METHANE-ENRICHED CUSTODIOL PRESERVATION SOLUTION IMPROVES GRAFT FUNCTION IN EXPERIMENTAL MODEL OF HETEROTOPIC HEART TRANSPLANTATION

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The key goal of cold storage is to maintain cell viability for a prolonged time during solid organ transplantation. Methane (CH_4) has been recognized as novel therapeutic gas exerting anti-inflammatory effects in ischemia-reperfusion (IR) injuries. We aimed to investigate whether cold storage of donor hearts in CH_4-enriched Custodiol preservation solution could protect against IR and preserve myocardial function in a rat model of heterotopic heart transplantation (HTX).
The hearts of donor Lewis rats were stored for 60 minutes in cold histidine-tryptophanketoglutarate (Custodiol [CS]) or CH4-saturated CS solution (CS-CH4) (n = 12 each). Standard heterotopic HTX was performed, and 60 minutes later, the left ventricular (LV) pressure-volume relationships LV systolic pressure (LVSP), systolic pressure increment (dP/dtmax), diastolic pressure decrement, and coronary blood flow (CBF) were measured. Tissue samples were taken to detect proinflammatory parameters, structural damage (by light microscopy), endoplasmic reticulum (ER) stress, and apoptosis markers, whereas mitochondrial functional changes were analyzed by high-resolution respirometry.
LV contractility, active relaxation and CBF values were significantly ($p < 0.05$) improved in CS-CH_4 grafts as compared to the CS group. CS-CH_4 storage significantly reduced the transcription of pro-apoptotic proteins and Bcl2/Bax ratios as compared to CS grafts. Increased mitochondrial oxidative phosphorylation, reduced leak respiration and cytochrome c release were demonstrated in response to CS-CH_4 preservation.
The addition of CH4 during 1 hour of cold storage improved early in vitro graft function and reduced mitochondrial dysfunction and activation of inflammation. Evidence shows that CH4 reduced ER stress−linked proapoptotic signaling.

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