MOLECULAR INSIGHT INTO THE LATE ANTIARRHYTHMIC EFFECTS OF NITRITES

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We have evidence that the inorganic sodium nitrite provides a significant antiarrhythmic effect: nitrite given 24 hours before coronary artery (LAD) occlusion and reperfusion (I/R) ('late effect') significantly decreased the incidence of severe ventricular arrhythmias and increased survival in dogs. The sudden increase of free radicals and the impaired calcium homeostasis could be the sources of arrhythmias upon reperfusion; therefore, we have focused on the mitochondria since mitochondria plays a substantial role in the regulation of intracellular reactive oxygen species (ROS) formation and calcium level. Our previous results have revealed that sodium nitrite attenuated ROS production by altering the mitochondrial respiration, decreased the diastolic calcium level during reperfusion and prolonged the effective refracter period which might contribute to this antiarrhythmic effect.
The present study focused on the possible molecular mechanisms: our objective was to examine the role of protein S-nitrosylation in this late protection.
Dog and rat left ventricular tissue samples were collected in the sham-operated (n=3) and nitrite treated groups (at 3h, 6h, 12h and 24h (n=3/time point)). In these samples we have assessed the total protein S-nitrosylation (SNOs) by biotin switch method.
Our results have shown that the administration of sodium nitrite significantly increased the total protein SNOs at 24h in dogs and rats compared to the sham-operated control group.
Our previous and present results suggest that protein S-nitrosylation might play a role in the late antiarrhythmic effect of sodium nitrite. In the future, we aim to identify the proteins (e.g. MCU and mNCX) altered by nitrite administration.

Keywords: arrhythmia, S-nitrosylation, mitochondrial bioenergetics, biotin switch