Oxidative Stress, Prostaglandins, Cytokines, and Cataract Surgery: How Incorporating a Low-Energy Laser Can Be Beneficial



BY JODHBIR S. MEHTA, BSc (HONS), MBBS, PHD, FRCOPHTH, FRCS(Ed), FAMS

aser cataract surgery has been a viable alternative to conventional cataract surgery for more than a decade now. Inflammation management remains important independent of the surgery type: Not only does it influence corneal edema and central macular thickness, but today's patients have high expectations for their visual recovery and for reduced pain postoperatively, so that they may return to their everyday activities as soon as possible after cataract surgery. With a handful of femtosecond laser platforms and one nanosecond platform available today to assist in a multitude of steps in cataract surgery, it is important for surgeons and their practices to consider the benefits of each platform and to contemplate how incorporating one of them could help to produce superior surgical outcomes for their patients.

I have conducted a number of studies proving the benefits of a low-energy laser (Femto LDV Z8, Ziemer) in corneal surgery¹ and in cataract surgery.² With new clinical data on the Femto LDV Z8 emerging, more benefits of this low-energy laser in cataract surgery have been coming to light in the recent years and months. For instance, it has previously been shown that, in a case-controlled study, 1-day postoperative corrected distance visual acuity was significantly better after laser cataract surgery with the Femto LDV Z8 than it was after conventional phacoemulsification.³ The indication here, then, is that a low-energy laser platform like the Femto LDV could offer advantages in early visual rehabilitation. It has also been hypothesized that a low-energy laser could potentially decrease the extent of prostaglandin surge compared to higher-energy lasers (Figure 1) and, in return, reduce oxidative stress (for more information on prostaglandins, oxidative stress, and other inflammation indicators, see the Table).

I recently conducted a trial to compare the oxidative stress, prostaglandin E2 (PGE2), and cytokine levels after conventional and laser-assisted phacoemulsification with the Femto LDV Z8.⁴ A cohort of patients were also given a topical NSAID preoperatively in the eye that received femtosecond treatment. In short, what we found was that, compared with conventional cataract surgery with phacoemulsification, the Femto LDV Z8 induced a significantly higher PGE2 level



Figure 1. Increase in inflammation with several femtosecond laser platforms.

and no significant difference in malondialdehyde (MDA) and aqueous flare levels. However, capsulotomy creation with the Femto LDV Z8 causes the lowest level of PGE2 release compared with high-energy systems. Further, we found that the addition of a topical NSAID preoperatively reduced PGE2 surge and, finally, that the amount of oxidative stress induced during phacoemulsification—both conventional and laser—strongly correlated with effective phacoemulsification time (EPT) and was independent of the surgery type.

RESULTS

Aqueous PGE2 and MDA levels. We found that the PGE2 level in the laser group was significantly higher (175.6 \pm 125.3 pg/mL) than it was in the conventional group (68.8 \pm 47.6 pg/mL) and that, in the laser group, PGE2 levels were significantly reduced among the eyes that received topical NSAID preoperatively (63.4 \pm 35.9 pg/mL). Again, this is much lower than compared with higher-energy laser systems. There was an increase in PGE2 levels in all groups immediately postoperatively (Figure 2), indicating that the preoperative NSAID only suppressed the rise in PGE2 after laser treatments at the beginning of surgery, but it had no effect at the end of the surgical procedure. Regarding MDA levels, the use of a topical NSAID did not suppress the increase of MDA caused by the laser pretreatment.

TABLE. TYPES AND FUNCTIONS OF OXIDATIVE STRESS AND INFLAMMATION INDICATORS

Oxidative Stress and Inflammation Indicators	Function
Malondialdehyde (MDA): a marker of oxidative physical or chemical stress	Short-term exposure and accumulation of oxygen radicals, produced by phacoemulsification, might result in oxidative damage to corneal endothelium.
Prostaglandin E2 (PGE2): a potent inflammatory mediator	PGE2 exerts diverse effects on cell proliferation, apoptosis, angiogenesis, inflammation, and immune surveillance.
Aqueous flare: increased protein concentration of the aqueous humour causes an optical phenomenon called <i>flare</i>	Occurs as a result of increased protein content and inflammatory cells in the aqueous humour. Visual impairment depends on the intensity of the flare.
Cytokines: involved in the up-regulation of inflammatory reactions	Linked to many disease conditions, such as immune responses, inflammation, and trauma. Certain pro-inflammatory cytokines such as IL-1 β , IL-6, and TNF- α are involved in the process of pathological pain.

