VII SUMMARY

Effects of vasoactive drugs on systemic and hepatic haemodynamics and oxygenation in an animal liver transplant model with different types and times of ischaemia

In the present study the effects of prostacyclin and noradrenaline on systemic and hepatic haemodynamics and oxygenation immediately before and after liver transplantation were investigated. To clarify if the postoperative effects depend on type and time of hepatic ischaemia, the liver allografts were exposed to different types and lengths of ischaemia prior to transplantation. The investigation was also expected to determine if in the present transplant model alterations in hepatic venous oxygen saturation are reflected in the mixed venous oxygen saturation and if a change in systemic haemodynamics is reflected in hepatic blood flow.

24 pigs were divided at prospective random into two groups of 12 pigs each, a donor and a recipient group. Depending on type and length of hepatic ischaemia the recipients were further divided into two subgroups (n = 6, each). For recipient group A the livers underwent a 4-hour cold ischaemia before transplantation (preservation in UW-solution). In recipient group B the liver allografts were exposed to 1 hour of warm ischaemia prior to the 4-hour cold ischaemia. After the necessary instrumentation and a phase of stabilization each animal received an intravenous prostacyclin infusion (5 ng/kg/min) for 30 minutes, directly before transplantation for donors and directly after transplantation for recipients. 15 minutes later a continuous infusion of noradrenaline (0,6 µg/kg/min) was administered for 30 minutes. Data of systemic and hepatic haemodynamics and oxygenation were taken before, during and after drug administration.

Only in recipients group A did Prostacyclin lead to a significant improvement in systemic and regional haemodynamics (cardiac outflow, $Flow_{AH}$) and oxygenation (DO_2, $D_{HEP}O_2$). During administration of noradrenaline, donors showed a distinct decline of liver blood flow without impairing the hepatic oxygen supply. Systemic catecholamine effects were not found in donors. In both recipient groups administering noradrenaline resulted in a significant deterioration of systemic hemondynamics (CO, intravascular pressures) (recipients group B > recipients group A). The systemic and hepatic oxygenation remained uneffected.

It was not possible to draw conclusions from mixed venous to hepatic venous oxygen saturation. A change in cardiac output was reflected in hepatic blood flow only in recipients group A.

The altered reactivity to vasoactive substances of the recipients compared to the healthy donors shortly after liver transplantation probably can be attributed to the imbalance between endogenous vasodilatators and vasoconstrictors. Seemingly, the 4-hour cold liver ischaemia (slight I/R injury) led to a discreet surplus of endogenous vasodilatators. The additional warm ischaemia (severe I/R injury) probably led to an increased production of endogenous vasoconstrictors. An interaction between these endogenous substances and the administered vasoactive drugs apparently led to a mutual strengthening and diminution of their particular effects respectively. Additionally, a reduced noradrenaline clearance after the transplantation could also be responsible for the increased systemic catecholamine effects in the recipients.

According to the results of our study the success of vasoactive therapy in the acute postoperative phase of liver transplantation depends among other things on the severity of hepatic I/R injury. It is assumed that systemic and hepatic haemodynamics and oxygenation be positively effected by prostacyclin only in recipients of slightly damaged livers. In contrast no significant prostacyclin effects can be expected in recipients of more severely injured livers.

Effects of noradrenaline seem to increase with severeness of I/R injury – at least effects on systemic haemodynamics (decrease of cardiac output, increase of intravasculare pressures). However, since no impairment of systemic or hepatic oxygenation is expected, the application of norardrenaline should not be harmful in this respect.