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EXPERIMENTAL PRESERVATION OF LIVER FROM HYPOTENSIVE DONOR AND WITH PROLONGED WARM ISCHEMIA

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Various experimental methods have been used for cooling the liver for transplantation and for short-term preservation. Electrolyte protein-free solutions produce major changes in hepatocytes and sinusoids. Plasma is the least harmful and most physiological fluid. Continuous perfusion-preservation for 8 hours with oxygenated plasma gave the best results, but the whole procedure seems too complex for clinical purposes.

In most publications on experimental liver preservation and transplantation, the liver used for transplantation is removed from a normotensive and living donor. Warm ischemia time is then limited to 1—3 minutes. Normal blood pressure and flow protect against development of ultrastructural changes in the liver cell. With such experimental technique, preservation of the liver up to 24 hours with subsequent successful transplantation has been achieved. The experimental setting does not, however, correspond to the clinical situation. Human liver donors usually remain hypotensive for several hours. After death, the liver remains warm and ischemic for at least 10 to 15 minutes before the mesenteric vein is cannulated and cold wash-out started.

The present investigation was undertaken to study how donor hypotension and prolonged warm ischemia time change the results of liver preservation and survival rate of the recipient.

MATERIAL AND METHODS

Sixty-two experiments divided in three groups were performed on mongrel dogs.

Donors were bled 30—35% of their blood volume, with a drop in arterial pressure to 60—80 mm Hg. They were sacrificed one hour later. Ten minutes after pharmacological cardiac arrest, the superior mesenteric

vein was cannulated and the liver washed out with 1500 ml buffered Ringer's solution at 4°C. Cooling of the liver from 37° to 10°C took about 25 minutes. The liver was then removed.

In group I (18 dogs) the liver was preserved in a perfusion system consisting of two diaphragm pumps, membrane oxygenator, and heat exchanger. For perfusion, cryoprecipitated plasma at 4°C, pH 7·8, 0·3—0·4 ml/g/min was used. In 9 animals perfusion preservation lasted for 4 hours, in the other 9 for 8 hours.

In group II (18 dogs) 9 livers were preserved by immersion in 4°C Ringer's solution, 9 were additionally washed out with buffered pooled plasma and also preserved in cold Ringer. No perfusion was used and an arbitrary 2·5 hours preservation time was chosen.

After preservation, the liver were transplanted orthotopically, Biochemical studies were carried out in the recipient 1 to 6, and 24 hours after transplantation, and daily afterwards until death of the animal. No immunosuppressive therapy was used.

In the control group (26 dogs), the donors were not bled, the liver was removed surgically from the living animal and no liver preservation was used.

RESULTS

Group I. Out of 9 dogs receiving livers preserved for 4 hours, 5 survived 24 hours and 4 longer than 3 days. Out of 9 dogs with liver preserved for 8 hours, 6 survived 24 hours, and 4 more than 3 days. Major biochemical changes were found in serum SGOT, potassium and hematocrit (Tables 1 and 2). They were evident in the first two hours after transplantation. Serum SGOT above 600 u, and hematocrit above 50% proved to be incompatible with survival. Marked hypokaliema was noted as early as one hour after transplantation, with return to almost normal values in 24 hours, but without any substantial differences between survivors and non-survivors.

Group II. Out of 9 livers preserved for 2·5 hours by immersion in cold Ringer's solution, 7 survived 24 hours, but only 3 more than three days. Out of 9 livers washed out with cold ACD plasma, only 2 lived for one day and 1 over three days. Serum SGOT was much higher in the non-survivors group than in the survivors. Serum potassium remained at its upper level, and hematocrit revealed hemoconcentration only slightly higher in the nonsurvivors (Tables 3 and 4).

Control group. Out of 26 dogs, 23 survived 24 hours and 21 more than three days. All deaths were due to technical problems. Serum SGOT

Table 1. Eight-hour liver perfusion preservation with cryoprecipitated plasma. Posttransplantation biochemical data.

