6. Dogru M, Erturk H, Shimazaki J, et al. Tear function and ocular surface changes with topical mitomycin (MMC) treatment for primary corneal intraepithelial neoplasia. Cornea 2003;22:627–39.

IOP after Triamcinolone Acetonide

Dear Editor:
We read with great interest the recent report by Jonas et al.[1] In their study, the authors have reported a rise in intraocular pressure (IOP) starting a week after the intravitreal injection of 20-mg triamcinolone acetonide.

We present the results of a study carried out at our department using 4-mg triamcinolone acetonide injected intravitreally for macular edema arising due to a variety of causes (cystoid macular edema including postcataract extraction, retinal vein occlusions and uveitis, diabetic macular edema, and edema associated with age-related macular degeneration).

In our series of 26 eyes, a rise in IOP was noted in 0.0% of eyes at 1 week, 15.8% of eyes at 6 weeks, 38.5% of eyes at 3 months, and 22.2% of eyes at 6-month follow up. The Friedman test was used on the data. There was a significant rise in mean IOP over the 6-month follow up ($P = 0.039$).

Maximum and mean IOPs remained within the normal range at week 1 and were observed to increase after week 6. All cases of raised IOP were controlled by available antiglaucoma medication, and none required surgical intervention.

The timing of raised IOP in our series was therefore later than that reported by Jonas et al. In their series, Chan et al[2] reported an IOP elevation at a mean of 5.2 weeks. A rise in IOP was noted by Young et al[3] 1 month or later after intravitreal triamcinolone injection.

We believe the later rise of IOP may be a result of the lower dose of intravitreal triamcinolone acetonide used in our case series. It is important to highlight this difference in outcomes, as 4 mg is the more commonly used intravitreal triamcinolone dose.

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References

1. Jonas JB, Degenring RF, Kreissig I, et al. Intraocular pressure elevation after intravitreal triamcinolone acetonide injection. Ophthalmology 2005;112:593–8.
2. Chan CK, Fan DS, Chan WM, et al. Ocular-hypertensive response and corneal endothelial changes after intravitreal triamcinolone injections in Chinese subjects: a 6-month follow-up study. Eye 2004;1–6.
3. Young S, Larkin G, Branley M, Lightman S. Safety and efficacy of intravitreal triamcinolone for cystoid macular oedema in uveitis. Clin Experiment Ophthalmol 2001;29:2–6.

Author reply

Dear Editor:
We thank Drs Dhir and Prasad for their interest in our article. They say that in their study population receiving a dose of 4-mg intravitreal triamcinolone acetonide for treatment of macular diseases similar to those in our study, intraocular pressure (IOP) increased significantly at 6 weeks after the injection, whereas at 1 week after the injection IOP did not differ significantly from baseline. They conclude that the later timing of the rise in IOP in their study with 4-mg triamcinolone compared with our study with about 20 mg of triamcinolone was due to the difference in the dose.

We agree with Drs Dhir and Prasad that the earlier increase in IOP may be associated with the higher dose used. It would agree with a previous dose-finding study on intravitreal triamcinolone acetonide for treatment of diabetic macular edema, in which the higher dose was associated with a slightly earlier (and markedly longer) increase in visual acuity than the lower dose.[1] In Dhir and Prasad's study, the peak in IOP rise was at about 3 months after the injection, whereas in the study with about 20 mg of triamcinolone, a decline in the frequency of an elevated IOP was noted at about 8 months after the injection. This disadvantage of a longer duration of the IOP rise with the higher dose may be associated with the advantage of a longer duration of the anti-edematous effect of triamcinolone, so that reinjections may become necessary at lower frequency with a higher dose.

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Reference

1. Spandau UH, Derse M, Schmitz-Valckenberg P, et al. Dosage-dependency of intravitreal triamcinolone acetonide as treatment for diabetic macular edema. Br J Ophthalmol 2005;89:999–1003.

Safe and Effective?

