1508 x 2

# Sodium Lactobionate Sucrose Solution for Canine Liver and Kidney Preservation

Y. Zhu, H. Furukawa, K. Nakamura, I. Hamamoto, Y. Wu, R. Xiaoshan, R. Venkataramanan, S. Todo, and T.E. Starzl

EVEN though the University of Wisconsin (UW) solution developed by Belzer and Southard[1] in 1988 has markedly prolonged the preservation time of most of the solid organs,[2,3] there still have been many efforts to improve the quality of UW solution.[4–6] Recently, Tokunaga et al[7] developed a new solution, sodium lactobionate sucrose (SLS) solution, which has been shown to be superior to UW solution in rat liver preservation. In the SLS solution, sucrose is substituted for the raffinose in the UW solution and the SLS solution has an extracellular type electrolyte composition. Additionally, chlorpromazine (CPZ) is added to SLS solution to maintain the microvasculature and membrane integrity. In the present study, we compared the performance of these solutions using canine liver and kidney transplantation models.

## MATERIALS AND METHODS

### Animals and Surgical Procedures

Female beagle dogs (9 to 11 kg) and mongrel dogs (18 to 23 kg) were used for liver and kidney transplantation, respectively. All of the dogs were fasted 12 hours before operation. The dogs were anesthetized with 25 mg/kg of IV sodium thiopental for induction, maintained with isoflurane, and oxygenated under mechanical ventilation.

### Liver Transplantation

Orthotopic liver transplantation was performed by a method described previously.[8–10] The donor livers were flushed in situ with either UW solution (group 1, n = 7) or SLS solution containing 1 mg/L of CPZ (SLS) (group 2, n = 7). One liter of preservation solution was perfused through the portal vein and 500 mL through the aorta. The livers were stored for 24 hours in the same solution prior to transplantation.[3]

Graft weight was measured before and after preservation. The occurrences of hypotension and outflow block after reperfusion were determined. Hepatic artery and the portal vein blood flows (before harvesting and at 1 hour and 2 hours after unclamping) were measured. Following transplantation, serum glutamic oxaloacetic transaminase (SGOT), lactate dehydrogenase (LDH), glucose, and total bilirubin were measured daily. All of the surviving animals were killed at 14 days. Autopsies were performed immediately on animals that died before 14 days. Liver tissue was taken before transplant, 2 hours after transplant, and at autopsy.

### Kidney Transplantation

The technique used for kidney autotransplantation was described previously.[2] The renal artery was flushed with 200 mL of cold heparinized lactated Ringer's solution, followed by 200 mL of cold UW (group 3, n = 6) or SLS solution (group 4, n = 6). The kidneys were stored in the same solution for 72 hours.

Graft weight was measured before and after preservation. Renal arterial blood flow was measured immediately before harvesting, and at 1 and 2 hours after revascularization. Graft function was estimated by urine output at 1 and 2 hours after unclamping and by daily serum creatinine (Cr) levels. All of the animals that survived for 15 days were killed. Autopsies were performed immediately on dogs that died before 15 days. A section of kidney was obtained for histopathologic analysis.

**Table 1. Animal Survival After Liver or Kidney Transplantation With UW or SLS Solution**

| | % Survival | Survival (d) |
|---|---|---|
| Liver | | |
| Group 1 (UW) | 86 | 1,* 14, 14, 14, 14, 14, 14 |
| Group 2 (SLS) | 28 | 1,* 1,* 2,* 2,* 9,† 14, 14 |
| Kidney | | |
| Group 3 (UW) | 100 | 15, 15, 15, 15, 15, 15 |
| Group 4 (SLS) | 83 | 5,‡ 15, 15, 15, 15, 15 |

*Liver failure.
†Cholangitis.
‡Thrombosis of the renal artery.

## RESULTS

Our general impression was that in situ flushing of the liver and the kidney was faster and smoother with SLS solution than UW solution.

### Liver

Six of the seven dogs (86%) in group 1 survived for 14 days, whereas only two of the seven dogs (28%) in group 2 survived for the same period (Table 1). Reperfusion of group 1 grafts was similar to that of immediately transplanted grafts. Disturbance of reperfusion, occurrence of outflow block, and poor bile production were rarely found in group 1 animals, but common in group 2 animals. Grafts in both groups 1 and 2 lost similar amounts of weight (−0.6% to −12.5%) during the preservation period. Hepatic artery and portal vein blood flows at 1 and 2 hours

From Pittsburgh Transplant Institute, University of Pittsburgh, Pittsburgh, Pennsylvania.

