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Endotoxemia in organ donors: graft function following liver transplantation

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Abstract Translocation of endotoxin (LPS) to the portal-venous system is produced by multiple factors. In the case of normal liver function, LPS is rapidly cleared from the portal blood by Kupffer cells; in impaired liver function, LPS can reach the systemic circulation. The objective of this study was to investigate whether elevated donor endotoxin levels affect graft function in the recipient. LPS levels in donor plasma were measured in 14 consecutive liver transplantations. Grafts with donor LPS levels ≤ 12 pg/ml had a function probability of 100% after 600 days ($n = 10$). LPS concentrations of > 12 pg/ml in donor plasma led to loss of function in 75% of the liver grafts ($n = 4$; $P = 0.003$; Wilcoxon). Elevated LPS values in donor plasma seem to impair the prognosis of the grafts and could predict poor graft function as early as at the time of brain death.

Key words Endotoxin · Liver transplantation · Graft function

Introduction

Translocation of the lipopolysaccharide component (LPS, endotoxin) of the gram-negative bacterial cell wall to the portal-venous system can be produced by multiple factors (i.e., intestinal bacterial overgrowth, deficiencies in host immune defences, and increased permeability of the intestinal mucosal barrier [1]). Low LPS concentrations in the portal blood represent a normal physiological situation [5]. If the liver function is normal, LPS is rapidly cleared from the portal blood by Kupffer cells, in impaired liver function, LPS is able to reach the systemic circulation [2].

The objective of this study was to investigate whether elevated donor endotoxin levels affect the graft function in the recipient.

Patients and methods

Donor plasma was obtained during 14 consecutive liver transplantations using endotoxin-free vacuum blood collection tubes (Chromogenix, Mölndal, Sweden), followed by centrifugation at 150 × g at 4°C. Endotoxin levels were measured using the Limulus amoebocyte lysate (LAL) assay (Chromogenix, Mölndal, Sweden) as described by Fukui et al. [3]. The grafts' function probabilities were analysed according to the method of Kaplan-Meier.

Seven donors were male and 7 female; their age ranged from 18–58 years (median 37 years). They had died from intracerebral haemorrhage (12), head injury ($n = 4$), sinus thrombosis ($n = 1$), subarachnoid haemorrhage ($n = 6$), and polytrauma ($n = 1$).

The recipients' ages ranged from 25–56 years (median 44 years); 8 of them were female, 6 male. The diagnoses of the recipients were acute liver failure ($n = 1$), alcoholic cirrhosis ($n = 2$), cirrhosis due to hepatitis B ($n = 1$) and C ($n = 2$), primary biliary cirrhosis ($n = 2$), primary sclerosing cholangitis ($n = 3$), retransplantation following acute ($n = 1$) or chronic ($n = 1$) rejection, and cholangiocarcinoma (Klatskin tumor) ($n = 1$).

Results

Grafts from donors who had LPS concentrations ≤ 12 mg/ml in plasma had a function probability of 100% after 600 days (Fig. 1: *continuous line*; $n = 10$). LPS concentrations > 12 pg/ml in donor plasma led to

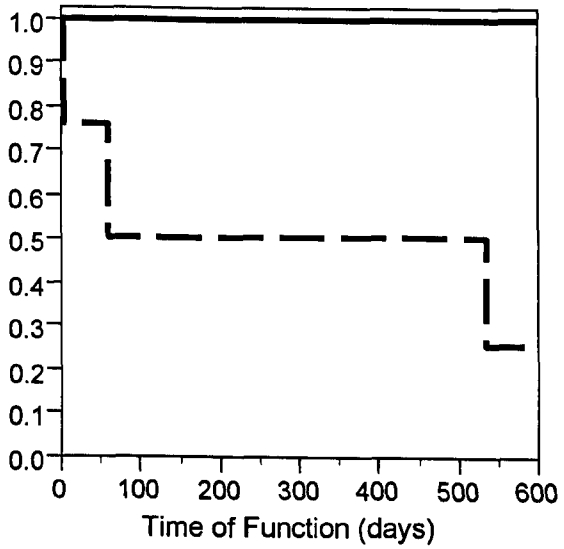

Fig. 1 Function probability according to Kaplan-Meier. *Continuous line* ($n = 10$): Liver function of the organs with LPS concentrations ≤ 12 pg/ml in donor plasma. *Broken line* ($n = 4$): Liver function of organs with LPS concentrations > 12 pg/ml in donor plasma ($P = 0.003$, Wilcoxon)

the loss of liver function in 75% of the grafts within the same period of time (Fig. 1: *broken line*; $n = 4$; $P = 0.003$, Wilcoxon).

Discussion

Elevated LPS concentrations in donor plasma indicate that the liver function may be impaired. It has been shown that patients with alcoholic and nonalcoholic liver disease have elevated plasma LPS concentrations within the same range as those patients of our study who had LPS concentrations above the cut-off value [4].

In conclusion, our results demonstrate that elevated LPS concentrations in donor plasma may adversely affect the prognosis of graft function and could predict poor graft function already at the time of brain death.

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