Dear Editor:
I enjoyed reading your editorial "Safe and Effective,"[1] and offer a few comments. It is common in ophthalmology journals for authors to describe interventional procedures such as surgical techniques, intraocular injections, or the use of topical and systemic drugs etc. and simply conclude that they are "safe and effective . . .." Although these interventions may be as safe and effective as claimed, there is an essential question: are there any absolute criteria for safety and efficacy, or are the claims simply accepted if the reviewers and editors do not object? Schachat et al appropriately remind that authors should take care when they use the charged words *safe* and *effective* and that reviewers should consider if the authors' proposed use is appropriate. The editorial writers announced that when they err, they would expect letters to editors. However, there are a lot of ophthalmologists who may miss reading these letters and may assume that the safety and efficacy claims are right.

The cornerstone for the public health is prophylaxis (rather than treatment); sending letters to the editor that gainsay the safety and efficacy claims may have a therapeutic role, but having proper criteria for publication of these charged words may have a prophylactic role.. I think that these adjectives (*safe* and *effective*) are more qualitative

rather than quantitative, and should be reconsidered. I hope that journals might find acceptable and scientific criteria before allowing their use.

There are a lot of busy ophthalmologists who read only the abstracts of the articles and even only the titles and their conclusions; they may be easily misled by these phrases. What are the practical guidelines to avoid these biases? I suggest the editorial board of each journal should clarify precisely the criteria that allow an intervention to be considered as safe and effective or require that the phrase *safe and effective* not be used in the report.

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Reference

1. Schachat AP, Chambers WA, Liesegang TJ, Albert DA. Safe and effective. Ophthalmology 2003;110:2073–4.

Author reply

Dear Editor:

Dr Mohammadpour agrees with our editorial that the terms *safe* or *effective* in relationship to drugs or procedures in journal articles are usually not appropriate, or that strict scientific criteria should be applied to apply those terms. Many journals—for example, the *American Journal of Ophthalmology*[1]—have specific guidelines in the author instructions addressing the use of statistics that should be applied for every manuscript. Even when not specifically dealt with in the author instructions, editors and reviewers are, or should be, familiar with the statistical nuances that Dr Mohammadpour recommends. Although ideal in theory, it is a fact that many published reports, including those describing some randomized clinical trials, have significant flaws[2] that may be known before publication (in which case they should be revealed in the "Discussion") or are sometimes only evident after publication. Flaws frequently relate to the methodology, and everything else, including the statistics and conclusions, consequently suffers.

To amplify the discussion further, *safe and effective* as applied to medications and procedures in humans is a somewhat subjective term that may circumvent statistics. The United States Food and Drug Administration (FDA) adopted the phrase *safe and effective* to indicate that a drug or device is effective for specific indications, provides benefits that outweigh the risks, is of high quality, and has directions for use that are sufficiently communicated. The FDA employs statisticians to evaluate the data to confirm that the study design, statistical analyses, and conclusions of safety and effectiveness are valid. *Safety* and *effectiveness* are not really scientific terms, but rather a consensus that the data submitted are sufficiently convincing to grant marketing approval. Postmarketing surveillance may detect clinically relevant side effects. Therefore, the term *safe and effective* as applied by the FDA is relative and may be reversed.

Treatments advocated in journal articles are usually for indications for which FDA approval has not been granted. We agree with Dr Mohammadpour that these articles cannot usually determine whether these treatments are either safe or effective. The studies reported in the literature can, at best, establish preliminary evidence of efficacy but usually need to be tested in further clinical trials. Further, these studies usually cannot be used to confirm safety, simply because the number of interventions is too low, so the chance of detecting rare but potentially serious adverse events generally is low.

Because no effective drugs or procedures lack side effects, safety assessment must be closely linked to the establishment of effectiveness. Physicians must establish the risk–benefit ratio themselves if they use drugs for indications that have not received FDA approval. We agree with Mohammadpour that journals have a pivotal role in assisting physicians in these decisions by attempting to verify the claims within each article. The reviewers and editors are always requested to scrutinize all the elements of a manuscript under their jurisdiction. Manuscripts are referred to a statistician or methodologist as appropriate, although most journal editors do not have ready access to these busy individuals. The process is not perfect, as we are dealing with human assessments.

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References

1. Guide for authors. Am J Ophthalmol 2005;139:A25–6. Available at: http://authors.elsevier.com/JournalDetail.html?PubID=601028&Precis=. Accessed April 19, 2005.
2. Altman DG. The scandal of poor medical research. BMJ 1994;308:283–4.