

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



IN THIS LETTER, WE RESPOND TO COMMENTS PRESENTED BY Drs. Kanclerz and Myers in their correspondence to the Editor regarding our article.¹

We conducted a randomized, prospective, double-masked, multicenter, phase III study to evaluate the efficacy and safety of a topical ophthalmic suspension combination of povidone-iodine (PVP-I; 0.6%) and dexamethasone (DEX; 0.1%) for infectious and inflammatory components of bacterial conjunctivitis. The primary endpoint was clinical resolution in the study eye, and the key secondary efficacy endpoint was bacterial eradication, both at the day 5 visit. We found that PVP-I/DEX did not demonstrate clinical efficacy compared with placebo in subjects with bacterial conjunctivitis. PVP-I/DEX had a favorable safety profile and was well tolerated.

In our study, treatment was administered 4 times a day for 7 days. Drs. Kanclerz and Myers suggested that more frequent dosing may be necessary, and referred to their recent review, which found that evidence on PVP-I treatment of bacterial conjunctivitis in adults is scarce.² We agree that more frequent dosing may be beneficial, but would like to note that patient compliance beyond 4 times daily dosing may be challenging, particularly because current Food and Drug Administration–approved antibiotic dosing is 3 times a day. In response to the comments made by Drs. Kanclerz and Myers regarding the fact that antiseptics act differently from antibiotics, we would like to note that, although we described the compound in our article, the differences were outside the scope of the current research.

Drs. Kanclerz and Myers commented that they did not find studies that reported benefits of applying a combination of PVP-I and a corticosteroid; they queried the rationale for this approach for bacterial conjunctivitis. Our rationale for using DEX was to reduce inflammation associated with the conjunctivitis. The usefulness of adding a steroid is described in the Introduction section of our paper, where we highlight how topical steroids have demonstrated usefulness in reducing the adverse effects of inflammation in the treatment of infections of the anterior segment of the eye.

In their letter to the Editor, Drs. Kanclerz and Myers commented on the concentration of PVP-I that should be applied in bacterial conjunctivitis, with the suggestion that the dose in the current study could have been higher. The concentration-dependent availability of free iodine is well discussed in our paper. The rationale for the 0.6% dose in the current study was based on data from previous studies (referenced in the article), although we acknowledge that

with the benefit of hindsight, adjustments in the concentration, dosing schedule, or both might have led to a different result. As noted in our article, previous evidence suggests that PVP-I concentrations >1.25% may decrease tolerability.^{3,4} Therefore, the concentration must be balanced against side effects and toxicity.

The final point raised by Drs. Kanclerz and Myers is that strong consideration should be given to substitute a placebo-controlled design with a noninferiority study in subsequent studies. In response, we believe that a placebo-controlled trial would be a more robust study, especially because most bacterial conjunctivitis cases are self-limiting.^{5,6}

CHRISTOPHER N. TA
Palo Alto, California, USA
MICHAEL B. RAIZMAN
Boston, Massachusetts, USA
ROBERT D. GROSS
Dallas, Texas, USA
SUNIR JOSHI
Fort Lauderdale, Florida, USA
SUSHANTA MALLICK
YUEMEI WANG
Lexington, Massachusetts, USA
BRUCE SEGAL
Delray Beach, Florida, USA

CONFLICT OF INTEREST DISCLOSURES: SEE THE ORIGINAL article for any disclosures of the authors.

REFERENCES

1. Ta CN, Raizman MB, Gross RD, et al. A prospective, randomized trial of povidone-iodine 0.6% and dexamethasone 0.1% ophthalmic suspension for acute bacterial conjunctivitis. *Am J Ophthalmol* 2020;215:56–65.
2. Grzybowski A, Kanclerz P, Myers WG. The use of povidone-iodine in ophthalmology. *Curr Opin Ophthalmol* 2018;29(1):19–32.
3. Isenberg SJ, Apt L, Valenton M, et al. A controlled trial of povidone-iodine to treat infectious conjunctivitis in children. *Am J Ophthalmol* 2002;134(5):681–688.
4. Isenberg SJ, Apt L, Yoshimori R, Pham C, Lam NK. Efficacy of topical povidone-iodine during the first week after ophthalmic surgery. *Am J Ophthalmol* 1997;124(1):31–35.
5. Morrow GL, Abbott RL. Conjunctivitis. *Am Fam Physician* 1998;57(4):735–746.
6. Patel PB, Diaz MC, Bennett JE, Attia MW. Clinical features of bacterial conjunctivitis in children. *Acad Emerg Med* 2007;14(1):1–5.

