Frequency-dependent Cardiotoxicity of Ropivacaine: Study in an Experimental Porcine Model

Primary Author: Sara Alvarez-Zaballos Medical student
Universidad Autónoma de Madrid

Co-Authors: Almudena Morales, Medical student; Arturo Melone, Anesthesia Resident; Carlos DÁez, Medical student; Cristina Cardenas, Medical student; David Callejo, MD; Jesºs Almendral, MD; PhD; Mª JosÁ© AnadÁ³n-Baselga, MD; PhD; Matilde Zaballos, MD; PhD; Olal

Introduction:
Ropivacaine is considered a less cardiotoxic local anesthetic in comparison with other local anesthetics. However, regardless of this consideration numerous clinical reports have been described, in which its accidental administration has caused severe complications including arrhythmias, episodes of ventricular tachycardia and even cardiac arrest. The cardiotoxicity of ropivacaine is related to the inhibition of the fast inward current during the depolarization of cardiac cells. Studies in vitro have showed that ropivacaine toxicity increases in a use-dependent fashion. Our aim was to characterize an in vivo model to evaluate the frequency-dependent cardiotoxicity of ropivacaine.

Material and methods:
The ethics committee on animal studies approved the study. Eight large white pigs were premedicated with ketamine and anesthetized with thiopental sodium 5 mg/kg. The anesthetic maintenance was performed with sevoflurane 1 MAC (2.6%). Three quadripolar catheters were inserted via the femoral veins under fluoroscopic control and were used for stimulation and intracardiac recordings. The catheters were positioned into the high right atrium, the right ventricular apex, and to the His bundle recording area. After a period of stabilization pacing was performed at a current strength of 30 mA with a programmable stimulator. Right ventricular pacing was performed for at least 10 beats at a cycle lengths of 400 and 500 ms. This pacing protocol was performed immediately before and at 1, 5, 10, 15 and 30 minutes of the administration of ropivacaine (6 mg/Kg in two animals and 5 mg in 6 animals). Statistics: Analysis of variance for repeated measures

Results: Two animals, which received 6 mg/Kg of ropivacaine, died due to severe hypotension. The rest of the animals received 5 mg/ Kg. Plasma ropivacaine levels ranged between 7.940 to 5450 ng/dl from 5 to 30 min respectively. Ropivacaine induced an intense toxicity effect in sinusual rhythm as well as in stimulated rhythm. After ropivacaine administration there was an important prolongation in QRS interval in sinusual rhythm: from 67Â±9 to 97Â±18 ms; p=0,0001; (Í° 45%) and at paced cycle length of 400 ms: from 99 Â±6 ms to 355Â±73 ms; p=0,0001); (Í° 258%) (Figure 1). Ten minutes after ropivacaine administration, still persisted and intense increment up to 90% in stimulated QRS, however, QRS interval in sinusual rhythm showed values in normal range (82 Â±6 ms).
Conclusion:

Ropivacaine has been associated with a huge cardiotoxic effect that has been shown with fast frequencies of stimulation. This experiment has unmasked a hidden cardiotoxic phenomenon that persists intensely even after 10 minutes since the administration of the drug. These findings suggest that in the context of an accidental ropivacaine intoxication precaution measures should be maximized as well as avoiding sympathetic simulation until cardiotoxicity parameters are completely restored.