in this issue by Bhandari et al.[14] aims to shed some light on this topic by analysing real-world data on patients having cataract surgery whilst undergoing intravitreal treatment for DMO from the Fight Retinal Blindness! (FRB!) Project. The FRB! Project is a collaborative web-based software collection tool used to collect data from routine clinical practice from centres in Australia, New Zealand, Switzerland and the United Kingdom.[15] They included all cases from 2007 to 2018 with DMO that underwent cataract surgery with at least 6 months of data before and after surgery. These were matched to a group of phakic controls receiving treatment for DMO with 147 eyes in each group. The vast majority (>90%) in both groups received anti-VEGF treatments, and this did not alter significantly post operatively in the surgery group (92% received anti-VEGF pre-operatively vs 91% post-operatively). As expected, the cataract surgery group experienced a drop in VA leading up to surgery, and a statistically significant gain in mean VA post-operatively of 10.6 letters at 6 months. More importantly, the VA at 6 months was very similar to those of the control group (68.8 vs 69.2, P=0.8) indicating that DMO can be adequately managed perioperatively with intravitreal injections. Interestingly, the cataract surgery group had a thicker mean CST leading up to surgery (341μm vs 316μm), which increased after surgery (360μm vs 315μm). The mild increase in CST

after cataract surgery at 6 months is not unexpected and is consistent with previous large real-world data studies and trials with predominant anti-VEGF usage.[7,16] In terms of intravitreal injections, the cataract surgery group had an increased number of injections both before surgery (2.4 vs 1.6 P=0.01) and after surgery (2.1 vs 1.5 P<0.001), likely representing the clinicians' attempts to optimise DMO before and after surgery.

The only factor found to be associated with visual outcome was the timing of intravitreal injections, with those receiving injections either at the time of surgery or within the 4 weeks preceding surgery being more likely to have a gain in VA, which is consistent with previous reports.[8, 10, 11] Although the vast majority of patients in this study received anti-VEGF treatment, there was a slightly higher usage of corticosteroids in the cataract surgery group (8% vs 3%), which may reflect the increased rate of cataract formation from corticosteroid use, or a conscious switch to corticosteroids due to their a longer lasting effect on DMO in this setting.[11] Nonetheless, Bhandari et al.'s report confirms that DMO can be effectively managed in the perioperative period with anti-VEGF agents in a non-trial setting on a large scale, although requiring relatively frequent injections.

There are, however, some key caveats to a large observational study such as this, including variable treatment indications, variable decision making and a variable population. Alternatively, this can be viewed as a strength, as this heterogenous study population and variable treatment paradigms were still able to show a significant improvement in VA and stabilization of the CMT post cataract surgery.

As the COVID-19 pandemic sweeps across the world, ophthalmology clinics are greatly reducing their services to urgent and vision threatening cases in an attempt to limit the spread of the disease. The slightly higher usage of corticosteroids in the

cataract surgery group is interesting and may highlight the fact that corticosteroids are more efficacious in requiring less frequent injections. This point may be particularly useful in helping guide ophthalmologists in how to best reduce their case load whilst still providing adequate ophthalmic care.

Although these results may not change how we treat patients clinically, it shows that in routine clinical practice patients are no longer destined to have a poor visual outcome when they undergo cataract surgery with concurrent DMO. Rather, these patients can expect to have a significant improvement in their vision if provided with the appropriate perioperative adjunctive treatment.

REFERENCES

1. Panozzo G, Staurenghi G, Dalla Mura G, et al. Prevalence of diabetes and diabetic macular edema in patients undergoing senile cataract surgery in Italy: The DIabetes and CATaract study. Eur J Ophthalmol 2019:1120672119830578.
2. Pollreisz A, Schmidt-Erfurth U. Diabetic cataract-pathogenesis, epidemiology and treatment. J Ophthalmol 2010;2010:608751.
3. Saeedi P, Petersohn I, Salpea P, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9(th) edition. Diabetes Res Clin Pract 2019;157:107843.
4. Gupta A, Gupta V. Diabetic maculopathy and cataract surgery. Ophthalmol Clin North Am 2001;14:625-37.
5. Schatz H, Atienza D, McDonald HR, Johnson RN. Severe diabetic retinopathy after cataract surgery. Am J Ophthalmol 1994;117:314-21.

6. Patel JI, Hykin PG, Cree IA. Diabetic cataract removal: postoperative progression of maculopathy--growth factor and clinical analysis. Br J Ophthalmol 2006;90:697-701.

7. Denniston AK, Chakravarthy U, Zhu H, et al. The UK Diabetic Retinopathy Electronic Medical Record (UK DR EMR) Users Group, Report 2: real-world data for the impact of cataract surgery on diabetic macular oedema. Br J Ophthalmol 2017;101:1673-1678.

8. Rauen PI, Ribeiro JA, Almeida FP, Scott IU, Messias A, Jorge R. Intravitreal injection of ranibizumab during cataract surgery in patients with diabetic macular edema. Retina 2012;32:1799-803.

9. Takamura Y, Kubo E, Akagi Y. Analysis of the effect of intravitreal bevacizumab injection on diabetic macular edema after cataract surgery. Ophthalmology 2009;116:1151-7.

10. Moshfeghi AA, Shapiro H, Lemmon LA, Gune S. Impact of Cataract Surgery during Treatment with Ranibizumab in Patients with Diabetic Macular Edema. Ophthalmol Retina 2018;2:86-90.

11. Kandasamy R, Constantinou M, Rogers SL, et al. Prospective randomised clinical trial of intravitreal bevacizumab versus triamcinolone in eyes with diabetic macular oedema undergoing cataract surgery: 6-month results. Br J Ophthalmol 2019;103:1753-1758.

12. Lam DS, Chan CK, Mohamed S, et al. Phacoemulsification with intravitreal triamcinolone in patients with cataract and coexisting diabetic macular oedema: a 6-month prospective pilot study. Eye (Lond) 2005;19:885-90.

13. Lim LL, Morrison JL, Constantinou M, et al. Diabetic Macular Edema at the time of Cataract Surgery trial: a prospective, randomized clinical trial of intravitreous bevacizumab versus triamcinolone in patients with diabetic macular oedema at the time of cataract surgery - preliminary 6 month results. Clin Exp Ophthalmol 2016;44:233-42.

14. Bhandari S, Biechl AC, Nguyen V et al.Outcomes of cataract surgery in eyes with diabetic macular oedema: Data from the Fight Retinal Blindness! Registry. Clin Experiment Ophthalmol 2020;48;pp-pp

15. Gillies MC, Walton R, Liong J, et al. Efficient capture of high-quality data on outcomes of treatment for macular diseases: the fight retinal blindness! Project. Retina 2014;34:188-95.

16. Diabetic Retinopathy Clinical Research Network Authors/Writing C, Bressler SB, Baker CW, et al. Pilot study of individuals with diabetic macular edema undergoing cataract surgery. JAMA Ophthalmol 2014;132:224-6.