Response to: Corneal collagen cross-linking by sun exposure and high dose oral riboflavin: a multicentric longitudinal observational study

Resposta para: Crosslinking de colágeno corneano por exposição solar e riboflavina oral em altas doses: um estudo observacional longitudinal multicêntrico

Edna Almodin[1], **Flávia Almodin**[1], **Juliana Almodin**[1]

[1] Provisão Hospital de Olhos de Maringá, Maringá, PR, Brazil.

How to cite:
Almodin E, Almodin F, Almodin J. Response to: Corneal collagen cross-linking by sun exposure and high dose oral riboflavin: a multicentric longitudinal observational study [letter]. Rev Bras Oftalmol. 2026;85:e0019.

doi:
https://doi.org/10.37039/1982.8551.20260019

Received on:
October 8, 2025

Accepted on:
October 24, 2025

Corresponding author:
Edna Almodin
E-mail: ealmodin@gmail.com

Institution:
Provisão Hospital de Olhos de Maringá, Maringá, PR, Brazil.

Conflict of interest:
no conflict of interest.

Financial support:
no financial support for this work.

Dear Editor,

We appreciate your thoughtful review of our recently published article. We fully agree that the ideal way to evaluate the potential of oral riboflavin combined with sun exposure would be through a prospective, controlled, large-scale study involving patients with documented progressive keratoconus. Only then would it be possible to unequivocally distinguish the effect of the intervention from natural variability, spontaneous stability, or co-interventions.

However, as rightly pointed out, an 'ideal' experiment faces significant practical barriers.[1] Ultraviolet radiation intensity varies depending on geography, season, and daily weather conditions, factors that are difficult to standardize. Therefore, in many real-world scenarios, the feasible study design differs from that considered theoretically optimal. Our aim was to present initial data, acknowledging their limitations, but encouraging discussion and the development of more structured investigations. We consider it equally important to emphasize that epidemiological data on keratoconus progression should be interpreted with caution. The frequently cited finding that "88% of patients under 18 will progress" comes from the study published by Chatis and Hafezi et al. [2], conducted at a crosslinking referral center. Naturally, such samples are enriched by more severe and aggressive cases. Extrapolating those numbers to the general population may be misleading. Using these data as justification for recommending crosslinking at the time of diagnosis in all young patients poses the risk of exposing individuals – who might otherwise remain stable under close follow up – to an unnecessary surgical procedure, which, although rare, may result in severe complications, such as haze, severe flattening, corneal thinning and melting, acanthamoeba, pseudomonas infections, etc., as mentioned in several reports in the literature.

I have cited the example of Hafezi's work precisely to emphasize that we are not always able to apply ideal methodological conditions. Nonetheless, this does not diminish its relevance: on the contrary, it is a fundamental study, which serves as a starting point for another related research. Likewise, our work aims to present results observed in clinical practice, acknowledging its limitations but providing support for more refined future investigations. At no point did we conclude that oral crosslinking could replace surgical crosslinking.

Furthermore, we do not consider it appropriate to classify studies as 'anecdotal'. Every study has its own value – not necessarily to definitively prove a hypothesis, but to serve as scientific groundwork and as a stimulus that encourages further research.[3]

This is how knowledge is built: from initial observations to more robust trials, in a continuous process of methodological refinement, just how you did with your article about Corneal Cross-linking with Riboflavin Using Sunlight.[4] Thus, we were very delighted to learn that our main goal, which was to spark the interest of genuine researchers to verify our hypothesis, was achieved at the *Universidade Federal de São Paulo* (UNIFESP).

Finally, we would like to reinforce that every research line requires initial studies that are gradually refined. The criticisms presented are valid and should serve as an incentive for other researchers to advance the field, reducing biases that, while not completely eliminated, can be mitigated. If our study represents only a first step in this field, we already consider its publication to be of great importance, always with the great purpose of providing the best possible care to our patients.

AUTHORS' CONTRIBUTION

Both authors actively contributed to the production of the manuscript.

REFERENCES

1. Corrêa M.P.Solar Ultraviolet radiation: Properties, characteristics and amounts observed in Brazil and South America. An Bras Dermatol. 2015;90(3):297-310.
2. Chatzis N, Hafezi F. Progression of keratoconus and efficacy of pediatric corneal collagen cross-linking in children and adolescents. J Refract Surg. 2012;28(11):753-8.
3. Torres-Netto EA, Abdshahzadeh H, Lu NJ, Kling S, Abrishamchi R, Hillen M, et al. Corneal crosslinking with riboflavin using sunlight. J Cataract Refract Surg. 2023;49(10):1049-55.
4. Campêlo ED. Efeito da riboflavina oral associada à exposição solar em pacientes com ceratocone em progressão [tese]. São Paulo: Universidade Federal de São Paulo; 2025. Available at: https://hdl.handle.net/11600/72901.