Abstract: P1735

Treatment of cardiogenic shock complicating peripartum cardiomyopathy with the calcium sensitizer, levosimendan - data from the german PPCM registry

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Background:
Peripartum cardiomyopathy (PPCM) is a life-threatening heart disease, characterized by acute or subacute heart failure due to reduced left ventricular ejection fraction (LVEF). Treatment of cardiogenic shock (CS) complicating PPCM is challenging; therapeutic regimes for PPCM patients with CS seem to influence the ability of patients to recover. We could recently show that dobutamine may be associated with progression to irreversible terminal heart failure in PPCM patients with acute severe heart failure.

The calcium sensitizer levosimendan (LE) is currently considered as a beneficial therapy in selected patients with acute heart failure/CS. However, recent analyses of sarcomere physiology in cardiac biopsies from PPCM patients point to impaired PKA-cAMP signaling and already increased Ca²⁺ sensitivity.

This study sought to investigate the effect of administration of LE on outcome and clinical course of PPCM patients with CS.

Methods and Results
Out of 19 PPCM patients with CS 13 patients obtained LE (LE-patients) and 6 patients did not obtain this drug (no-LE-patients). Notably LE-patients had a significant lower LVEF at diagnosis (18.5±8.29 vs 27.0±5.62; p: 0.0297) and a trend to higher NT-proBNP values (12716±10196 ng/l vs 4414±5451 ng/l; p: 0.0733) compared to no-LE-patients. Both groups were comparable regarding age, parity, comorbidities and lactate levels. The Card-Shock-Score, SAPS II-Score, APACHE II-Score and initial SOFA-Score did not differ significantly between the two groups. All patients survived the acute phase of CS but more patients in the LE-group were treated with mechanical circulatory support (Impella or ECMO) compared to the no-LE group (8/13 vs. 0/6; p: 0.1358).

At follow up (FU: 20.5 [3-67] vs. 15 [1-76] months) none of the no-LE patients (0/6) had received a HTX, LVAD or had died, while 69.2% (9/13) of the LE-patients underwent LVAD implantation or HTX (p: 0.0108) and 23.1% (3/13) LE-patients had died.

In our mouse model of PPCM (mice with a cardiomyocyte specific STAT3 deficiency, CKO), we observe similar impairment of cAMP and Ca²⁺ signaling. Postpartum treatment (on day 1-2 and day 8-9 after delivery, 2 pregnancies and nursing periods) of CKO mice with LE (0.012 mg/kgBW) showed a trend to a reduced cardiac function and accelerated PPCM.

Conclusion:
PPCM patients treated with LE displayed a higher rate of terminal heart failure, HTX, LVAD and less LV recovery, compared to no-LE-patients. Although both groups were comparable regarding several heart failure markers and shock-scores, worse LVEF and higher NT-proBNP levels at diagnosis show that CS was more severe in LE-patients and the two groups are not statistically comparable. Therefore, these data have to be interpreted with great caution, and outcome can not be attributed directly to the treatment with LE. However, first experimental data support the notion that LE may not be beneficial in all PPCM patients.