Pump-Priming Grant

Report

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Ex situ renal replacement therapy during normothermic liver perfusion.

Objective:

To assess different techniques of ex situ renal replacement during normothermic liver perfusion, according to impact on: (i) perfusate electrolyte balance and osmolality, (ii) removal of metabolic waste (urea), (iii) haemolysis, (iv) perfusate cytokines and DAMPs.

Methods:

Three ex situ renal replacement therapy techniques were evaluated during 28-hour normothermic perfusion of slaughterhouse pig livers: (i) haemofiltration using haemoconcentrator (n = 3); (ii) haemodiafiltration using standard dialysis filter (n = 3); (iii) haemodialysis using high cut-off filter (n = 3). These were compared to control perfusions that underwent standard normothermic perfusion with renal replacement therapy (n = 3).

Results:

All three renal replacement therapy techniques improved maintenance of physiological perfusate concentrations of potassium, sodium, and ionised calcium; reduced accumulation of metabolic waste (urea); and improved maintenance of physiological perfusate osmolality. This was associated with lower levels of cell-free/total haemoglobin. High cut-off haemodialysis removed substantial amounts of interleukin-6, TNF-a, and interleukin-1b, low amounts of interleukin-10 and HMGB1, and no interleukin-18. Haemofiltration using a haemoconcentrator removed similar amounts of interleukin-6 but minimal amounts of the other cytokines/DAMPs. Haemodiafiltration using a standard dialysis filter did not remove significant amounts of cytokines/DAMPs. Volume neutrality during renal replacement therapy was most consistent using the haemofiltration method.

Outputs:

This study was presented as an oral presentation at the British Transplantation Society congress 2025.
Haemofiltration using a haemoconcentrator has been incorporated into the extra-corporeal liver cross-circulation protocol to correct perfusate electrolyte balance prior to recipient connection.

Next steps:

Extra-corporeal liver cross-circulation will be evaluated in upcoming phase-1 clinical trials: haemofiltration using a haemoconcentrator will be a central component of the pre-connection isolated normothermic perfusion phase.
In the context of organ preservation, this study demonstrated that all three renal replacement therapy techniques may improve perfusate composition during normothermic perfusion. High cut-off haemodialysis and, to a lesser extent, haemofiltration using a haemoconcentrator additionally remove perfusate cytokines/DAMPs. The potential clinical benefit of this could be assessed in a large animal transplant model.