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Patients treated with intravitreal triamcinolone acetonide

The paper by Kocabora and coworkers (2008) underlines the message that patients treated with intravitreal triamcinolone acetonide are at risk of increased intraocular pressure (IOP) even after the clearance period of the drug. Furthermore, the development of intractable secondary glaucoma requiring surgical intervention is clear advice to monitor these patients carefully.

However, the study was performed in the period 2003–2006, before the prescribing information for the drug changed in 2007. The new information states that the intravitreal use of triamcinolone acetonide is not suggested because the high risk of complications, particularly because of the increase of IOP. After this modification, intravitreal triamcinolone acetonide is now an *against-label* and no more an *off-label* drug.

Currently, other drugs based on triamcinolone from different producers can be injected in vitreous. A recently introduced micronized gel triamcinolone (on-label for vitreous staining during vitreoretinal surgery) if used for intravitreal therapy (AMD, Myopia, Diabetes, CRVO/BRVO) is also correlated with increased IOP increase and can lead to filtering surgery in more than 50% of patients. In these cases the filtering surgery is frequently ineffective, leading to valve surgery in more than 25% of all cases. It must be underlined that this intravitreal use is absolutely off-label and that micronized triamcinolone is not a drug, but a surgical device.

To remain adherent to the on-label indications (verified by GCP trials) is mandatory for routine therapy. The European Commission document for "'Detailed guidance on the collection, verification and presentation of adverse reaction reports arising from clinical trials on medicinal products for human use, April 2004" is a useful guide to communicate these adverse reactions to the central national/supranational Agency (EMEA, FDA).

Pharmacovigilance is always important and the Ophthalmological Community must continue to be aware of the potential harm of these important drugs.

Reference

Kocabora MS, Yilmazli C, Taskapili M, et al. 2008. Development of ocular hypertension and persistent glaucoma after intravitreal injection of triamcinolone. *Clin Ophthalmol*, 2:167–71.

Response to correspondence from Gallenga and Lobefalo Re: Patients treated with intravitreal triamcinolone acetonide

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We thank Dr. Gallenga and Dr. Lobefalo for their interest in our article (Kocabora et al 2008) and for their comments.

We agree with them on the importance of pharmacovigilance and of warning the ophthalmology community about the potential risks of intravitreal triamcinolone (IVTA). We should always follow the principle of *primum, non nocere* in our medical practices. On the other hand, if we consider that the therapeutic effect of IVTA

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is almost 'miraculous' in select cases, then we also feel obligated to offer our patients the benefit of this treatment until a safer and effective alternative becomes available. This dilemma originates from the nature of our profession. Our main responsibilities are to inform our patients and obtain their consent for treatment by off-label use of trimancinoloneD and also to evaluate the risk-benefit ratio for each individual patient and eye, which is a prerequisite in selecting candidates for IVTA.

We do not think that off-label use of triamcinolone should be considered illicit; many well known drugs are used off-label in routine ophthalmological practice, including mitomycin-C (adjunct to trabeculectomy), cefuroxime (intracameral), and vancomycin (intravitreal), etc. Moreover, many approved drugs carry the risk of serious side effects with on-label use.

Steroid use in general comes with serious side effects regardless of the disease and administration route. Secondary intraocular pressure (IOP) elevation is observed even with approved uses of steroids such as ocular topical and systemic (oral and parenteral) uses. For that reason we do not consider IOP elevation to be a specific side effect of triamcinolone, although there is no doubt that the administration site exacerbates it. On the other hand, the retinal toxicity of preserved triamcinolone has been demonstrated in animal studies; hence, this toxicity can be avoided by use of a preservative-free triamcinolone formulation.

In conclusion, based on scientific rationale and guided by the results of medical studies, we believe that triamcinolone has become the de facto standard for treatment of certain edematous, inflammatory, and neovascular eye diseases as an off-label drug, but we also agree that its use should be limited according to precisely determined criteria

Reference

Kocabora MS, Yilmazli C, Taskapili M, et al. 2008. Development of ocular hypertension and persistent glaucoma after intravitreal injection of triamcinolone. *Clin Ophthalmol*, 2:167–71.