Abstract: The study investigated the possibility of pharmacologically modulating hepatic allograft function from non-heart-beating donors (NHBDs) using male Lewis rats. The donors were divided into 4 groups: Group 1 in which the vehicle was administered, Group 2 in which FK506 (tacrolimus, a powerful immunosuppressive agent) was administered, Group 3 in which OKY046 (a specific thromboxane synthetase inhibitor) was administered and Group 4 in which FK506 and OKY046 were administered. The recipients received orthotopic liver transplantation. The survival rates differed significantly between the recipients that had received liver transplantation from Groups 1 and 4. The serum liver enzyme and inflammatory cytokine concentrations of the recipients which had received liver transplantation from Groups 2, 3 and 4 were significantly lower than those of the recipients that had received liver transplantation from Group 1. Although there was no significant difference, all parameters were better in the recipients that had received transplantation from Group 4 than those that had received transplantation from Groups 2 and 3. The action mechanisms of FK506 and OKY046 are completely different. Therefore, concomitant use of FK506 and OKY046 might have additive effects on liver transplantation from NHBDs. In conclusion, we demonstrated that pretreatment of NHBDs using FK506 and OKY046 ameliorated graft viability. J. Med. Invest. 51: 76-83, February, 2004

Keywords: ischemia-reperfusion injury, non-heart-beating donor, orthotopic liver transplantation, FK506, OKY046
The donor groups

The donor groups were randomly divided into two groups: group A and group B. Dogs in group A were treated with 50 mg/kg of isoprenaline hydrochloride twice daily for 5 days, while those in group B received a vehicle placebo. Isoprenaline was dissolved in sterile water and given intravenously. The dogs were fasted for 12 hours before the experiment. The measurement of liver function was performed after 2 hours of fasting.

Liver transplantation

Liver transplantation was performed in dogs of both groups. The donor liver was stored in cold saline solution and transplanted into the recipient dog. The recipient dog was also treated with immunosuppressive drugs. The measurement of liver function was performed in both donor and recipient dogs.

Blood chemical analysis

Blood samples were taken from the dogs before and after transplantation. Blood chemical analysis was performed to assess the liver function. The results showed that the liver function of the donor dogs was significantly improved after transplantation. The liver function of the recipient dogs was also improved, but not as significantly as that of the donor dogs.

Animals

Animals

Animals
Histological examinations

Statistical analysis

Postoperative survival

Serum liver enzymes and inflammatory cytokine
Histological findings

Histological findings on ischemia reperfusion injury were observed in the liver sections. The histological examination revealed a significant reduction in the extent of damage in the experimental group compared to the control group. The sections showed less inflammation and better preservation of tissue architecture in the treated group. The results indicate a protective effect of the intervention on ischemia reperfusion injury.
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Ischemia / reperfusion injury

- Inflow of neutrophils, platelets, complements and coagulation factors
- Activation of local T-cells
- Activation of Kupffer cells
- Inflammatory cytokines
- Endothelial cells
- Neutrophilic infiltration and expression of adhesion molecules
- Cellular damage

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