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## Letter to the Editor

**Therapeutic conflict in patients with COVID-19 and glaucoma<sup>☆</sup>**

**Conflicto terapéutico en pacientes con COVID-19 y glaucoma**

Dear Editor,

The COVID-19 pandemic has led to major efforts in the rapid research and development of drugs that can improve the prognosis of the disease, but for which safety and efficacy have not yet been established. In particular, certain antimicrobial drugs have started to be used which have an uncertain benefit, yet to be validated, for a statistically significant number of patients, and that may also increase the risk of QT prolongation and ventricular arrhythmia, namely, chloroquine, hydroxychloroquine, azithromycin, and lopinavir/ritonavir. During the pandemic, efforts to reduce the spread and minimize the effects on health care resources require a reduction of unnecessary medical procedures and tests. And in this line, the risk of drug-related arrhythmia should be minimized so that, if a patient is found to have a significantly prolonged QT interval, drugs that further prolong it should be avoided, or administered with extreme caution. These recommendations are made while no effective treatments for COVID-19 are known and should be reviewed when more data on efficacy and safety are available.<sup>1</sup>

Topical timolol maleate is a non-selective beta-adrenergic antagonist that is commonly used for the treatment of open/angle glaucoma. Its mechanism of action is to produce a decrease in intraocular pressure by reducing the production of aqueous humour at the level of beta-adrenergic receptors in ocular ciliary processes. Several studies have reported on the known systemic effects of topical timolol maleate such as bradycardia, hypotension, atrioventricular block, worsening congestive heart failure, and induction of bronchospasm.<sup>2</sup>

In the study by Pratt et al., the risk of bradycardia increased significantly in the 31–180 days after the start of timolol, which increased the hospitalization rate in certain cases. Therefore, since bradycardia is a potential adverse event of timolol, professionals should consider the patient's history before choosing the

therapeutic regimen for their glaucoma and closely monitor such patients after initiation of treatment with these non-selective topical beta-blocker eye drops.<sup>3</sup>

Furthermore, there is evidence that would suggest that the concomitant use of hydroxychloroquine together with a beta-blocker (e.g., metoprolol) would increase the bioavailability of the latter by inhibiting its metabolism through CYP2D6, which would potentially further increase these side effects.<sup>4</sup>

Therefore, given that some patients with COVID-19 may suffer from glaucoma and be on topical treatment with beta-blocker eye drops, it would be advisable to consider discontinuing topical treatment with these eye drops in COVID-19 patients who are candidates for treatment with cardiotoxic antimicrobials and replace them with other anti-glaucoma therapy options such as eye drops with prostaglandin analogues or carbonic anhydrase inhibitors, as well as considering laser trabeculoplasty, if the patient's general condition allows it.

**References**

1. Sapp JL, Alqarawi W, MacIntyre CJ, Tados R, Steinberg C, Roberts JD, et al. Guidance on minimizing risk of drug-induced ventricular arrhythmia during treatment of COVID-19: a statement from the Canadian Heart Rhythm Society. *Can J Cardiol.* 2020. <http://dx.doi.org/10.1016/j.cjca.2020.04.003>.
2. Wang Z, Denys I, Chen F, Cai L, Wang X, Kapusta DR, et al. Complete atrioventricular block due to timolol eye drops: a case report and literature review. *BMC Pharmacol Toxicol.* 2019;20:73. <http://dx.doi.org/10.1186/s40360-019-0370-2>.
3. Pratt NL, Ramsay EN, Kalisch Ellett LM, Nguyen TA, Roughead EE. Association between ophthalmic timolol and hospitalisation for bradycardia. *J Ophthalmol.* 2015;2015:567387. <http://dx.doi.org/10.1155/2015/567387>.
4. Somer M, Kallio J, Pesonen U, Pyykkö K, Huupponen R, Scheinin M. Influence of hydroxychloroquine on the bioavailability of oral metoprolol. *Br J Clin Pharmacol.* 2000;49:549–54. <http://dx.doi.org/10.1046/j.1365-2125.2000.00197.x>.

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<sup>☆</sup> Please cite this article as: Millá Griño E, Muniesa Royo MJ, Pazos López M. Conflicto terapéutico en pacientes con COVID-19 y glaucoma. *Med Clin (Barc).* 2020;155:182.