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RESCUE THERAPY FOR ISCHEMIC HUMAN KIDNEY ALLOGRAFTS:

LIFOR® SOLUTION IMPROVES PUMP PERFUSION (PP) PARAMETERS COMPARED WITH STANDARD BELZER SOLUTION IN DISCARDED HUMAN RENAL ALLOGRAFT

Introduction:

Marginal kidneys are currently assessed for transplant suitability by pump perfusion (PP) with a modified UW solution (Belzer), which does not deliver oxygen in any significant amounts. Kidney allografts are mechanically pumped under constant pressure (40-60 mmHg) and changes in the flow and resistance are used to assess kidney suitability for transplant. An increased flow with a concomitant decrease in resistance signifies potentially transplantable kidneys. A resistance of $>0.3-0.4$ is currently used as parameter indicating a kidney unusable for transplant.

Lifor® solution is a nutrient-rich media containing a patented nanoparticle capable of delivering oxygen that has been shown to be effective in the preservation of rat kidney allografts and hamster heart grafts. We hypothesize that Lifor® can be used as a pump perfusate to deliver oxygen to the organ tissue in the attempt to reverse ischemia and resuscitate the organ, potentially rescuing organs and making them transplantable. Our aim is to examine the efficacy of Lifor® as a pump perfusion media compared to that of Belzer's solution. Our hypothesis is that because Lifor® solution can deliver oxygen, perfusion with Lifor® will lead to improved pump parameters and may potentially rescue ischemic kidney allografts.

Materials and Methods:

Kidneys discarded due to poor pump parameters with the standard Belzer's solution will be pumped with Lifor® solution and the parameters compared. The discarded kidneys will be pumped at 4⁰C initial to compare baseline parameters for approximately 4-6 hours. The temperature will then be increased to 22⁰C, the temperature at which Lifor® works optimally and, theoretically, the kidney should be able to repair ischemically damaged tissue. Kidney biopsies will be obtain prior to and after perfusion with Lifor® and histology will be obtained.

Results:

PP parameters in discarded kidneys significantly improved with Lifor® compared to Belzer's at 4⁰C. Three of four (3/4) kidneys discarded due to high resistance (0.35, 0.48, 0.42) in pumping with Belzer's showed immediate improvement within 6 hours of pumping with Lifor® (0.25, 0.34, 0.33, respectively). These parameters would render the

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kidneys suitable for transplantation. The fourth kidney showed no change in resistance (0.45 -> 0.45) which may reflect an irreversibly ischemic kidney.

Normothermic (22⁰C) perfusion with Lifor® improves pump parameters. Two of two (2/2) kidneys pumped with Lifor® at 4⁰C and subsequently at 22⁰C showed immediate improvement in their resistive indices (0.35, 0.48 to 0.16, 0.21, respectively) within 3 hours. Resistance improvements were sustained for a further 16 hours after which the experiment was terminated.

Normothermic perfusion with physiologic pressures (>90 mmHg) may reverse ischemic tissue. One (1) discarded kidney was perfused with Lifor® at 22⁰C and at pressures of 90/40 mmHg. The contralateral kidney, which was not perfused but kept at 22⁰C, was used as control. Routine histology was taken in both kidneys before and after perfusion. Blind reading by an experienced pathologist at Allegheny General Hospital showed progression of ischemia and cell death in the control. The kidney perfused with Lifor® actually showed improvement of cellular integrity and repair.

Conclusion:

Preliminary results suggest that Lifor® may help to rescue ischemic kidneys and potentially render them transplantable. Further work needs to be done to confirm or refute these findings.