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TRANSPLANTATION

Hydrogen sulphide reduces warm renal ischaemic injury

New research has shown that modifying organ preservation solution with hydrogen sulphide (H_2S) can reduce the damage caused to kidneys after warm ischaemia. The work—conducted in rat models—suggests that a similar approach in humans might improve transplantation outcomes.

To keep up with demand, an increasing number of kidneys are harvested from donors after cardiac death. These organs invariably experience prolonged periods of warm ischaemia, which can impart deleterious effects on endothelial, glomerular and renal tubular structure and function.

"Clinically, these processes translate to increased rates of delayed graft function, acute rejection and reduced overall graft survival," explained lead investigator Alp Sener. Sener and his team looked at mitigating ischaemic injury by supplementing standard organ-preservation solutions (phosphate-buffer saline, PBS) with the gasotransmitter H_2S, which is endogenously produced and has known antiapoptotic, free-radical-scavenging and anti-inflammatory effects. Using uninephrectomized rats, they clamped the remaining renal pedicle for 1 h, and then reperfused the organ for 2 h, during which time the abdomen of the animals were filled with PBS with or without H_2S. The raised serum creatinine levels observed after renal clamping were lower in animals in the H_2S-supplementation group than in the PBS-only group, indicating improved renal function.

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"H_2S supplementation also limited distant organ (liver) dysfunction after renal ischaemic reperfusion injury, with a decrease in hepatic sinusoidal vasodilatation and decreased leukocyte infiltration in postsinusoidal venules," continued Sener. This curbing of the inflammatory response was also observed in the histological and PCR analyses, which revealed improved acute tubular necrosis and apoptosis scores in the H_2S group. Downregulation of several proinflammatory markers was also apparent following H_2S supplementation.

Overall, these results are most promising for patients because the techniques avoids the use of systemic H_2S in the donor or recipient, which might have adverse effects. Importantly, the simple modification to the organ preservation solution will not alter any established institutional protocols. However, whether these results will translate to benefits for transplantation recipients remains to be seen. "Human trials are in the works," concluded Sener.

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Original article Zhu, J. X. G. *et al.* Detrimental effects of prolonged warm renal ischaemia-reperfusion injury are abrogated by supplemental hydrogen sulphide: an analysis using real-time intravital microscopy and polymerase chain reaction. *BJU Int.* doi:10.1111/j.1464-410X.2012.11555.x