

A warning against associating doxycycline with isotretinoin

Um alerta contra a associação de doxiciclina com isotretinoína

Alexandre Xavier da Costa¹ , Gabriel Lima Benchimol², Tulio Frade Reis³ 

1. Department of Ophthalmology and Visual Sciences, Universidade Federal de São Paulo, São Paulo, SP, Brazil.

2. Universidade Estácio de Sá, Rio de Janeiro, RJ, Brazil.

3. Department of Ophthalmology, Otorhinolaryngology and Head and Neck Surgery, Universidade de São Paulo, Ribeirão Preto, SP, Brazil.

Dear Editor:

After reading with great interest the article recently published by Andrade et al.⁽¹⁾ about the use of isotretinoin and doxycycline to treat rosacea, we became concerned about an inadvertent possible treatment effect when using both drugs simultaneously.

The use of isotretinoin to treat severe forms of rosacea has been reported, but this medication can also worsen ocular symptoms as a result of dry eye, blepharitis, and hordeolum, as well described by Andrade et al.⁽¹⁾.

Although the authors indicate that low-dose isotretinoin may be associated with a good treatment response in patients with rosacea along with reduced general side effects, worsening of ocular symptoms was notably pronounced in these patients, in contrast to what was observed in the doxycycline group. This might suggest to readers, especially dermatologists and ophthalmologists, that the use of doxycycline might be a good choice for patients suffering from blepharitis and rosacea combined with isotretinoin. Nonetheless, the authors did not mention that the association of both drugs is contraindicated because of the elevated risk of pseudotumor cerebri⁽²⁾.

In their systematic review on drug-induced intracranial hypertension (DIH), Tan et al.⁽³⁾ identified that the drugs most strongly associated with DIH are vitamin A derivatives (especially isotretinoin) and tetracycline-class antibiotics (minocycline, tetracycline, and doxycycline).

One previous observational case series reported 179 cases of intracranial hypertension associated with isotretinoin use, of whom, based on spontaneous reports, 43 (24%) patients had taken tetracycline-class antibiotics beforehand⁽⁴⁾.

Physicians should understand the strength of association of each of the aforementioned DIH medications and exercise caution when prescribing them. A washout period of seven days is recommended when switching between tetracycline-class antibiotics and isotretinoin⁽⁵⁾. Physicians should also notice that these seven days are the theoretically calculated seven half-lives needed to achieve 99% drug clearance after the last dose. There is no clinical evidence on the ideal interval, but it is important to stress the danger of associating the two drugs and to understand that because of the rareness of the event, a clinical study on that matter would be hard to perform.

REFERENCES

1. Andrade FMX, Picosse FR, Cunha LP et al. Ocular surface changes in the treatment of rosacea: comparison between low-dose oral isotretinoin and doxycycline. *Arq Bras Oftalmol.* 2020;83(2):109-12.
2. Lee AG. Pseudotumor cerebri after treatment with tetracycline and isotretinoin for acne. *Cutis.* 1995;55:165-73.
3. Tan MG, Worley B, Kim WB et al. Drug induced intracranial hypertension: a systematic review and critical assessment of drug-induced causes. *Am J Clin Dermatol.* 2020;21:163-72.
4. Fraunfelder FW, Fraunfelder FT and Corbett JJ. Isotretinoin-associated intracranial hypertension. *Ophthalmology.* 2004;111:1248-50.
5. Caruana DM, Wylie G. "Washout" period for oral tetracycline antibiotics prior to isotretinoin. *Br J Dermatol.* 2016;174:929-30.

Submitted for publication: April 20, 2020

Accepted for publication: May 10, 2020

Funding: This study received no specific financial support.

Disclosure of potential conflicts of interest: None of the authors have any potential conflicts of interest to disclose.

Corresponding author: Alexandre X. da Costa.
E-mail: dr.alexandre.x@gmail.com

 This content is licensed under a Creative Commons Attributions 4.0 International License.