Correspondence

Comment on: A Prospective, Randomized Trial of Povidone-Iodine 0.6% and Dexamethasone 0.1% Ophthalmic Suspension for Acute Bacterial Conjunctivitis

EDITOR

WE HAVE READ THE ARTICLE BY TA AND COLLEAGUES[1]; however, we believe that some discussion is required. In this interesting article, the investigators evaluated the efficacy and safety of a topical ophthalmic suspension combination of povidone-iodine (PVP-I) and dexamethasone (DEX) for acute bacterial conjunctivitis.

Within the study, subjects with bacterial conjunctivitis were randomized to receive either PVP-I 0.6%/DEX 0.1%, PVP-I 0.6% alone, or placebo. The treatment was administered 4 times a day (QID) for 7 days. Our recent review found that the evidence on PVP-I treatment of bacterial conjunctivitis in adults is scarce.[2] The investigators referred to an investigation by Schuhmann and Vidic in which PVP-I 0.3% was a reasonable alternative to gentamicin-sulphate (0.3%).[3] Nevertheless, in this study, PVP-I was applied every 2 hours for the first 3 days.[3] Antiseptics differ from antibiotics in their bactericidal kinetics; antibiotics require hours to act and interrupt bacterial enzymatic processes. Antiseptics, such as PVP-I, act within 30 seconds via free iodine interacting with amine (-NH), thiole (-SH) and phenol groups, as well as with lipids simultaneously.[4] Choosing a QID dosing schedule may not be ideal, because application of fresh free iodine is additionally effective within 30-second intervals.[5] Our review found that PVP-I could be an alternative in developing countries due to the low cost of manufacturing, because the price of a PVP-I solution ranges from 1.4% to 30% of the cost of most antibiotics.[2] Moreover, it can be transported as powder, which provides additional advantages in remote areas. We did not find studies that reported benefits of applying a combination of PVP-I and a corticosteroid.[2] What is the rationale for this approach for bacterial conjunctivitis?

Another issue is the concentration of PVP-I that should be applied in bacterial conjunctivitis; lower concentrations of PVP-I have been shown to be more effective in conditions in which no organics are present to inactivate the free iodine.[6] When the bacterial load is higher, low PVP-I concentrations might not have sufficient total available iodine for the bactericidal effect. Silas et al. showed that in an agar plate *in vitro* model of maximally, but subclinically contaminated conjunctiva, PVP-I 0.7% used 3 consecutive times over 2 min was the minimum concentration sufficient to reduce the bacterial population by the Food and Drug Administration—required 3-$\log_{10}$.[5] Even higher concentrations and/or iterations would be required for clinically apparent conjunctivitis. In contrast, the toxicity to the corneal epithelium is directly correlated with the concentration of PVP-I.[2]

Finally, in the study by Ta et al.[1] some patients did not receive a standard accepted treatment. Strong consideration should be given to substitute a placebo-controlled design with a noninferiority study in subsequent studies.

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