Clinical Alert
Intraocular Use of Epinephrine to Maintain Mydriasis during Cataract Surgery

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A recent alteration in the formulation of epinephrine from one of the more common sources of preservative-free epinephrine has contributed to a shortage or impending shortage of this product for ophthalmologists. In January 2017, PAR Pharmaceutical updated and began shipping the new formulation of epinephrine which in addition to containing 0.457 mg of sodium metabisulfite, will also contain 2.25 mg of tartaric acid per ml.

Currently, there is no published data or experience with intracameral administration of solutions containing tartaric acid. ASCRS has become aware of several reports of TASS that appear to have resulted from inadvertent use of the PAR product. The updated PAR product is not for intraocular use and the indication of induction and maintenance of mydriasis during intraocular surgery has been removed from the Prescribing Information. PAR has sent out updated Prescribing Information to providers on several occasions. Although, their 30 ml bottles of epinephrine 1 mg/ml (1:1000) specifically state on the label "Not for Ophthalmic Use," the smaller 1 ml single-use vials do not display this warning. This could potentially result in inadvertent use of the new product in hospitals or ambulatory surgery centers. We advise surgeons to check with their centers to ensure that the PAR Pharmaceutical epinephrine is not being ordered for intracameral use.

The reduction in supply of preservative-free epinephrine has led many surgeons to inquire about alternative sources of epinephrine or alternative pharmaceutical agents for maintaining mydriasis especially in patients with IFIS. For pharmaceutical agents, the term "preservatives" is used only for antimicrobials, such as methylparaben, chlorobutanol, and benzalkonium chloride.[1] Many of these products will contain bisulfite 0.1% which is added to improve stability by delaying the oxidation of the active substance. Corneal endothelial damage has been demonstrated with exposure to bisulfite 0.1%.[2] Although a preservative-free/bisulfite-free (PFBF) formulation of epinephrine is ideal, studies have revealed that corneas exposed to sodium bisulfite 0.05% demonstrated no functional or ultrastructural endothelial changes. Thus, diluting preservative-free epinephrine containing bisulfite 0.1% 1:4 with balanced salt solution (BSS) or mixing epi-Shugarcaine [3] (9 cc BSS Plus, 4 cc 1:1000 epinephrine, and 3 cc non-preserved lidocaine 4%) utilizing bisulfite-containing epinephrine will create a bisulfite concentration that should be safe for the corneal endothelium. Diluting epinephrine containing bisulfite in the irrigating bottle will of course also be safe due to the final low concentration of bisulfite.

Currently, we are aware of only limited pharmaceutical companies that are producing PFBF epinephrine. Belcher Pharmaceuticals (Largo, Fl) produces PFBF epinephrine but is a small supplier. Hospira (a Pfizer company) produced epinephrine containing metabisulfite but recently discontinued production. American Regent (a Luitpold Pharmaceutical company) was a large supplier of PFBF epinephrine but changed their formulation to contain bisulfite in 2012. Imprimis Pharmaceuticals (San Diego, CA) produces a non-preserved, methylparaben-free epinephrine. Other alternatives include compounded phenylephrine 1.5% with lidocaine 1.0% without bisulfite. Phenylephrine solutions have been well

tolerated by the corneal endothelium [4] and should remain stable for 1 month at room temperature.[5] Ophthalmologists should consider utilizing a 503B approved outsourcing facility for compounded intraocular medications. These facilities are held to a higher standard as a manufacturer requiring full current good manufacturing practice (CGMP) compliance. And finally, Omidria (Omeros Corporation, Seattle, WA) (phenylephrine 1%/ketorolac 0.3%) can be used in the irrigating bottle to help maintain mydriasis. [6] If Omidria is injected into the anterior chamber prior to beginning the procedure, it should not be used in the concentrated form but should be drawn from the irrigating bottle after dilution.

In an attempt to increase the available supply of PFBF epinephrine, ASCRS has been in communication with the Director of Medical Affairs and the Director of Marketing for American Regent in order to stress the need for a PFBF formulation of epinephrine. American Regent states that they will be releasing this formulation in May of 2018. Although the labeling will not state that the product will be approved for ophthalmic use, it will not contain preservatives, tartaric acid, or bisulfite and thus it should be safe for intracameral use. Until that time, we recommend judicious use of current supplies of PFBF epinephrine. If epinephrine is utilized in the irrigating bottle, it is recommended to reserve epinephrine containing bisulfite for this use since supplies of bisulfite-containing epinephrine will be more abundant than PFBF epinephrine. Bisulfite-containing epinephrine can be used safely intracamerally if it is diluted 1:4 or diluted in the irrigating bottle. We currently recommend NOT using epinephrine with tartaric acid (even in dilution) until more studies and information becomes available.

ASCRS Cataract Clinical Committee

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