Comment on: Accuracy of Intraocular Lens Formulas in Eyes With Keratoconus



EDITOR:

WE READ WITH GREAT INTEREST THE EXCELLENT ARTICLE by Wang and associates.¹ We recognize that intraocular

lens power calculation in patients with keratoconus is challenging. Determining the accurate keratometry readings, axial length, and anterior chamber depth can be difficult in these eyes, which can lead to inaccurate and unpredictable results with a tendency to hyperopic refractive surprises.¹⁻⁴ To the best of our knowledge, this is the first study that reports the Barrett Universal II as the most accurate formula in mild keratoconus (stages I and II).

Wang and associates¹ noted that it was not possible to apply the Barrett Universal II formula in more advanced stages (stage III) because the online calculator did not allow include keratometry entries >55 diopters (D). Currently, the online calculator provided by the Asia-Pacific Association of Cataract and Refractive Surgeons and other online calculators,^{5,6} allow the input of keratometric powers ranging from 30 D-60 D (≤ 65 D in the Kane formula), which enables the inclusion of more advance stages of keratoconus.

Savini and associates² reported that the SRK/T formula was superior to the Barrett Universal II formula, providing the lowest predicted error and highest percentage of eyes with a predicted error within ± 0.5 D, with the worst median absolute error in stage III eyes regardless of the formula.

Recently, Kane and associates⁶ demonstrated that formulas with adjustments for keratoconus can be an interesting option, being even slightly superior to traditional formulas. Regarding traditional formulas, SRK/T and Barrett Universal II remain the best options, which is consistent with the findings in the study by Wang and associates.¹

Considering the lower accuracy of intraocular lens power calculations in more severe cases of keratoconus,¹⁻⁴ we believe it would be interesting to explore the Barrett Universal II formula in severe cases such as those reported by Wang and associates, to determine its efficacy in more advanced cases that are usually the most questionable.

EDUARDO GONZALEZ-LUBCKE
NICOLAS KAHUAM-LOPEZ
ALEJANDRO NAVAS
ARTURO RAMIREZ-MIRANDA
ENRIQUE O. GRAUE-HERNANDEZ

*Department of Cornea and Refractive Surgery
Instituto de Oftalmología "Conde de Valenciana"
Mexico City, Mexico*

ALL AUTHORS HAVE COMPLETED AND SUBMITTED THE ICMJE form for disclosure of potential conflicts of interest. Funding/Support: The authors indicate no financial support or financial conflict of interest. All authors attest that they meet the current ICMJE criteria for authorship.

1. Wang K, Jun A, Ladas J, Siddiqui A, Woreta F, Srikumaran D. Accuracy of intraocular lens formulas in eyes with keratoconus. *Am J Ophthalmol* 2020;212:26-33.
2. Savini G, Abbate R, Hoffer KJ, et al. Intraocular lens power calculation in eyes with keratoconus. *J Cataract Refract Surg* 2019;45(5):576-581.
3. Watson MP, Anand S, Bhogal M, et al. Cataract surgery outcome in eyes with keratoconus. *Br J Ophthalmol* 2014; 98(3):361-364.
4. Piñero DP, Camps VJ, Caravaca-Arens E, et al. Estimation of the central corneal power in keratoconus: theoretical and clinical assessment of the error of the keratometric approach. *Cornea* 2014;33:274-279.
5. Barrett G. Barrett Universal II formula. Available at: http://calc.apacrs.org/barrett_universal2105/. Accessed April 13, 2020.
6. Kane JX, Connell B, Yip H, et al. Accuracy of intraocular lens power formulas modified for patients with keratoconus. *Ophthalmology* 2020; <https://doi.org/10.1016/j.optha.2020.02.008>. In press.

Reply to Comment on: Accuracy of Intraocular Lens Formulas in Eyes With Keratoconus



EDITOR:

WE APPRECIATE THE COMMENTS AND INQUIRY FROM Gonzalez-Lubcke and associates. Intraocular lens (IOL) power calculations in eyes with keratoconus is indeed more unpredictable than in normal eyes using third and fourth-generation IOL formulas.

An exclusion criterion of our study was postoperative best spectacle-corrected visual acuity (BSCVA) of 20/40 or better, and many eyes with stage III keratoconus were contact lens-dependent and not able to achieve BSCVA of 20/40 or better. Thus, there were only 5 eyes with stage III keratoconus that were included in our study.¹ The Barrett Universal II calculator on the Asia-Pacific Association of Cataract and Refractive Surgeons (APACRS) website is able to accept input variables from 2 of our 5 stage III eyes.² In the 3 eyes where the online calculator is unable to be applied, 1 has a corneal power >60 diopters (D) and 2 have IOL models implanted that are not compatible with the Barrett calculator. In the 2 eyes where the online calculator is able to be used, the predicted errors are 3.82 D and 0.43 D. This result is only from 2 eyes; therefore, we cannot reliably assess the performance of the Barrett Universal II formula in stage III keratoconus.

Savini and associates³ previously showed that the SRK/T formula was superior to the Barrett Universal II formulas in