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EDITORIAL

Management of supraventricular arrhythmias in the intensive care unit: a step in the right direction

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Supraventricular arrhythmias (SVAs) are frequent in the intensive care unit (ICU). Data suggest that the incidence of SVAs, especially atrial fibrillation (AF), ranges between 8% and 23% in patients with sepsis and septic shock [1]. Observational studies suggest that developing SVAs during critical illness negatively impacts the overall outcome and that this impact may persist beyond the ICU stay [2, 3]. Therefore, controlling ICU-related arrhythmias may help improve both short-term and long-term outcomes. Based on previously published surveys, amiodarone seems to be the most frequently used antiarrhythmic drug in the ICU [4, 5]. Beta-blockers (BBs), calcium blockers, digoxin, magnesium and electrical cardioversion are also used either as monotherapy or adjunct therapy using different combinations [4, 5].

The popularity of amiodarone in critical care may be partly explained by (i) its efficacy in suppressing different types of supraventricular and ventricular arrhythmias, especially in patients with structural heart diseases, (ii) combined with limited negative inotropic effect compared with other antiarrhythmics [6]. However, amiodarone also carries serious downsides, including (i) slow clearance leading to a prolonged half-life, and (ii) potentially severe toxicity to the thyroid gland, the lung, the liver, the cardiovascular, ophthalmologic and neurologic systems [6]. BBs are commonly prescribed in patients with different cardiovascular comorbidities admitted for myocardial infarction due to their beneficial effect on mortality [7]. Whilst there is data suggesting cardioprotective and immunomodulating effects of BBs in sepsis [8, 9], their impact on ICU outcome is still debated [10]. Preliminary data also suggest a potential benefit of propafenone, a class 1 antiarrhythmic agent with beta-adrenoceptor antagonist properties amongst patients with septic shock [11, 12]. But will this translate into a clinically relevant benefit? Previous literature on the management of SVAs in critically ill patients is very illustrative of promising preliminary results based on very small and low-quality studies, thereby leaving the question largely unanswered.

In this issue of Intensive Care Medicine, the paper from Balik and colleagues represents a welcome exception. The authors present a two-centre randomised, blinded clinical trial comparing propafenone vs. amiodarone to achieve rhythm control in patients with septic shock, and a new-onset supraventricular arrhythmia with a left ventricular ejection fraction greater than 35% [13]. In this trial, patients were randomised to receive either intravenous propafenone (70 mg bolus followed by 400–840 mg/24 h) or amiodarone (300 mg bolus followed by 600–1800 mg/24 h). The primary outcome was included rhythm control at 24 h. All eligible patients had an echocardiographic evaluation, an optimisation of their preload and a correction of any electrolyte disturbances as part of the pre-specified study protocol [13]. There was no significant difference between propafenone and amiodarone for rhythm control at 24 h in the study population (73% vs. 67%; $p = 0.4$). In the propafenone group, the time-to-cardioversion was shorter with a median time of 3.7 h (95% confidence interval (CI) 2.3–6.8) vs. 7.3 h (95% CI 5–11; $p = 0.022$) for the amiodarone group. Also, the arrhythmia recurrence rate was lower for patients treated with propafenone compared to amiodarone (52% vs.

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76%; p <0.001) [13]. There was no difference between the groups in any of following secondary outcomes: course of vasopressors, detected electrocardiogram abnormalities, ICU length of stay or mortality. Interestingly, a subgroup analysis indicated better rhythm control for patients with left atrial enlargement who were randomised to the amiodarone group [13]. The authors concluded that propafenone did not provide better rhythm control at 24 h but resulted in faster cardioversion and an overall lower arrhythmic burden than amiodarone.

How should we interpret these findings? Propafenone and amiodarone may both be useful in achieving rhythm control in patients with septic shock. Whilst propafenone may represent an interesting alternative to amiodarone, the choice may depend on the presence of an underlying structural heart disease. Indeed, based on the results by Balik et al., patients with left atrial enlargement may respond better to amiodarone. However, these findings and conclusions are hampered by low statistical power, concurrent use of other antiarrhythmics and the heterogeneity of the population in terms of SVAs. Another essential point to highlight is the absence of a placebo group, making it impossible to determine the effect size of both antiarrhythmics in controlling SVAs in critically ill patients. Although antiarrhythmics are well-established treatments for a variety of SVAs, uncertainty remains regarding the overall beneficial effect of antiarrhythmics in critically ill patients [14]. Unsurprisingly, AF was the most frequently reported SVA in this study. Spontaneous conversion rates of AF have been reported to vary between 9 and 83% with an increased likelihood of spontaneously returning to sinus rhythm in patients with no previous history of arrhythmia, no known cardiovascular disease and a prolonged 'watch-and-wait' strategy before initiating any active treatment [15]. Hence, in the absence of placebo, it remains unclear how amiodarone and propafenone conversion rates compare to spontaneous conversion. From a clinical perspective, initiating an antiarrhythmic treatment should be based on a proven reduction in the rate of SVA-related complications, more than a conversion rate. Finally, the risk–benefit balance of using antiarrhythmics should always be taken into account. The present study was not powered to look into side effects. Pharmacovigilance studies will be very important to better understand the safety profile of propafenone in critically ill patients.

To our knowledge, only a very limited number of trials have evaluated the actual benefit of active treatments compared with placebo or a 'watch-and-wait' strategy in critically ill patient populations. Thus, translating the real effects of antiarrhythmics on short-term and long-term outcomes is subject to great uncertainty. This is especially true for ICU patients.

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Declations

Conflicts of interest
The authors declare that they have no conflict of interest.

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