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CORRESPONDENCE

Comment on: 'A randomized masked pilot clinical trial to compare the efficacy of topical 1% voriconazole ophthalmic solution as monotherapy with combination therapy of topical 0.02% polyhexamethylene biguanide and 0.02% chlorhexidine in the treatment of *Acanthamoeba* keratitis'

Alfonso Iovieno[1] · Sonia N. Yeung[1]

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To the Editor:

We have read with interest the randomised clinical trial by Bagga et al. on the use of topical Voriconazole as single agent for treatment of *Acanthamoeba* keratitis (AK) [1]. Despite a relatively small number of cases enroled, the authors observed non-inferiority of voriconazole to double biguanide treatment in regard to several parameters including time to clinical resolution and final visual acuity. Moreover, topical Voriconazole had a higher percentage of clinical resolution and a lower percentage of worsened patients, although not statistically significant.

One element that is not clear to us is the length of follow-up for patients in each group. How exactly were the cases "in clinical resolution" defined in relationship to the length of follow-up? In other words, could an extension of treatment or follow-up in those cases have resulted in complete healing?

As the authors reported in their manuscript, several in vitro studies have explored the amoebicidal properties of Voriconazole against amoeba cysts and trophozoites, including one from our group [2]. The conflictive results of these studies have been largely attributed to a lack of uniformity in laboratory methodology and, to a minor extent, to the use of different strains of *Acanthamoeba*.

While oral Voriconazole has gained a certain popularity as an adjunctive treatment in cases of recalcitrant AK [3], the use of topical voriconazole in the clinical setting has been underwhelming in the experience of many clinicians, including ourselves (unpublished data).

This difference may depend on several factors. Similar to in vitro studies, clinical trials could also reflect geographical prevalence of certain strains or genotypes of *Acanthamoeba*, with variable sensitivity to Voriconazole. Genotyping of the organisms was not reported in this study. One other element to be taken into account is that in previous reports Voriconazole has largely been used in combination with other antiamoebics and not as monotherapy [4]. Given the reported antagonism of Voriconazole in vitro on the cysticidal activity of chlorhexidine and propamidine [5], the poor response to topical Voriconazole might have been, at least in some cases of AK, secondary to the use of concomitant medications.

We conclude by congratulating the authors on their interesting findings and we look forward to further clinical evidence on the topic.

Author contributions AI (conception of manuscript, revision and analysis of previous literature, writing of manuscript) SNY (revision and analysis of previous literature, revision of manuscript).

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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✉ Alfonso Iovieno
alfonsoiovieno@hotmail.com

[1] Department of Ophthalmology and Visual Sciences, University of British Columbia, Vancouver, BC, Canada

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