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Hypothermic Perfusion with the Adsorptive Cartridge Persorb Limits Ischemia-Reperfusion Injury of Pig Kidneys by Sustaining Mitochondrial Function and Inhibiting Senescence of Tubular Epithelial Cells



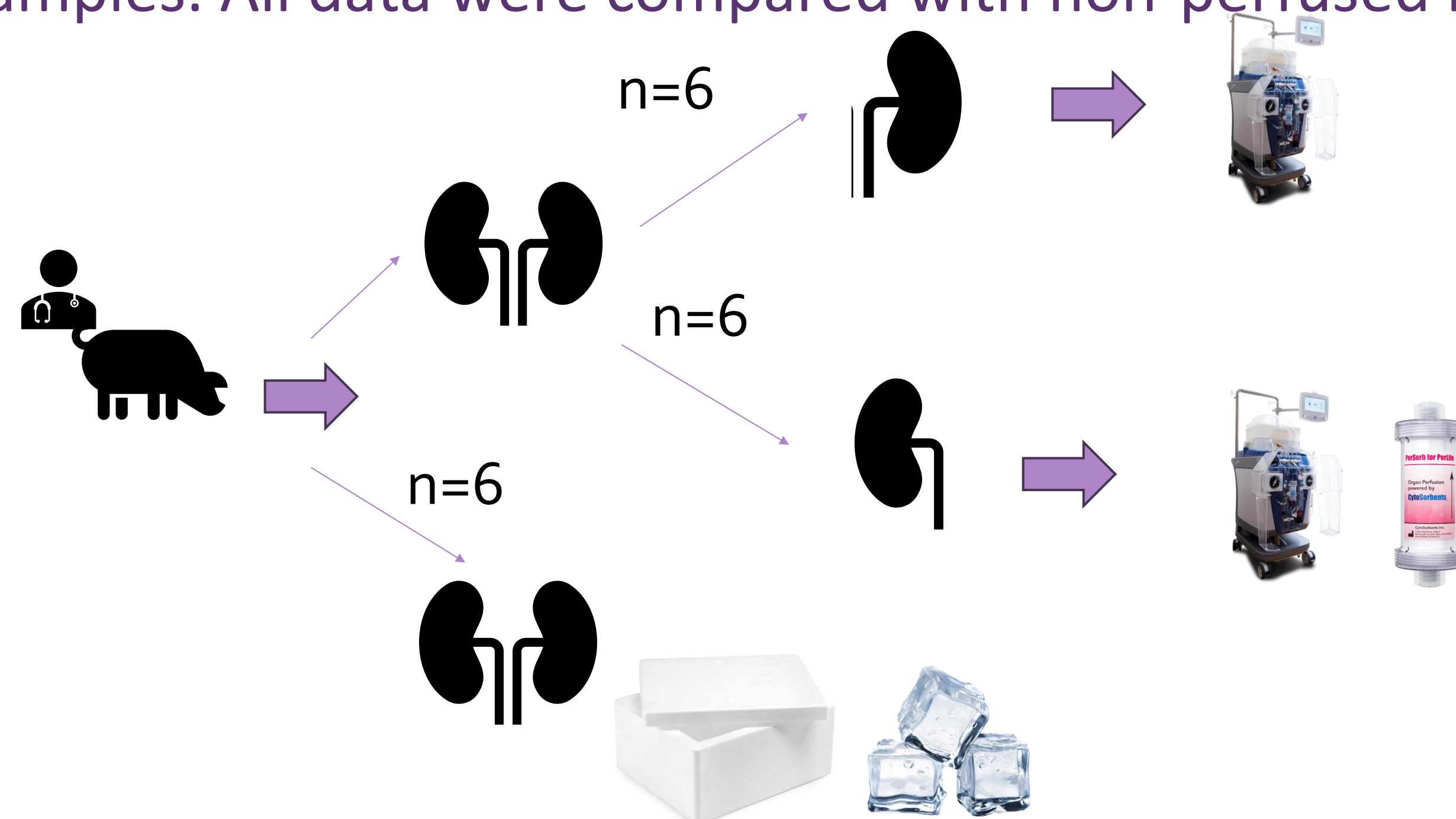
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Background

Hypothermic perfusion limits kidney ischemia-reperfusion injury (IRI) and Delayed Graft Function (DGF) in high-risk donors, prolonging graft survival. Study aim: to evaluate the protective effect of the PerSorb sorbent on mitochondrial dysfunction and senescence of pig kidneys during hypothermic perfusion.

Methods

Pig kidneys were subjected to hypothermic perfusion with (n=6) or without (n=6) PerSorb (Aferetica srl, Bologna, Italy). Metabolomics analysis of tryptophan pathways by LC-MS/MS and quantification of extracellular vesicles (EVs) by Nanotrack analysis (NTA) were also performed in liquid perfusion samples. All data were compared with non-perfused kidney pair (n=6).



Results

In comparison to cold storage, hypothermic perfusion with PerSorb reduced tubular injury score, NGAL, IL-6 and Klotho gene expression. PerSorb also increased citrate synthase, malate dehydrogenase and succinate dehydrogenase levels, ATP production and mitochondrial electron transport chain, concomitantly reducing mitoROS. Metabolomic analysis of tryptophan metabolism showed the presence of a limited number of solutes including tryptophan (Trp), nicotinamide (NAM), nicotinamide mononucleotide (NMN), Nicotinic Acid (NA), nicotinamide riboside (NR) and Indoxyl Sulfate (IS). Of note, PerSorb was able to adsorb the nephrotoxic compound IS and other indole derivatives such as indole-3-pyruvic acid (I3PA), indole-3-carboxaldehyde (I3A), 3-indoleacetic acid (I3AA), tryptamine (TRYP), indole-3-propionic acid (IPA), 3-indoxyl sulfate potassium salt (IS), and melatonin (5-MT). Last, PerSorb reduced in the perfusate the concentration of EVs released by damaged and inflamed cells and potentially involved in tissue damage. All the described protective effects were more pronounced in presence vs. absence of PerSorb in the perfusion circuit.

Conclusions

Hypothermic perfusion with the adsorptive cartridge Persorb can limit kidney IRI by sustaining mitochondrial function and inhibiting senescence of tubular epithelial cells. Further experiments including a higher number of organs and/or human kidneys discarded from the clinical use are needed to confirm these preliminary results.