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 NE$_{0,04-0,08-0,16}$ (µg/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 (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, dP/dt$\text{max}$, dP/dt$\text{min}$ (1779±313 and -1967±322 mmHg/s) were increased by 56±15, 49±15 Δ% (p<0,001). There was further increase in dP/dt$\text{max}$ with combination of LEVO and CAs, maximal effect was observed with LEV+DA$_{16}$ (+73±19 Δ%, p<0,001). LVEDP tended to decrease during LEV+DOB$_{12}$ and to increase at LEV+NE$_{0,16}$ (ns). In the CAs-only group (II.) basal haemodynamic parameters (BP, LVEDP, dP/dt$\text{max}$, 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 LEV+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.