cokinetic profile was favourable. Three patients in the study group and one in the placebo group had delayed graft function. After 60 months, there had been 5 graft losses, all in the study group. The estimated glomerular filtration rate was significantly higher in the placebo group than in the study group at 12 months ($p=0.028$), 56 months ($p=0.0027$), 48 months ($p=0.0143$) and 60 months ($p=0.0573$) following the transplant.

Conclusions

APT070 can be used as an ex vivo flush prior to renal transplantation. The safety and side effect profiles are favourable although efficacy has not yet been demonstrated.

Nitric oxide levels following perfusion differ in donation after circulatory death and donation after brain death transplants

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Introduction

Donation after circulatory death (DCD) kidneys graft survival is similar to that of donation after brain death (DBD) donors. These kidneys have a higher incidence and duration of delayed graft function (DGF) that does not have the same impact on survival as in DBD kidneys. Nitric oxide (NO) is a free radical that plays a role in ischaemic reperfusion injury. Following reperfusion with the recipient blood, interferon-gamma increases significantly and induces iNOS synthesis and NO production. The aim of this study was to see whether the pattern of change of NO level following reperfusion differs between DBD and DCD kidneys, and whether it could explain their different behaviour.

Methods

Blood was collected prior to and following perfusion (2 hours) from 32 DCD and 32 DBD kidney recipients. NO was measured with a calorimetric method as NO3. The ratio of the postperfusion to the preperfusion values (reperfusion ratio [RRt]) was compared between the two groups and also correlated to known risk factors for DGF.

Results

The median postperfusion value of NO was not correlated with kidney disease, sex or recipient age. The median postperfusion NO value was affected by the baseline value. This is why the RRt was considered the best estimate of the change of NO following perfusion. The median RRt was 0.82 (mean: 0.86) in DBD kidneys whereas it was 0.89 (mean: 1.15) in DCD kidneys (Mann–Whitney U test, $p=0.05$).

In univariate analysis, the level of RRt was dependent on the type of transplant and CIT but not the presence of DGF. In addition, in DCD kidneys, the NO RRt in recipients with CIT of more than 12 hours was 1.29, significantly higher than the RRt of 0.86 measured in recipients with CIT less than 12 hours ($p=0.005$). In DCD kidneys, patients with donors under 55 years of age had an RRt of 0.96. This was not significantly different to the RRt of 0.85 in patients with older donors ($p=0.3$). In DBD kidneys, the post/prereperfusion ratio was not correlated with either donor age, sex or CIT.

Conclusions

The RRt of NO is significantly higher in DCD than in DBD kidney transplants, perhaps because DCD recipients' NO following reperfusion is significantly affected by long CIT, unlike in DBD recipients. In DCD kidneys, the level of NO increases following reperfusion with increasing CIT.

Activation of CD40 with platelet derived CD154 promotes necro-apoptosis of hepatocytes

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Introduction

Hypoxia and hypoxia-reoxygenation (H-R) are important mediators of hepatocyte death during liver transplantation as a result of reactive oxygen species (ROS) accumulation. The tumour necrosis factor superfamily member CD154 can also induce hepatocyte apoptosis via activation of its receptor CD40 and induction of autocrine/paracrine Fas ligand/CD178 but the relationship between CD40 activation, ROS generation and apoptosis is poorly understood. We hypothesised that CD40 activation and ROS accumulation act synergistically to drive human hepatocyte apoptosis.

Methods

Human hepatocytes were isolated from liver tissue and exposed to an in vitro model of hypoxia and H-R in the presence or absence of CD154 and/or various inhibitors. Hepatocyte ROS production, apoptosis and necrosis were determined by labelling cells with 2',7'-dichlorofluorescein, annexin V and 7-aminoactinomycin D respectively in a three-colour reporter flow cytometry assay.

Results

Exposure of human hepatocytes to recombinant CD154 or platelet derived soluble CD154 augments ROS accumulation during H-R, resulting in nicotinamide adenine dinucleotide phosphate oxidase-dependent apoptosis and necrosis. The inhibition of c-Jun N-terminal kinase and p38 attenuated CD154-mediated apoptosis but not necrosis.

Conclusions

CD154 mediated apoptosis of hepatocytes involves ROS generation that is amplified during H-R. This finding provides a molecular mechanism to explain the role of platelets in hepatocyte death during ischaemia-reperfusion injury.