Cytokines, chemokines, and growth factor. The concentrations of IL-1RA were significantly higher in the laser group than in the conventional phacoemulsification group. Yet, when the preoperative NSAID was delivered in the laser group, there was a significantly lower concentration of a number of inflammatory mediators. This is beneficial, as inhibiting cytokines, chemokines, and growth factor has the potential to limit the amount of pseudophakic cystoid macular edema. Capsulotomy creation with the Femto LDV Z8 causes the lowest level of PGE2 release compared with high-energy systems.⁵⁻⁸ Authors have reported PGE2 levels ranging from 182.1 to 1911.4 pg/mL with high-energy laser platforms.^{5,6,9,10} This is much higher than our reported level of 175.6 ±125.3 pg/mL (Figure 1).

CONCLUSION

PGE2 levels increase after both laser cataract surgery and conventional phacoemulsification, but significantly higher PGE2 levels are typically seen with laser cataract surgery. Compared to the levels of PGE2 previously reported with high-energy laser platforms, the low-energy laser induces less release of the PGE2. When a topical NSAID was incorporated, the release of PGE2 in the low-energy laser was further reduced, to the levels seen in the conventional phacoemulsification group.

The oxidative stress induced during phacoemulsification strongly correlated with EPT and not the type of the surgery. EPT after femtosecond laser pretreatment of the



Figure 2. Changes in aqueous PGE2 levels.

lens is significantly shorter than with conventional cataract surgery,¹¹ which could potentially lead to reduced oxidative stress. Also noteworthy is that the laser group had higher concentrations of IL-1RA than the conventional phaco-emulsification group. Seeing that IL-1RA has been shown to suppress the proliferation of lens epithelial cells, this may be another positive attribute of laser cataract surgery in the battle against posterior capsular opacification.

1. Riau AK, et al. Comparative study of nJ- and muJ-energy level femtosecond lasers: Evaluation of flap adhesion strength, stromal bed quality, and tissue responses. *Invest Ophthalmol Vis Sci*. 2014;55(5):3186-3194.

2. Williams GP, et al. The effects of a low-energy, high frequency liquid optic interface femtosecond laser system on lens capsulotomy. *Sci Rep.* 2016;6:24352.

3. Pajic B, Čvejic Z, Pajic-Eggspuehler B. Cataract surgery performed by high frequency LDV Z8 femtosecond laser: Safety, efficacy, and its physical properties. Sensors (Basel). 2017;pil:E1429.

4. Liu Y-C, Setiawan M, Ang M, et al. Changes in aqueous oxidative stress, prostaglandins, and cytokines: Comparisons of low-energy femtosecond laser—assisted cataract surgery versus conventional phacoemulsification. J Cataract Refract Surg. 2019;45:196–203.

 Schultz T, Joachim SC, Kuehn M, Dick HB. Changes in prostaglandin levels in patients undergoing femtosecond laser-assisted cataract surgery. J Refract Surg. 2013;29:742–747.

6. Jun JH, Yoo YS, Lim SA, Joo CK. Effects of topical ketorolac tromethamine 0.45% on intraoperative miosis and prostaglandin E2 release during femtosecond laser–assisted cataract surgery. J Cataract Refract Surg 2017; 43:492–497.

7. Wang L, Zhang Z, Koch DD, Jia Y, Cao W, Zhang S. Anterior chamber interleukin 1b, interleukin 6 and prostaglandin E2 in patients undergoing femtosecond laser-assisted cataract surgery. *Br J Ophthalmol* 2016;100:579-582.

8. Schultz T, Joachim SC, Szuler M, Stellbogen M, Dick HB. NSAID pretreatment inhibits prostaglandin release in femtosecond laser-assisted cataract surgery. J Refract Surg 2015;31:791–794.

9. Kiss HJ, Takacs AI, Kranitz K, Sandor GL, Toth G, Gilanyi B, Nagy ZZ. One-day use of preoperative topical nonsteroidal antiinflammatory drug prevents intraoperative prostaglandin level elevation during femtosecond laser-assisted cataract surgery. *Curr Eye Res.* 2016;41:1064-1067.

10. Nishi O, Nishi K, Ohmoto Y. Effect of interleukin 1 receptor antagonist on the blood-aqueous barrier after intraocular lens implantation. Br J Ophthalmol. 1994;78:917-920.

11. Dick, H. B. and T. Schultz A review of laser-assisted versus traditional phacoemulsification cataract surgery. *Ophthalmol Ther.* 2017;6(1):7–18.

JODHBIR S. MEHTA, BSc (Hons), MBBS, PHD, FRCOPHTH, FRCS(Ed), FAMS

- Head, Corneal and External Eye Disease Department; Senior Consultant, Refractive Surgery Department, Singapore National Eye Centre
- Head, Tissue Engineering and Stem Cells Group, Singapore Eye Research Institute
- jodmehta@gmail.com
- Financial disclosure: Travel support (Ziemer)