



Reply

Effect of anti-inflammatory regimen on early postoperative inflammation after cataract surgery

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Reply: Effect of anti-inflammatory regimen on early postoperative inflammation after cataract surgery.



We would like to thank Yusuf et al. for participating in the discussion of our article during the April 2021 ESCRS journal club.^{1,2} We appreciate the discussion and are thankful for the opportunity to comment on the points highlighted by the authors. Choosing the right anti-inflammatory prophylaxis is indeed an important issue.

Our article was part of a randomized, investigator-initiated, single-site trial, Study for Optimizing Anti-inflammatory Prophylaxis, registered on www.ClinicalTrials.gov (NCT03383328). The aim of the article was to evaluate the effect of different anti-inflammatory regimens on early postoperative inflammation. Treatment regimens were ketorolac monotherapy vs ketorolac and

prednisolone vs dropless approach in a design where the eyedrops could be started 3 days preoperatively or on the day of surgery. The main outcome of this study was macular thickening at 3 months, but the specific aim of our article was early postoperative inflammation. Macular thickening and the association between macular thickening and early inflammation will be reported separately, and we are happy to learn that readers are awaiting these reports.

We welcome the suggestions on how to design future studies of dropless surgery vs eyedrops. We believe that dropless surgery should be a genuinely drop-free approach if it is to replace the use of eyedrops in standard cataract surgery. Thus, adding an active (eyedrop) treatment to participants in the dropless group to prevent report bias may cause inability to assess dropless surgery as a drop-free approach. In addition, sham injections may be associated with a risk for eyeball perforation, and we did not find that it was ethically justified.

We agree that the PREMED study is currently the best available study for evaluating combination of steroid and nonsteroidal anti-inflammatory drugs (NSAIDs) eyedrops vs steroid or NSAID monotherapy, and our article supports the findings of the PREMED study by providing results on the early inflammatory response, which was not assessed in that study.³ However, the PREMED study did not show that combination was superior to NSAID monotherapy; it reported that incidence of pseudophakic cystoid macular edema (PCME) was lowest in the combination group, but pairwise comparisons with NSAID monotherapy showed no statistically significant differences.² Similarly, the observation by Donnenfeld et al. that preoperative initiation of NSAID prophylaxis reduced the incidence of PCME was not statistically significant.⁴ To accurately estimate relative risks for developing PCME, even larger prospective clinical trials than the PREMED study or meta-analyses of large studies are required, and an internationally accepted definition and classification of PCME is needed.

Yusuf et al. state that the pursuit of dropless surgery should not end with our study and we agree. But, we recommend investigating other approaches than sub-Tenon dexamethasone and that future studies compare dropless surgery with eyedrop regimens containing NSAID eyedrops and not steroid monotherapy.

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