Supported by research grants from the Veterans Administration and project grant no. DK 29961 from the National Institute of Health, Bethesda, Maryland.

Address reprint requests to Thomas E. Starzl, MD, PhD, 5C Falk Clinic, 3601 Fifth Ave, Pittsburgh, PA 15213.



0041-1345/93/$3.00/+0

**Table 2. Liver Function**

| | 1 h | 6 h | 24 h |
|---|---|---|---|
| SGOT (U/L) | | | |
| Group 1 | 2,037 ± 1,021 | 2,151 ± 822 | 1,798 ± 1,233 |
| Group 2 | 2,689 ± 1,525 | 2,802 ± 1,605 | 836 ± 836 |
| LDH (U/L) | | | |
| Group 1 | 1,357 ± 645 | 923 ± 348 | 614 ± 321 |
| Group 2 | 2,442 ± 1,159 | 1,365 ± 885 | 836 ± 764 |
| Glucose (mg/dL) | | | |
| Group 1 | 200 ± 58 | 226 ± 147 | 93.2 ± 33.9 |
| Group 2 | 324 ± 150 | 217 ± 155 | 107 ± 85 |

after graft reperfusion were not significantly different between the groups. However, 6 hours after liver transplantation, group 2 animals exhibited higher SGOT and LDH levels than group 1 (Table 2). No remarkable histopathologic differences were noted between two groups in pretransplant, 2-hour posttransplant, and autopsy samples.

### Kidney

All of the group 3 dogs survived for 15 days (100%), while 5 of the 6 group 4 dogs survived for 15 days (83.3%) (Table 3). Graft weight loss during the preservation period was similar between groups (−8% to −31%). Group 3 urine output for the first 2 hours after unclamping was higher than group 4 (658 ± 582 vs 385 ± 360 μL/h/g kidney), but it was not statistically significant (Table 3). Kidneys in groups 3 and 4 reperfused well after reimplantation, but the arterial blood flow was slightly lower than the value before harvesting for both groups. No histopathologic differences were seen in the grafts of either group. Group 4 posttransplant Cr levels were lower than group 3, with day 2 Cr being significantly lower (Table 3).

**Table 3. Kidney Function**

| | 2 d | 5 d | 15 d |
|---|---|---|---|
| Creatinine (mg/dL) | | | |
| Group 3 | 10.98 ± 5.36 | 7.05 ± 3.05 | 3.92 ± 4.1 |
| Group 4 | 5.27 ± 1.53* | 6.92 ± 4.23 | 2.75 ± 0.7 |

*$P < .05$ vs group 3 by Student's $t$ test.


## SUMMARY

With 24-hour preservation of canine liver, SLS solution showed inferior animal survival to UW solution. The lactobionate, raffinose, glutathione, and hydroxyethyl starch in UW solution have been shown to be important for liver preservation.[11,12] However, our results suggest that sucrose should not be substituted for raffinose for the preservation of livers.

In contrast to the liver, SLS solution performed the same or even better than UW solution for kidney preservation. The substitution of sucrose for raffinose, along with the addition of CPZ has either no effect or a slightly positive effect on kidney preservation.[12,13]

In conclusion, SLS solution may be a suitable solution for preserving canine kidneys, but is not suitable for liver preservation. These findings suggest that future development of preservation solutions should be focused on the needs of specific organs and not toward a generic, all encompassing preservation solution.


## REFERENCES


1. Belzer FO, Southard JH: Transplantation 45:673, 1988
2. Ueda Y, Todo S: Transplantation 48:913, 1989
3. Jamieson NV, Sundberg R, Lindell S, et al: Transplantation 46:517, 1988
4. Sumimoto R, Jamieson NV, Wake K, et al: Transplantation 48:1, 1989
5. Wahlberg J, Jacobsson J, Tufveson G: Transplantation 48: 400, 1989
6. Moen J, Claeson K, Pienar H, et al: Transplantation 47:940, 1989
7. Tokunaga Y, Wicomb WN, Concepcion W, et al: Surgery 110:80, 1991
8. Todo S, Kam I, Lynch S, et al: Semin Liver Dis 5:309, 1985
9. Todo S, Podesta L, Ueda Y, et al: Clin Transplant 3:253, 1989
10. Kam U, Lynch S, Todo S, et al: Surg Gynecol Obstet 163:33, 1986
11. Jamieson NV, Lindell S, Sundberg R, et al: Transplantation 46:512, 1988
12. Cheim KR, Abrams J, Serroni A, et al: J Biol Chem 253:4809, 1978
13. London EJ, Jaiswenl RK, Naukam RJ, et al: Biochem Pharmacol 33:3553, 1984