

Clinical Statement

Drug Shortage: Non-preserved, bisulfate-Free Epinephrine

Background

Drug shortages are becoming more frequent in the US, because of a dwindling number of makers of some drugs, deteriorating conditions in factories, and low prices for generics leading to a lack of investment to upgrade plants. FDA is working with manufacturers to find solutions, but their priority has been on critical care and cancer drugs.

Earlier in 2012, American Regent which was the sole source in United States for non-preserved, bisulfate-free epinephrine, suspended its manufacture of drug products. As of December 18 2012, this product is still not available from American Regent, although manufacturing has resumed and product is expected to be restocked but they have not issued a resupply date. Non-preserved, bisulfate-free epinephrine is the basic component of the intracameral epi-Shugarcaine solution used for intraoperative floppy iris syndrome (IFIS) and pupil dilation.

Options

Ophthalmologists have devised a few options during this shortage period. Other companies make preservative-free epinephrine but these still contain bisulfites. One option has been to limit the use of remaining supplies of non-preserved, bisulfate free epinephrine to selected patients. Another option is to dilute non-preserved, bisulfate-containing epinephrine, because bisulfates can cause toxicity in the eye, leading to corneal edema and inflammation.^{1,2} One more option is to explore the use of non-preserved, bisulfate-free phenylephrine. Studies have suggested that the use of preservative-free phenylephrine, with or without the addition of lidocaine, provides adequate pupil dilation for cataract surgery using phacoemulsification.³⁻⁴ A prospective, randomized fellow eye study of 42 patients using tamsulosin and undergoing cataract surgery using phacoemulsification compared patients receiving nonpreserved, bisulfite free phenylephrine 1.5% solution and 1% lidocaine hydrochloride to patients receiving only balanced salt solution (BSS).³ The mean pupil diameter was $7.57 \text{ mm} \pm 1.04 \text{ (SD) mm}$ after hydrodissection in the group receiving phenylephrine, compared to $6.46 \pm 1.18 \text{ mm}$ in the group receiving BSS. The incidence of intraoperative floppy eye syndrome was 88% in the group receiving BSS but none in the group receiving phenylephrine. Another prospective, randomized, double-masked study compared 42 patients using different concentrations of

intracamerally injected epinephrine from 0.15 mg/mL to 30.00 mg/mL⁴ The pupil dilations were similar for the 0.15 to 5.00 mg/mL concentrations but the 15.0 mg/mL (1.5%) provided a larger pupil dilation of 5.80 ± 0.79 mm, and the 30.0 mg/mL (3.0%) produced a pupil dilation of 6.65 ± 0.57 mm.

One study looked at a case series of 57 patients using intracameral nonpreserved lidocaine 1% compared to topical cyclopentolate and phenylephrine 5%.⁵ The results showed that the mean pupil dilation was $4.52\text{mm} \pm 0.08$ in the group receiving intracameral lidocaine, compared to 4.05 ± 0.09 mm in the group receiving topical mydriatics. However, the authors cautioned that the duration of pupil dilation after intracameral lidocaine injection was unknown.

Phenylephrine may be obtained through compounding pharmacies. When using compounding pharmacies, its best to ensure that the pharmacy is accredited by the Pharmacy Compounding Accreditation Board and adheres to quality standards for aseptic compounding of sterile medications (USP <797>).

Resources

Here are some useful links to check on the availability of non-preserved, bisulfate-free epinephrine:

American Regent is posting daily updates on their website regarding product availability.
<http://www.americanregent.com/>

FDA updates a table on current drug shortages based on information from the manufacturers:

<http://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm314740.htm>

American Society of Health-System Pharmacists updates a list of drug shortages:

<http://www.ashp.org/DrugShortages/Current/Bulletin.aspx?id=685>

Here is information about compounding pharmacies:

Pharmacy Compounding Accreditation Board's website allows you to search accredited pharmacies by state or by name: <http://www.pcab.org/accredited-pharmacies>

Academy statement on Verifying Source of Compounded Bevacizumab for Intravitreal Injections has suggestions about selecting a compounding pharmacy:

http://one.aao.org/CE/PracticeGuidelines/ClinicalStatements_Content.aspx?cid=2409cf9a-7700-4342-a857-a6098e848f6a

Ophthalmic Mutual Insurance Company has some recommendations when using compounding pharmacies: <http://www.omic.com/intravitreal-anti-vegf-treatment-for-adults-patientsrisk-management-recommendations/>

References

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