A. Survived more than 3 days,

	1—6 hr	24 hr
SGOT (u.)	413 (284—482)	485 (458—1170)
K (mEq/L)	2·0 (1·8—2·4)	3·7 (3·3—4·2)
Htc (%)	47 (39—60)	38 (29—54)

B. Died within 1—3 days.

SGOT (u.)	622 (482—890)	3222 (635—6700)
K (mEq/L)	2·1 (1·6—2·7)	4·1 (3·5—4·7)
Htc (%)	59 (54—67)	47 (40—57)

Table 2. Four-hour liver perfusion preservation with cryoprecipitated plasma. Posttransplantation biochemical data.

A. Survived more than 3 days,

	1—6 hr	24 hr
SGOT (u.)	521 (284—920)	610 (264—1300)
K (mEq/L)	3·2 (2·4—3·7)	3·2 (2·6—3·3)
Ht (%)	46 (42—48)	40 (35—42)

B. Died within 1—3 days.

SGOT (u.)	540 (510—570)	1210
K (mEq/L)	1·9 (1·9—2·0)	3·0 (2·3—3·5)
Ht (%)	57 (52—64)	50 (45—56)

Table 3. No perfusion, wash-out with Ringer's solution, preservation for 2·5 hours. Posttransplantation biochemical data.

A. Survived more than 3 days,

	1—6 hr	24 hr
SGOT (u.)	365 (300—398)	468 (264—572)
K (mEq/L)	4·3 (3·2—4·8)	4·6 (3·5—5·2)
Ht (%)	43 (32—48)	45 (35—55)

B. Died within 1—3 days.

SGOT (u.)	492 (280—1070)	608 (464—792)
K (mEq/L)	4·8 (3·6—6·3)	4·9 (4·0—6·2)
Ht (%)	38 (33—48)	48 (45—52)

Table 4. No perfusion, wash-out with ACD plasma, preservation for 2·5 hours. Posttransplantation biochemical data.

A. Survived more than 3 days.

	1—6 hr	24 hr
SGOT (u.)	452	342
K (mEq/L)	3·6	4·5
Ht (%)	54	37

B. Died within 1—3 days.

SGOT (u.)	657 (450—918)	—
K (mEq/L)	4·8 (4·6—5·0)	—
Ht (%)	54 (48—62)	—

Table 5. No preservation. Ischemia in less than 60 minutes. Posttransplantation biochemical data.

Survived more than 3 days.

	1—6 hr	24 hr
SGOT (u.)	338 (50—492)	419 (408—820)
K (mEq/L)	4·5 (3·4—5·6)	4·7 (4·3—5·8)
Ht (%)	38 (31—50)	47 (33—61)

Table 6. Survival with various methods of liver preservation.

Group	Type of preservation	Time hr	Number	Survivals 3 days
		4	9	4
I	Perfusion with cryoprecipitated plasma	8	9	4
II	No perfusion, wash-out with Ringer's cold immersion	2,5	9	3
	No perfusion, wash-out with ACD plasma, cold immersion	2·5	9	1
Control	No preservation	1	26	21

and potassium remained at an average level; only slight hemoconcentration was noted 24 hours after transplantation (Table 5).

The overall results are summarized in Table 6.

CONCLUSIONS

1. Liver was procured for transplantation simulating clinical setting (hypotension + prolonged warm ischemia). Only 40% survivors were found after 8 hour preservation with perfusion and 30% after 2·5 hour non-perfusion preservation.

2. Perfusion-preservation of the liver, despite its technical complexity, is still a superior method to the non-perfusion preservation.

3. Serum SGOT activity, K^+ concentration, and hematocrit are the most reliable in vivo indices of liver graft vitality in the first 24 hours.

4. SGOT activity above 600 and hematocrit above 50 are usually incompatible with survival.

5. Marked hypokalemia occurs following transplantation of the perfused-preserved liver.

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