Arquivos Brasileiros de
Oftalmologia

Response to: topical cyclosporine A 0.05% before and after surgery to prevent pterygium recurrence

Resposta para: Ciclosporina A 0,05% antes e após a cirurgia do pterígio para a prevenção da recorrência

Goksu Alacamli[1]

1. Ophthalmology Departmant, Mugla University Education and Research Hospital, Mugla, Turkey

Dear Editor,

We have read with interest the article by Roberta Lilian Fernandes de Sousa Meneghim et al.[1]. In response to this article[1] which is a well-thought out and written paper, I would like to draw attention to some critical points in this study. As presented in most studies, topical cyclosporine drops require at least 3-6 months for their effectiveness to begin[2-4]. In the article by Meneghim et al.[1], topical cyclosporine was used for only 10 days before and after the operation. In our clinic, Mugla Education and Research Hospital, we prescribe topical cyclosporine 3 months before and 6 months after the pterygium operation. In this article[1], it seemed obvious that topical cyclosporine used for such a short time before and after the operation would not have a statistical or clinical effect.

Pterygium pathogenesis has been mainly associated with ultraviolet light exposure; however, this association remains quite controversial. The complete pathophysiology of pterygium also remains to be clarified[5]. To reduce recurrences, new study and treatment methods are needed.

REFERENCES

1. Meneghim RLFS, Satto LH, Natsuaki KL, Oliveira AC, Padovani CR, Viveiros MMH, et al. Topical cyclosporine A 0.05% before and after surgery to prevent pterygium recurrence. Arq Bras Oftalmol. 2019;82(5):372-6.
2. de Paiva CS, Pflugfelder SC, Ng SM, Akpek EK. Topical cyclosporine A therapy for dry eye syndrome. Cochrane Database Syst Rev [Internet]. 2019[cited 21 sep 2020] ;9(9):CD010051. Available from: Topical cyclosporine A therapy for dry eye syndrome - de Paiva, CS - 2019 | Cochrane Library
3. Özülken K, Koç M, Ayar O, Hasiripi H. Topical cyclosporine A administration after pterygium surgery. Eur J Ophthalmol. 2012;22 Suppl 7:S5-10.
4. Hwang S, Choi S. A comparative study of topical mitomycin C, cyclosporine, and bevacizumab after primary pterygium surgery. Korean J Ophthalmol. 2015;29(6):375-81.
5. Wanzeler ACV, Barbosa IA, Duarte B, Borges D, Barbosa EB, Kamiji D, et al. Mechanisms and biomarker candidates in pterygium development. Arq Bras Oftalmol. 2019;82(6):528-36.

Submitted for publication: November 9, 2021
Accepted for publication: November 16, 2021

Funding: This study received no specific financial support.

Disclosure of potential conflicts of interest: The author have any potential conflicts of interest to disclose.

Corresponding author: Goksu Alacamli.
E-mail: goksualacamli@yahoo.com

 http://dx.doi.org/10.5935/0004-2749.20220092

Response to: topical cyclosporine A 0.05% before and after surgery to prevent pterygium recurrence

Resposta para: Ciclosporina A 0,05% antes e após a cirurgia do pterígio para a prevenção da recorrência

Roberta Lilian Fernandes de Sousa Meneghim[1], Larissa Horikawa Satto[1], Kryscia Leiko Natsuaki[1], Alessandro Carvalho de Oliveira[1], Carlos Roberto Padovani[2], Magda Massae Hata Viveiros[1], Silvana Artioli Schellini[1]

1. Department of Ophthalmology, Botucatu Medical School, Universidade Estadual Paulista "Julio de Mesquita Filho", Botucatu, SP, Brazil.
2. Department of Biostatistic, Biosciences Institute, Universidade Estadual Paulista "Julio de Mesquita Filho", Botucatu, SP, Brazil.

