Comparative study on corneal cross-linking with isotonic and hypotonic riboflavin: can hypotonic riboflavin be applied in thinner corneas?

Reviewer 1
The authors propose to compare the results of corneal cross-linking (CXL) with isotonic (IR) and hypotonic riboflavin (HR) in patients with keratoconus and to verify the efficacy of keratoconus in thinner corneas. To do so, they deeply study several parameters (1-year follow-up): best corrected visual acuity (BCVA), sphere and cylinder, central and finer pachymetry, mean and maximum keratometry (Km and Kmax respectively).

Finally, authors demonstrate that the use of HR seems to be a valid alternative for performing the traditional CXL technique in eyes with a central corneal thickness of <400 μm.

In my opinion, it is an interesting paper and reports a very novel case. It is a well written manuscript and I only have minor comments.

Point 1: Page 2. The keywords may not appear in the title.

Point 2: Page 3. "Retrospective study of 29 eyes of 29 patients with keratoconus from the Cornea Clinic of the Ophthalmology Department at the Hospital Professor Doutor Fernando Fonseca EPE (HFF, Lisbon, Portugal), submitted to CXL between 2012 and 2018, 15 eyes with IR application (IR group) and 14 eyes with HR application (HR group). Inclusion criteria consisted of: keratoconus in stages 1 to 3, according to Amsler-Krumeich classification; keratoconus with documented progression in the 12 months prior to the start of treatment, through refraction and/or corneal topography. Exclusion criteria consisted of: previous corneal surgery; history of herpetic keratitis; recurrent corneal infections; severe dry eye, and stable keratoconus in stage 4. All consecutive patients meeting the criteria during the period considered were included and the principles of the Helsinki Declaration (2008)”. Authors should update the Declaration of Helsinki, there is currently a new version.

The authors must indicate whether the study has been approved by the local ethical committee and indicate the IRB number.

Point 3: In general, the quality of the figures should be improved.

Response: Regarding the ethics committee issue, we wrote in the revised manuscript that we have the approval by the hospital ethical committee, but we were not given the IRB number in the declaration of approval.

Reviewer 2
1. Power of the study should be mentioned
2. Comparison of Delta changes of both groups will be more valuables
3. Correlation between the different preoperative dependent variables and the results like age, k readings, cone location are important
4. The authors did not mention information about the Epithelial healing and the corneal haze in both groups
5. I believe that contrast sensitivity and data bout the quality of the vision will be valuable
6. Is the pachymetry was measured intraoperatively after application of riboflavin in the group < 400
7. The authors should discuss that some studies noticed that there are no complications occurred
after standard CXL in patients < 400 with standard isotonic riboflavin

**Response:** Regarding the point 5 ("I believe that contrast sensitivity and data about the quality of the vision will be valuable"): these tests are not routinely done in our hospital, so not all clinical files had this complete information and we decided not to include in the list of parameters to study.