

# CORRESPONDENCE

## Treatment Duration and Side Effect Profile of Long-term Use of Intravitreal Preservative-free Triamcinolone Acetonide in Uveitis



EDITOR:

GANAPATHY AND ASSOCIATES' RECENT PUBLICATION ON the dose-response of long-term use of intravitreal preservative-free triamcinolone acetonide (Triesence) in uveitis was of interest to me. My issue is *not* the limitations of this retrospective, nonrandomized study, which the authors present in their discussion.<sup>1</sup> Rather, my issue is the use of the phrase "side effects," which in this paper refers primarily to the development of either glaucoma or cataracts, well known to be associated with the use of corticosteroids. While both physicians and patients use the phrase "side effects" in our daily conversations, the appropriate term is "adverse event," as noted in the International Conference on Harmonisation E2A and E6 guidances.<sup>2,3</sup>

The E2A guidance states "...The term 'side effect' has been used in various ways in the past, usually to describe negative (unfavorable) effects, but also positive (favorable) effects." The guidance further recommends that this term no longer be used. The recommended use is "adverse event," which is "any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment." A subset of adverse events is "adverse drug reactions," which are "a response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease or for modification of physiological function."

In the case of chronic corticosteroids, the adverse events of cataracts and glaucoma are clearly undesirable. However, in the case of prostaglandin analogs used therapeutically to treat elevated intraocular pressure, eyelash growth may be either desirable or undesirable. And in the case of prostaglandin analogs used therapeutically to increase eyelash growth, lowered intraocular pressure may also be desirable or undesirable. So the "side effect" is in the eye of the beholder. When first reported, the nature of the relationship of eyelash growth to prostaglandin use was unknown, although it later became clear to be the same pharmacology as the ocular hypotensive effect.

I propose that the *Journal* should make an effort to use the more correct term, "adverse events," rather than "side effects" in the future.

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## Concerns Regarding Nd:YAG Laser Posterior Capsulotomy in Children



EDITOR:

WE READ WITH GREAT INTEREST THE ARTICLE TITLED "Long-term outcome of Nd:YAG laser posterior capsulotomy in children: Procedural strategies and visual outcome" by Choi and associates.<sup>1</sup> This is an interesting study in which Choi and associates report the benefits of performing neodymium:yttrium-aluminum-garnet (Nd:YAG) laser posterior capsulotomy selectively in a pediatric population without serious complications.<sup>1</sup> Laser helps restore and maintain the visual acuity for a long period of time.

However, there are a few concerns that we would like to highlight. The mean number of laser shots (single burst) was  $60.4 \pm 21.0$ , which is far greater than that may be required for making an adequate size cruciate opening in a mesopic pupil. Was it because the authors gradually increased the power or because the posterior capsular opacification was dense? There is no mention of the step increase in power each time, and the large number of shots required is unexplainable. The total amount of laser energy

used was  $99.5 \pm 36.1$  mJ, which is quite high compared with laser energy use reported in adults (around 40–70 mJ).<sup>2</sup> Also, the authors do not mention the size of capsulotomy achieved.

The mean age of the children undergoing cataract surgery was  $6.7 \pm 3.2$  years, and the majority had hydrophobic acrylic intraocular lens insertion.<sup>1</sup> The type of posterior capsular opacification is not mentioned, although given the age and type of intraocular lens the proliferative type of posterior capsular opacification is more likely.<sup>2</sup> The proliferative type of posterior capsular opacification is less resistant to capsulotomy than the fibrous type and should therefore have required less laser energy for disruption.<sup>2</sup>

Choi and associates<sup>1</sup> mention complications, such as clinically insignificant laser pitting of the intraocular lens and transient elevation of intraocular pressure arising from the laser procedure. There is no mention of the laser burst offset settings used for the cases. The authors conclude that Nd:YAG laser posterior capsulotomy can be successfully performed in the pediatric population without serious complications. However, there is no mention whether serious complications, such as uveitis, retinal detachment, and cystoid macular edema, were looked for in the methodology as well as the results section. Although a causal relationship is not established between the laser energy levels and the rate of these complications, these complications occur more frequently when the cumulative energy levels are high ( $>70$  mJ in adults) because of disruption of the anterior hyaloid face and accelerated vitreous degeneration.<sup>2,3</sup> Given that the energy levels were too high in this study, it is imperative to perform a good macular and dilated peripheral fundus evaluation to search for these complications.

Nd:YAG laser posterior capsulotomy is a good therapeutic option for posterior capsulotomy in select cooperative pediatric patients, but it has its own adverse effects and complications.<sup>1,4</sup> In view of the lack of evidence regarding the posterior segment pathologies in these cases, the safety of this procedure with the high laser energy remains questionable.

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## Reply



EDITOR:

WE APPRECIATE DRS. JUMAWAT, SAHAY, AND SACHAN FOR their interest in our article.

In our study, the average energy per shot was  $1.67 \pm 0.36$  mJ (range 1.03–2.47 mJ),<sup>1</sup> which is comparable to previous studies.<sup>2,3</sup> As described in the Methods section, the single burst of neodymium:yttrium-aluminum-garnet laser was applied starting at 0.9 mJ and gradually increased in power until a complete opening of the posterior capsule was made. Cruciate opening ( $\geq 3$  mm) was created according to the size and shape of the pupil. Regarding the type of the posterior capsular opacity, it was difficult to clearly differentiate the Elschnig pearl type from the fibrous type, but most of them were the combined type, including a dense fibrous component requiring more laser energy for disruption.

We deeply sympathize with the authors' concern that high total laser energy can cause various complications, including intraocular pressure elevation, uveitis, and retinal detachment.<sup>2</sup> The total amount of laser energy used in our study was  $99.5 \pm 36.1$  mJ (range 49–190 mJ), which is a little higher than that used in adult patients<sup>2</sup> but is comparable or even lower than previously reported laser energy used in pediatric patients. Atkinson and Hiles<sup>4</sup> reported an average of total amount of laser energy as 223.97 mJ (range 37–1700 mJ), and Stager and associates<sup>3</sup> reported a total laser energy ranging from 15 to 700 mJ. Elkin and associates<sup>5</sup> reported a median total energy of 149.6 mJ (range 26.4–617.4 mJ) after implanting the same hydrophobic acrylic IOL. The increase in total energy is believed to be related to the relatively dense membrane of children compared with adults.<sup>5</sup> On the other hand, considering that it is difficult to accurately target every laser onto the membrane because of the poor cooperation of pediatric patients, the actual energy effectively transferred to the membrane and the posterior segment might be less than this estimated value.

Knowing that the risk of various retinal complications, including cystoid macular edema and retinal detachment, is higher when higher laser energy is delivered to the