Dear Dr. Alacamli,

Thank you for your interest in our study involving pterygium and the use of cyclosporine A (CsA) as an adjuvant drug to prevent pterygium recurrence after lesion removal.

According to a recent review, the main risk factor of pterygium progression remains ultraviolet exposure[1], and one of the most challenging aspects involving this lesion is still the prevention of recurrence.In a previous *in vitro* study, we found that 0.05% CsA is effective in inhibiting fibroblast proliferation, both in primary and in recurrent pterygium[2]. Also, *in vitro*, a combination of CsA with bevacizumab can reduce fibroblast outgrowth from cultured pterygium tissue explants, playing an important role in fibroblast migration and preventing T-helper cell activation and inflammatory cytokine production[3].

However, when using CsA for 10 pre- and 10 postoperative days, as stated in our article, we observed that CsA did not prevent or reduce the recurrence of pterygium, probably because of the short period of use[4]. As you also reinforced, the results can be influenced by the short period that the drug was used for, which should be not enough.

In addition to the short period of use, there are other *biases* that can directly affect the outcome of the pterygium studies, as the inclusion of a few patients, application mode (topically or by subconjunctival injection), and variations in surgical techniques. Because of this, a meta-analysis was conducted, suggesting that adjuvant use of CsA can significantly reduce the risk of pterygium recurrence compared with pterygium excision alone, whereas CsA may not reduce the risk of pterygium recurrence if pterygium excision is associated with limbal conjunctival autograft or conjunctival flap rotation[5].

Our study concluded that "Topical 0.05% CsA, when used for 10 days before and 10 days after the pterygium removal, does not prevent or reduce the recurrence of primary pterygium", and we suggested that "further studies are necessary to evaluate the efficacy of CsA to prevent pterygium recurrence when used for different time periods and assess which number of days of preoperative CsA use provides benefit if any".

According to others, postoperative topical 0.05% CsA (4 times a day for 6 months) can prevent recurrence of pterygium[6].

In conclusion, further studies are still needed to prove the best way to prevent pterygium recurrence and the role of CsA in it.

Submitted for publication: November 20, 2021
Accepted for publication: November 22, 2021

Funding: This study received no specific financial support.

Disclosure of potential conflicts of interest: The author have any potential conflicts of interest to disclose.

Corresponding author: Silvana Artioli Schellini.
E-mail: s.schellini@unesp.br

REFERENCES

1. Shahraki T, Arabi A, Feizi S. Pterygium: an update on pathophysiology, clinical features, and management. Ther Adv Ophthalmol. 2021;13:25158414211020152.
2. Viveiros MM, Kakizaki FY, Hercules LA, Padovani CR, Candeias JM, Schellini SA. In vitro study of cyclosporine A 0.05% on primary and recurrent pterygium fibroblasts. Int Ophthalmol. 2016;36(2): 237-42.
3. Kim YH, Jung JC, Gum S, Park SB, Ma JY, Kim Y, et al. Inhibition of pterygium fibroblast migration and outgrowth by bevacizumab

and cyclosporine A involves down-regulation of matrix metalloproteinases-3 and -13. PLoS One. 2017;12(1):e0169675. doi.org/10.1371/journal.pone.0169675

4. Meneghim RLFS, Satto LH, Natsuaki KL Oliveira AC, Padovani CR, Viveiros MMH, et al. Topical cyclosporine A 0.05% before and after surgery to prevent pterygium recurrence. Arq Bras Oftalmol. 2019;82(5):372-6.
5. Zhang Q, Bao N, Liang K, Tao L. Adjuvant use of cyclosporine A in the treatment of primary pterygium: a systematic review and meta-analysis. Cornea. 2018;37(8):1000-7.
6. Turan-Vural E, Torun-Acar B, Kivanc SA, Acar S. The effect of topical 0.05% cyclosporine on recurrence following pterygium surgery. Clin Ophthalmol [Internet]. 2011[cited 21 sep 2020];5: 881-5.