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Resuscitation Science Symposium

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Abstract 195: Cardioprotective and Anti-inflammatory Effects of Treatment With Adenocaine/mg²⁺ in a Porcine Model of Endotoxemia

Asger Granfeldt¹; Hayley L Letson²; Geoffrey P Dobson²; WeiWei Shi³; Jakob Vinten-Johansen⁴; Else Tønnesen⁵

¹ Dept of Anesthesiology, Aarhus Univ Hosp, Aarhus, Denmark

² James Cook Univ, Townsville, Australia

³ Emory Univ Sch of Medicine, Atlanta, GA

⁴ Emory Univ Sch of Medicine, Atlanta, GA

⁵ Aarhus Univ Hosp, Aarhus, Denmark

Introduction: The combination of adenosine + lidocaine (adenocaine) and Mg²⁺ (ALM) has demonstrated cardioprotective properties in models of cardiac arrest and hemorrhagic shock, and anti-neutrophil effects in vitro. This study evaluates whether ALM also demonstrates cardioprotective and anti-inflammatory properties in an endotoxemic porcine model.

Methods: Pigs (37–42kg) received lipopolysaccharide (LPS) at 1 µg/kg/h for 5 hours, and were randomized to: LPS (control) (n=8) or LPS + ALM (n=8). Pigs received a bolus of ALM at start of LPS infusion followed by 4 hours of infusion. Cardiac function was evaluated using pressure–volume loops, and inflammation was assessed by plasma TNF-α and leukocyte superoxide generation.

Results: Infusion of ALM maintained mean arterial pressure (MAP) at a lower level during the 4 hour infusion period (ALM: 47 ± 1.6 mmHg vs. control: 80 ± 2.9 mmHg, p<0.0001). After discontinuation of ALM, MAP immediately returned to and was maintained at baseline group values (ALM: 89 ± 5 mmHg vs. control: 86 ± 3 mmHg).

The slope of the end-systolic pressure–volume relationship (ESPVR) was unchanged during the experiment in both groups. However, a rightward shift of the volume axis intercept (V₀) in the control group indicated decreased contractility; this shift was not observed in the ALM group (control: -0.1 ± 12 ml vs. ALM: -32.5 ± 7.6 ml, p= 0.04). Preload recruitable stroke work (PRSW), an index of overall cardiac performance, decreased in the control group (baseline: 71 ± 4; end: 37 ± 4 mmHg · ml / ml), but was preserved in the ALM group (baseline: 72 ± 5; end: 62 ± 4 mmHg · ml / ml, p<0.001 between groups). Diastolic function evaluated by dP/dt_{min} (ALM 2221 ± 170 vs. 1793 ± 89 mmHg/sec; p=0.04) and Tau (ALM 36 ± 1.2 vs. 44 ± 2.2 msec; p=0.007) was also significantly improved in the ALM group. Peak TNF-α levels were lower in the ALM group (ALM 7653 ± 1092 vs. 11989 ± 1057 pg/ml; p=0.01). While neutrophil superoxide anion release increased by 19 ± 27 % in the control group, it decreased by 74 ± 8% in the ALM group (p=0.0006).

Conclusions: In this porcine model of endotoxemia, ALM improved cardiac function and reduced the inflammatory response to LPS, thereby extending the beneficial effects of ALM as reported for cardiac surgery, hemorrhagic shock and cardiac arrest.

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