

Positive inotropic support in acute cardiac decompensation - haemodynamic and arrhythmogenic effects of levosimendan and catecholamines combined treatment in experimental heart failure

Background: Ca^{2+} -sensitiser levosimendan became first-line treatment in acute systolic dysfunction besides catecholamines (CAs). We aimed to evaluate haemodynamic and arrhythmogenic effects of levosimendan (LEV) administered together with catecholamines (dobutamine, DOB; dopamine, DA; norepinephrine, NE) in a canine heart failure (HF) model.

Methods: HF (n=12) was induced by chronic right ventricular tachy-pacing (240/min), continued until acute cardiac decompensation. Two experimental groups of anesthetized (ketamine-midazolam) animals were constituted: *Group I.* - continuous infusion of LEV (0.1 g/kg/min iv.) combined with 10-10 minutes infusion of different CA doses: DOB_{3-6-12} , DA_{4-8-16} és $\text{NE}_{0,04-0,08-0,16}$ ($\mu\text{g/kg/min}$, iv.); *Group II.* – CAs were given in same doses without LEV. Measured variables: blood pressure (BP), left ventricular end-diastolic pressure (LVEDP), contractility ($\text{dP/dt}_{\text{min-max}}$), duration of monophasic action potential at 50%, 90% of repolarisation (MAPD_{50} , MAPD_{90}). Number of ventricular premature beats (VES), ventricular tachycardias were also counted.

Results: In Group I. LEV alone did not alter mean BP (105 ± 13 mmHg) and LVEDP (28 ± 5 mmHg). However, $\text{dP/dt}_{\text{max}}$, $\text{dP/dt}_{\text{min}}$ (1779 ± 313 and -1967 ± 322 mmHg/s) were increased by 56 ± 15 , 49 ± 15 $\Delta\%$ ($p < 0,001$). There was further increase in $\text{dP/dt}_{\text{max}}$ with combination of LEV and CAs, maximal effect was observed with $\text{LEV} + \text{DA}_{16}$ ($+73 \pm 19$ $\Delta\%$, $p < 0,001$). LVEDP tended to decrease during $\text{LEV} + \text{DOB}_{12}$ and to increase at $\text{LEV} + \text{NE}_{0,16}$ (ns). In the CAs-only group (II.) basal haemodynamic parameters (BP, LVEDP, $\text{dP/dt}_{\text{max}}$, $\text{dP/dt}_{\text{min}}$) did not differ from Group I. Moreover, CAs without LEV exerted cardiovascular responses similar to those in LEV+CA group.

Malignant ventricular arrhythmias or increase in VES occurrence were not observed in both groups. During LEV infusion LV MAPD_{50} decreased significantly (214 ± 8 vs 242 ± 9 msec, $p < 0,01$), which was further shortened by $\text{LEV} + \text{NA}_{0,16}$ (204 ± 20 msec, $p < 0,02$).

Conclusion Co-administration of levosimendan and catecholamines elicited similar improvement in cardiac contractility to catecholamines given separately. This beneficial effect was not accompanied by malignant arrhythmias, despite of MAPD_{50} shortening during LEV infusion.