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EDITORIAL

Safety and efficacy of beta-blockers and amiodarone in the management of new-onset atrial fibrillation in critically ill patients with sepsis

Seguridad y eficacia de betabloqueantes y amiodarona en el manejo de la fibrilacion auricular de nueva aparición en el paciente crítico con sepsis

This issue of the Journal publishes a retrospective analysis by Guoge Huang et al., based on the MIMIC-IV database that compares the safety and efficacy of beta-blockers and amiodarone in the pharmacological cardioversion of septic patients with new-onset atrial fibrillation (AF). Given the characteristics of these two types of drugs, it could be said that we are comparing a rhythm control strategy with a rate control strategy, although according to the study by Drikite et al.,[1] in critically ill patients, both types of drugs seem to have effects on rhythm control, which could suggest that the adrenergic system plays an important role in the generation of arrhythmic burden at this level of disease severity. The analysis presented in the article offers some interesting aspects but also has some drawbacks due to its retrospective nature.

This is a study in which treatment assignment is not randomized, which is why ̈propensity score matching ̈is used. This approach seeks to simulate randomization to make the cohorts comparable, though this has significantly reduced the size of the cohorts. It would be desirable to have a prospective randomized trial to better compare one pharmacological strategy with another. Moreover, it would be advisable to include in future studies the analysis of the presence of septic cardiomyopathy, since this can strongly influence pharmacological management in the acute phase, as well as to reflect the type and doses of inotropic drugs used. As pointed out in previous experiences,[2] it is noteworthy to have introduced the role of esmolol, which, used in continuous perfusion and due to its short half-life, can facilitate verification of the tolerance and efficacy of a beta-blocker for the management of new-onset rapid AF, before prescribing one with a longer half-life. Comparison of the cohorts in terms of mortality, mean length of stay and days of mechanical ventilation is reasonable. Even with the observation of a shorter duration of AF in the amiodarone group, the mortality rate was higher in this group, and this may be due to other adverse effects of this type of long half-life antiarrhythmic drug in severe septic patients with frequent multiorgan involvement—though this is only a hypothesis.

New-onset AF in critically ill patients has an overall incidence of between 10–15%. There is sufficient evidence, although not unanimous, that its presence worsens the prognosis and is associated with an increased average length of stay[3] and cost. Higher in-hospital and one-year mortalities[4,5] have been reported, as well as a higher incidence of thromboembolic events, as in the meta-analysis of Garside et al. involving 561,797 patients. On the other hand, the independent effect of AF on mortality appears to be less clear after adjusting for age and severity.[6]

The systematic review of 42 studies conducted by Drikite et al. to analyze management strategies for new-onset AF in critically ill patients suggests that beta-blockers and amiodarone may have similar efficacy in terms of rhythm control, based on four non-randomized studies. However, beta-blockers may be associated with longer survival compared with amiodarone, calcium channel blockers and digoxin, and although this conclusion may be influenced by confounding factors, it is consistent with the study by Guoge Huang.

In the study by Fernando et al., no association with in-hospital mortality was found, but there was an association between new-onset AF and sepsis; the presence of both of these conditions was associated with a higher likelihood of in-hospital mortality. This association has been reported by other authors such as Xiao et al.[7] in a meta-analysis of 225,841 patients in 13 studies that aimed to describe the impact of new-onset AF on the prognosis of sepsis. The authors reported an association between AF and the prognosis, and highlighted that it can be present

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in up to 46% of the cases of septic shock. The pathophysiology underlying this association could be explained by multiple mechanisms, ranging from the presence of major adrenergic discharge, the use of vasoactive drugs, disorders of the internal environment with electrolyte alterations, inflammatory cytokines such as IL-6 and TNF-α, which affect electrical conduction and myocardial function, myocardial ischemia due to hypoperfusion, hypoxia, increased demand that compromises myocardial oxygenation, alteration of the autonomic nervous system, and many others that may lead to cardiac arrhythmias or converge in the presence of septic cardiomyopathy.[8]

The chances of reversal of new-onset AF are greater the shorter its evolution, and its presence has a negative impact on the hemodynamic condition of the patient, mediated either by the loss of atrial contribution to cardiac output or by an elevated heart rate - with some studies establishing a cut-off point of prognostic value of 120 beats per minute.[9] Reversal of AF more than 48 h after its onset also complicates management, so attempts seeking early reversal are justified. Pharmacological cardioversion is less effective than electrical cardioversion, with the latter achieving efficacy rates of 80%.[10] Nevertheless, pharmacological cardioversion is often chosen because it avoids the side effects of sedoanalgesia and provides a relatively controlled hemodynamic situation.

The experience reported by Guoge Huang on the impact of new-onset AF in the critically ill patient therefore merits further prospective, randomized studies to determine the best strategy to improve survival and reduce morbidity and side effects.

A separate, but no less interesting issue, is whether anticoagulation of these patients is indicated and when and how to commence it - this being an aspect for which there is no established evidence.

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