VENO-VENOUS ECMO-INDUCED KIDNEY INJURY – DEVELOPMENT OF A LARGE ANIMAL MODEL

Dániel Érces[1], Noémi Vida[1], Gyöngyvér Vigyikán[1], Antal Szabó-Biczók[2], Gábor Bari[2], Ádám Hodoniczki[1], Zoltán Varga[1], Attila Rutai[1], Szabolcs Péter Tallósy[1], László Juhász[1], Anna Nászai[1], Mihály Boros[1], Gabriella Varga[1]

[1]Institute of Surgical Research, University of Szeged, Szeged, Hungary
[2]Division of Cardiac Surgery, Second Department of Internal Medicine and Cardiology Center, University of Szeged, Szeged, Hungary

Veno-venous extracorporeal membrane oxygenation (vvECMO) is a life-saving intervention in severe respiratory distress. Our aim was to establish a large animal model to study the pathomechanism of complications and the development of vvECMO-induced acute kidney injury (AKI) in a clinically relevant time frame.
The experiments were performed on anaesthetised minipigs. In group 1 (n=6) 24-hr vvECMO was started after l.a. cannulation, followed by a 6-hr post-ECMO period. In the control group (n=6) the animals were observed for 30 hr, without ECMO initiation. Haemodynamics were recorded, renal artery flow (RAF) was measured post-ECMO with ultrasound flowmeter. At the end of the experiments, renal biopsies were taken for histopathological examination, mitochondrial functional measurements (by high-resolution respirometry), and detection of myeloperoxidase and xanthine-oxidoreductase activities. Plasma and urine samples were collected for neutrophil gelatinase-associated lipocalin (NGAL) determination.
RAF was decreased in post-ECMO period (96.3±21 vs 223.6±32 ml/min) and hourly diuresis was lower compared to the controls (3.25±0.4 vs 4.83±0.6 ml/h/kg). Kidney histology demonstrated ischemic structural lesions. In the vvECMO group, urine (4.24±0.25 vs 2.57±0.26 ng/ml) and plasma (4.67±0.1 vs 3.22±0.2 ng/ml) NGAL levels, xanthine-oxidoreductase (5.88±0.8 vs 2.57±0.2 pmol/min/mg protein) and myeloperoxidase (11.93±2.5 vs 4.34±0.6 mU/mg protein) activity were increased. A decrease in complex I-dependent oxidative capacity (174.93±12.7 vs. 249±30.07 pmol/s/ml) indicated mitochondrial dysfunction.
This 30-hrs experimental protocol provided clear evidence for significantly impaired renal function with explicit signs of structural damage and mitochondrial dysfunction. The established large animal model offers basis for studying the pathomechanism, biomarker combinations or potential therapeutic options for vvECMO-linked AKI.
Keywords: veno-venous ECMO, acute kidney injury, mitochondrial function, experimental model, inflammation

NKFIH-K120232, NKFIH-K116861, TKP2020 NKFIH-1279-2/2020