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LETTER

Toxic anterior segment syndrome and intracameral injection of cefuroxime axetil

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Dear editor

We read with concern the findings of toxic anterior segment syndrome in patients receiving intracameral injection of cefuroxime axetil, as described in the report by Çakir et al[1] in the March 2015 issue of *Clinical Ophthalmology*. Notably, the authors state that the form of cefuroxime used to extemporaneously compound cefuroxime for intracameral injection was cefuroxime axetil and that 17 cases of toxic anterior segment syndrome ensued. With over one million doses of intracameral cefuroxime administered to date, and with extensive clinical experience,[2] the unfortunate scenario described by the authors has not been realized elsewhere.

Based on information offered in the report, the root of the problem may lie in the inadvertent, or inappropriate, use of the axetil form of the antibiotic. Use of cefuroxime axetil does not conform with the guidelines published by the European Society of Cataract and Refractive Surgery,[3] and does not reflect the form of cefuroxime used in Aprokam®, the approved injectable form of cefuroxime that has recently become commercially available in Europe and in Turkey.

The axetil form of cefuroxime could be obtained from various sources, but is a form of cefuroxime not intended for injection. The axetil form of cefuroxime is used in, for example, tablets or oral suspensions where the drug particles do not remain in solution, but in a solid form or suspension. Cefuroxime axetil is an ethyl ester of cefuroxime that requires hydrolysis by esterases in the body to yield free cefuroxime. The axetil moiety of cefuroxime axetil is then metabolized to acetic acid and acetaldehyde.

Aside from the improper use of the axetil form of cefuroxime, and any effects from metabolic byproducts in the eye, concerns also surround the extemporaneous compounding procedure itself. One assumes the axetil form would have had to be placed into a liquid vehicle, and sterilization attempted prior to injecting into the anterior chamber of the eye. This procedure poses challenges in terms of accurate dose determination from a suspension and also sterilization of the suspension, both of which would likely interfere with accurate assessment of any dose actually delivered.

Once inside the eye, both the particulate matter of the axetil form and the metabolic acetic acid and acetaldehyde byproducts of axetil could have been noxious to the eye, in addition to uncertainties surrounding the delivered dose and sterility. Each of these factors, excluding the cefuroxime base, would themselves likely produce toxic anterior segment syndrome after intracameral injection. We hope our communication to the corresponding author is received and that such practices are discouraged in the region.

This report again underscores the hazards of extemporaneous compounding of products for injection into the eye. In answer to the clinical demand for a commercially

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available cefuroxime product, Aprokam was approved by the European Medicines Agency, with an indication for intracameral injection as prophylaxis for endophthalmitis after cataract surgery.

Aprokam does not use cefuroxime axetil, but does use the proper base for formulation into an injectable product. We thank the authors for bringing attention to the potential hazards of improper extemporaneous compounding as described in this publication.

Disclosure

The authors report no conflicts of interest in this communication.

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Authors' reply

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Dear editor

We are grateful to Gardner et al for their attention and interest in our paper. In our study, we investigated possible causes of an outbreak of toxic anterior segment syndrome step by step and finally we focused on the use of cefuroxime axetil at the end of surgery. This drug was not produced for intracameral use, and dilution problems have been reported previously.[1,2] While we had our suspicions about the agent and changed from cefuroxime axetil to moxifloxacin, Aprokam® was not commercially available in our country.

Despite the European Society of Cataract and Refractive Surgery (ESCRS) recommendations, use of intracameral cefuroxime has not been fully adopted. An ESCRS survey of member ophthalmic surgeons conducted in 2012 reported that the most common reasons for not using intracameral cefuroxime during cataract surgery were: the unavailability of a country/clinic-specific protocol, unavailability of an approved preparation, and concern over the risk of dilution errors.[3] These major concerns are directly addressed by Aprokam, which, as per the UK National Health Service National Patient Safety Agency injectable risk assessment proforma, is likely to be classified as a lower-risk product. Aprokam is currently the only product licensed for prophylaxis of postoperative endophthalmitis, and received approval from the European Medicines Agency in 2012.

In summary, we agree with the concerns of Gardner et al about the extemporaneous compounding of products delivered into the eye, and we recommend use of approved commercial and single-unit products to avoid the risk of dilution errors and contamination.

Disclosure

The authors report no conflicts of interest in this communication.

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