IS THERE A CENTRAL ROLE FOR SECRETORY PHOSPHOLIPASE A2 IN THE INITIATION OF ISCHE-MIA-REPERFUSION INJURY IN NON-HEART-BEATING DONOR LIVERS ? D. Monbaliu, C. Dubuisson, M. Zeegers, V. Heedfeld, K. Vekemans, T. Crabbé, J. Pirenne, J.F. Van Pelt. KULeuven.

Introduction : Secretory Phospholipase A_2 ($sPLA_2$) degrades cell membranes and plays a role in the synthesis of pro-inflammatory mediators and the induction of cytokines. It is immerging as an important factor playing a key role during inflammatory events such as ischemia-reperfusion injury (IRI).
Aim and methods : We evaluated changes in $sPLA_2$ enzyme activity and pro-inflammatory cytokines in serum early after reperfusion of livers exposed to Warm Ischemia (WI) in our previously validated pig model of liver transplantation (LT) from non-heart-beating donors (NHBD). Livers were exposed up to 60 minutes of WI, procured and transplanted after 4 hours cold ischemia. Serum samples were collected prior to and 15, 60 and 180 minutes and 1 and 4 days after reperfusion. $sPLA_2$ enzyme activity, Tumor Necrosis Factor-a (TNF-a) and Interleukin-6 (IL-6) levels were determined.
Results : After reperfusion, $sPLA_2$ activity in the serum increased and peaked at 60 min in primary non-function (PNF) recipients (8.35 ± 0.88 mU/ml) vs non-PNF recipients (6.35 ± 0.98 mU/ml) ($p = 0.045$). This was followed by a peak of TNF-a and IL-6. To investigate whether the organism is capable of protecting itself against high levels of $sPLA_2$, we determined the level of natural inhibitors of $sPLA_2$ in serum. We added a known amount of purified $sPLA_2$ to pig serum and determined the activity and compared this to the activity in buffer. The levels of inhibition at base line were not different between PNF and non-PNF recipients ($72.5 \pm 12\%$ vs $75.2 \pm 14.5\%$). 60 minutes after reperfusion the natural inhibition was reduced to around 50% in both groups. The level returned to base line at day 1 after transplantation in surviving non-PNF recipients and remained constant thereafter.
Conclusions : These findings suggest that a higher activity of $sPLA_2$ activity at 60 minutes after reperfusion is associated with PNF. In addition, natural sPLA2 inhibition seems to be important for it is restored within 24 hours. However, natural inhibition is not sufficient to counteract the increased $sPLA_2$ activity during and early after LT. Therefore we suggest that biological interventions aimed at improving WI injury following LT from NHBD should also include the inhibition of $sPLA_2$ activity.

BLOODLESS CADAVERIC LIVER TRANSPLANTATION : EXPERIENCE WITH JEHOVAH'S WITNESS RECIPIENTS. O. Detry, A. De Roover, C. Coimbra, M.F. Hans, J. Monard, M.H. Delbouille, J. Delwaide, J. Joris, M. Meurisse, J. Belaiche, P. Honoré. CHU Liège.

Background and aim : Modern medical management is marked by a trend to a decreased use of blood products or to transfusion-free strategies. In liver transplantation (LT), the use of blood products (red cells, platelets, plasma components) was reduced these last ten years due to better medical and surgical management, but the interest of transfusion-free LT is debated. The authors developed a transfusion-free LT program for Jehovah's witnesses (JW), and analysed its outcome to evaluate the potential interest of bloodless strategies in LT for the JW and non-JW LT recipient population.
Methods : Over an 8-year period, 16 selected JW underwent LT in the authors' department, including 5 right lobes living related LT and one pediatric LT. We analysed herein the outcome of the 10 adult patients (4 males, 6 females, mean age : 49 years) who underwent cadaveric whole LT. They received preoperative erythropoietin (EPO) therapy, with iron and folic acid to increase preoperative haematocrit (Ht). A cell saving system was used during the surgical procedures. No patient was lost to follow-up (mean : 43 months).
Results : No blood product was used in the whole follow-up. During the operative procedure a mean of 1,180 ml (ranges : 300-2,600 ml) were scavenged by the cell-saving system, allowing the reinfusion of a mean of 405 ml (ranges : 0-1,000 ml) of concentrated red cells. Mean total graft ischemia was 385 min (ranges : 205-684 min). Due to preparation, Ht level rose from $38.3\% \pm 1.9$ at first visit, to $44.3 \pm 1.8\%$ just before LT ($p < 0.05$). Postoperative day 1 mean Ht was $34.4 \pm 1.9\%$, significantly lower than the pre transplant level ($p < 0.05$), and further decreased during the post transplant period (mean lowest Ht : $31,2 \pm 1,9\%$, $p < 0.05$). Mean Ht at discharge was $34.1 \pm 2.1\%$. No patient experienced complication linked to anemia. Graft and patient survival is 100% at follow-up.
Conclusions : These excellent results justify the development of a bloodless LT program for JW patients. They also raise questions on the interest of a prospective evaluation of bloodless strategies in non-JW patients undergoing LT, and on the possible protective effects of EPO against ischemia-reperfusion injury and apoptosis (1).

Reference

1. Fliser D. *et al.* Mechanisms of disease : erythropoietin – an old hormone with a new mission ? *Nature Cardiovasc. Med.*, 2006, **3** : 563-572.