Abstract

Malignant ventricular arrhythmias are a common cause of sudden cardiac death. Moderate therapeutic hypothermia (MTH) is routinely used in post-resuscitation care for anticipated neuroprotective effects. However, the safety of MTH in terms of the electrical stability of the heart has not been satisfactorily proved yet. Also, the increased sympathetic tone in patients with heart failure contributes to a higher incidence of malignant ventricular arrhythmias. The aim of this work was to verify the safety of MTH as regards the inducibility of ventricular fibrillation (VF) in the pig biomodel, especially in relation to spontaneous changes in the kalemia and QT interval. Furthermore, we assumed that renal denervation (RDN) could reduce the inducibility of VF.

In the first part of the thesis, the extracorporeal cooling was introduced in fully anesthetized swine (n = 6) to provide MTH. Inducibility of VF was studied by programmed ventricular stimulation (8 basic stimuli with up to 4 extrastimuli) three times in each biomodel under the following conditions: during normothermia (NT), after reaching the core temperature 32 °C (HT) and after another 60 minutes of stable hypothermia (HT60). VF inducibility, effective ventricular refractory period (ERP), QTc interval, and potassium plasma level were measured. In the second part of the thesis,
a controlled electrophysiological study was performed in 6 biomodels 40 days after RDN (RDN group) and in 6 healthy animals (control group). Inducibility of VF was tested three times for each biomodel using peripheral extracorporeal membrane oxygenation for hemodynamic support. Furthermore, resting heart rate (HR), PQ and QT intervals, and ERP were measured. The technical success of the RDN was evaluated by histological examination.

Starting at normothermia of 38.7 (IQR 38.2; 39.8) °C, HT was achieved within 54 (39; 59) minutes and the core temperature was further maintained constant. Overall, the inducibility of VF was 100% (18/18 attempts) at NT, 83% (15/18) after reaching HT ($P = 0.23$) and 39% (7/18) at HT60 ($P = 0.0001$) using the same protocol. Similarly, ERP prolonged from 140 (130; 150) ms at NT to 206 (190; 220) ms when reaching HT ($P < 0.001$) and remained 206 (193; 220) ms at HT60. QTc interval was inversely proportional to the core temperature and extended from 376 (362; 395) at NT to 570 (545; 599) ms at HT ($P < 0.0001$). Kalemia changed spontaneously: decreased during cooling from 4.1 (3.9; 4.8) to 3.7 (3.4; 4.1) mmol/L at HT ($P < 0.01$), then began to increase and returned to baseline level at HT60 (4.6 (4.4; 5.0) mmol/L, P = NS).

According to histological findings, RDN procedure was successfully performed in all biomodels. Comparing the groups, basal HR was lower in RDN group: 79 (58; 88) vs. 93 (72; 95) beats per minute ($P = 0.003$); PQ interval was longer in RDN group: 145 (133; 153) vs. 115 (113; 120) ms ($P < 0.0001$) and QTc intervals were comparable: 402 (382; 422) ms in RDN vs. 386 (356; 437) ms in control group ($P = 0.1$). ERP was prolonged significantly in RDN group: 159 (150; 169) vs. 140 (133; 150) ms ($P = 0.001$), but VF inducibility was the same (18/18 vs. 18/18 attempts).

We can conclude that MTH does not increase the risk of VF in the pig biomodel. In addition, combined with normokalemia, MTH exerts an antiarrhythmic effect despite prolonged QTc interval. RDN reduced the sympathetic nerve system tone, but the electrophysiological study did not prove a decrease of VF inducibility after RDN.

Keywords: ventricular fibrillation, mild therapeutic hypothermia, renal denervation, hypokalemia, QT interval.