

Challenge of Anesthesia Management in Brugada Syndrome

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In this issue of ANESTHESIOLOGY, Flamée *et al.* present a randomized controlled trial on the electrocardiographic effects of propofol *versus* etomidate for induction of anesthesia in Brugada syndrome patients.¹ Due to its randomized controlled nature, this study is unique within the few scientific contributions to this matter. The authors could not find any evidence of a worsening electrocardiographic pattern in propofol-treated patients, conversely showing a decrease in ST-elevation (a favorable electrocardiographic change) in 30% of these patients.¹

The Brugada syndrome is an inherited disease characterized by coved-type ST-segment elevation in the right precordial leads on the electrocardiogram and increased risk of ventricular fibrillation and sudden cardiac death, in the absence of structural heart disease. There are three different electrocardiographic patterns in Brugada syndrome. The type 1 electrocardiographic pattern is characterized by a pronounced elevation of the J point, a coved-type ST segment, and an inverted T wave in V1 and V2. The type 2 pattern has a saddleback ST-segment elevated by more than 1 mm, and in the type 3 pattern, the ST segment is elevated less than 1 mm. The type 1 electrocardiographic pattern is diagnostic of Brugada syndrome, whereas types 2 and 3 patterns require antiarrhythmic drug challenge to be unmasked and converted into type 1.²

The prevalence of Brugada syndrome ranges from 1 in 5,000 to 1 in 2,000, and the incidence of Brugada syndrome pattern on electrocardiogram from 0.12 to 0.8%,³ while malignant arrhythmias may be triggered by a number of conditions (the most common is fever) and drugs. Among these, the most important to be avoided are some



“...[P]ropofol appears to be a safe anesthesia induction agent in Brugada syndrome...”

antiarrhythmic drugs (ajmaline, flecainide, procainide, propafenone, and others); psychotropic drugs (amitriptyline, clomipramine, lithium, and others); and local anesthetics (procaine, bupivacaine).⁴

Propofol is considered a drug to be avoided (class IIa: there is conflicting evidence and/or divergence of opinion about the drug, but the weight of evidence/opinion is in favor of a potentially arrhythmic effect in Brugada syndrome patients),⁴ based on a limited number of observations. Given the wide use of this drug for induction and maintenance of anesthesia, the inclusion of propofol within the list of drugs to be avoided in Brugada syndrome has serious implications for the daily clinical practice of anesthesia. The mechanism by which propofol may induce

a Brugada syndrome-like electrocardiographic pattern or trigger malignant arrhythmias in overt Brugada syndrome patients is related to its induction of a block of sodium currents in cardiac myocytes at concentrations that are comparable to those used during anesthesia.⁵

The great majority of the reports linking propofol to malignant arrhythmias in patients with overt Brugada syndrome or unmasked Brugada syndrome-like electrocardiographic patterns is related to prolonged propofol infusion in the setting of critical care patients, often within the context of a propofol infusion syndrome. Conversely, the use of propofol for induction of anesthesia seems not to be associated with the appearance of Brugada syndrome-like electrocardiographic patterns, worsening of preexisting Brugada syndrome electrocardiographic patterns, or induction of malignant arrhythmias. In a recent study,⁶ our group analyzed the electrocardiographic effects of propofol induction of anesthesia in 36 type 1 Brugada syndrome patients undergoing epicardial ablation of the arrhythmogenic substrate. Seventy-eight percent of the patients showed a reversal of the electrocardiogram to a nondiagnostic pattern, with

Image: J. P. Rathmell.

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a significant decrease of the ST elevation and J-wave amplitude, and no malignant arrhythmias. The study by Flamée *et al.*¹ is largely confirmative of these effects of propofol on the Brugada syndrome electrocardiographic pattern, and its randomized controlled nature with an active comparator strengthens the information that propofol appears to be a safe anesthesia induction agent in Brugada syndrome patients of any degree. Therefore, this study is important, and may change the existing practice by allowing the use of propofol as an anesthesia induction agent in Brugada syndrome patients. It must be admitted that the sample size of this study is relatively low; however, no signals of propofol-induced malignant arrhythmias were detected.

The two major existing studies^{1,6} demonstrate the safety and even favorable propofol-induced electrocardiographic changes after administration of a bolus dose for induction of anesthesia. This potentially protective effect of propofol may be explained by its inhibition of the transient outward potassium current in human myocytes. A high density of the transient outward potassium current in right ventricle outflow tract epicardial cells is considered an important mechanism underlying the repolarization abnormalities associated with the arrhythmogenic substrate in Brugada syndrome. Consequently, the administration of single-dose propofol may exert a rebalancing of ion channel currents, resulting in a reduction of the ST-segment elevation.

However, this message should not yet be automatically translated into reassuring information about the effects of long-term propofol infusion in Brugada syndrome patients. The setting of prolonged propofol infusion in critical care patients has a number of additional factors that may concur in creating a tendency toward malignant arrhythmias: among these, the most common are fever (*i.e.*, in septic patients), electrolyte imbalance, and the use of proarrhythmic drugs (catecholamines). Therefore, until adequate studies on large patient populations are conducted, caution remains for the use of prolonged propofol infusion in Brugada syndrome patients. Additionally, no information is available with respect to the use of propofol infusion for maintenance of anesthesia or sedation during prolonged surgical procedures. This may be an interesting field for further studies.

Competing Interests

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