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TITLE: EFFECT OF APROTININ ON FIBRINOLYSIS DURING ORTHOTOPIC LIVER TRANSPLANTATION
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Hemorrhagic diathesis¹ during the anhepatic and postanhepatic period of orthotopic liver transplantation (OLT) is due to the occurrence of disseminated intravascular coagulation (DIC) associated with hyperfibrinolysis i.e. increase of tissue type plasminogen activator (tPA) and reduction of PA-inhibitor (PAI). Aprotinin inhibits many serine proteases including kallikrein and plasmin. Aprotinin has recently been reported to reduce blood loss in OLT². The goal of this study was to unravel the mechanism of action of aprotinin.

After informed consent and institutional approval were obtained, we studied the coagulation and fibrinolytic parameters in 9 patients undergoing OLT. In group A, patients (n=3) received Aprotinin at a loading dose of 2 000 000 kallikrein inhibitor units (KIU) followed by an infusion of 500 000 KIU/h. In group B, patients (n=6) had no aprotinin treatment (Table 1). Blood samples were collected preoperatively and at regular times during OLT. We report the results of the preoperative period (T 1) and at the end of anhepatic phase (T 6). The Man-Whitney U-test was used for comparison of data. P < 0.05 was considered to be statistically significant.

Two mechanisms can be distinguished (table 1):

1) Hyper-fibrinolysis was confirmed by high levels of tPA in all patients at T1, with a further increase during and after the anhepatic phase. However PAI and 2AP levels were significantly increased after aprotinin administration.

2) Activation of coagulation was similar in both groups with very high levels of thrombin antithrombin complex (TAT). During OLT, fibrin degradation products (FbDP) were increased in both groups whereas fibrinogen degradation products (FgDP) were higher in Group B, especially after reperfusion.

In conclusion, the results suggest that the reduction of hyperfibrinolysis during OLT is associated with an increase of fibrinolysis inhibitors PAI and 2AP, with plasmin neutralisation (low levels of FgDP) after aprotinin administration whereas no effect is observed on the activation of coagulation and thrombin generation.

REFERENCES

1. Thrombosis and haemostasis, 1989, p 179
2. Lancet 6 : 886 - 887, 1990

TABLE 1	GROUP A (n = 3)		GROUP B (n = 6)		Normal Range
	T 1	T 6	T 1	T 6	
tPA (ng/ml)	42.3±37	57±41	27.6±28	41.6±48	1 -12
PAI (UA/ml)	0.6±0.8	27.4±17*	7.2±16	0.3±0.5	0.3 - 3.5
α 2AP (IU/ml)	46.6±12	135±7.5*	86±18	55.7±25	0.8 - 1.3
TAT (µg/l)	6.1±8.8	127±44	5.7±5.8	105±63	< 3
FbDP (µg/ml)	2.1±2.1	2.9±0.7	3±4	4.2±2.1	< 0.4
FgDP (µg/ml)	0.6±0.5	0.9±0.1	0.9±1.3	9.4±13.8	< 0.4

* P < 0.05 vs. Group B (without aprotinin)

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TITLE: COMPARATIVE EVOLUTION OF RENAL HEMODYNAMICS DURING ORTHOTOPIC LIVER TRANSPLANTATION WITH AND WITHOUT VENO-VENOUS BYPASS.
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Introduction: Postoperative renal failure is a frequent problem after orthotopic liver transplantation (OLT). During the anhepatic phase, the increase of inferior vena cava pressure (IVCP) may be responsible for a decrease of renal perfusion pressure (RPP) (1, 2). Routine use of venous bypass (BP) has been advocated to improve early postoperative renal function (3). The aim of this study was to compare renal hemodynamics variations during OLT with and without BP and to evaluate their consequences on perioperative urine output and postoperative renal function.

Methods: Thirty eight cirrhotic patients undergoing OLT were prospectively studied after institutional approval. BP was used in 17 patients for easier surgical dissection or because mean arterial pressure (MAP) decreased by more than 30 % and/or cardiac index (CI) decreased by more than 50 % during the trial of clamping. For the other 21 patients, BP was not used (NBP). All patients had a normal preoperative renal function (creatinine serum level in NBP group: 73 ± 13 µmol.l⁻¹; in BP group: 72 ± 18 µmol.l⁻¹) (mean ± SD). Intraoperative measurements were made 2 hours after induction of anesthesia, 10 min before the end of the anhepatic phase and 2 hours after IVC unclamping. Variables included MAP, thermomodulation CI, superior vena cava pressure (SVCP), IVCP (measured through a 6F 30 cm catheter inserted via the femoral vein) and renal perfusion pressure (RPP = MAP - IVCP). Urine output (UO) was recorded during each phase of the surgery. Creatinine serum level was measured before surgery and on the third day after OLT. Results are expressed as mean ± SD. Statistical analysis was performed using repeated measures ANOVA followed by appropriate post-hoc tests and two-tailed student t test for normally distributed variables (P < 0.05 significant).

Results (Table). IVC clamping resulted in a significant increase in IVCP with and without BP. The increase in IVCP was greater without BP. UO was not modified during the clamping period in the BP group when it decreased significantly in the NBP group. After unclamping, UO was similar in both groups although greater than during the dissection phase. Creatinine serum levels were similar in both groups at Day 3 (NBP group: 126 ± 95 µmol.l⁻¹, BP group: 107 ± 49 µmol.l⁻¹). In either group during the anhepatic phase, no correlations were found between UO and RPP, UO and MAP or UO and IVCP.

Conclusion: In this study, BP does not seem to protect early postoperative renal function even if it allows a greater UO during the anhepatic phase.

Table: Results (mean ± SD). * P < 0.05 versus preceding sample. # P < 0.05 vs NBP.

		2 hours after induction	anhepatic phase	2 hours after IVC unclamping
SVCP (mmHg)	NBP	10 ± 3	6 ± 5*	9 ± 3*
	BP	8 ± 3	12 ± 4#	10 ± 4
IVCP (mmHg)	NBP	14 ± 5	32 ± 9*	14 ± 6*
	BP	13 ± 5	19 ± 7#	13 ± 5*
MAP (mmHg)	NBP	93 ± 17	92 ± 14	90 ± 14
	BP	90 ± 11	94 ± 13	82 ± 18
PPR (mmHg)	NBP	79 ± 20	60 ± 17*	76 ± 13*
	BP	77 ± 14	74 ± 16#	69 ± 20
UO (ml.kg ⁻¹ .h ⁻¹)	NBP	1.7 ± 2.0	0.7 ± 0.6*	2.8 ± 1.8*
	BP	1.5 ± 0.8	1.7 ± 1.6#	3.2 ± 2.0*
CI (l.min ⁻¹ .m ⁻²)	NBP	6.0 ± 1.6	3.2 ± 0.9*	5.7 ± 2.3*
	BP	5.4 ± 2.1	4.0 ± 1.6*	4.9 ± 1.6

- References:** 1- Transpl. Proc., 21, 3500-3505, 1989.
 2- Anesthesiology, 73, A304, 1990.
 3- Ann. Surg., 200, 524-533, 1984.