The use of the University of Wisconsin (UW) and Euro-Collins (EC) solutions either alone or in a combined method*


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Abstract. From June 1988 to October 1990, a total of 100 orthotopic liver transplantations (OLTs) in 91 patients were performed at the Hospital Clinic of Barcelona. Euro-Collins (EC) solution was used as the flush and storage solution in 29 livers, and the University of Wisconsin (UW) solution was used in 24. A combined method, consisting of flushing and harvesting the liver with UW solution through the portal vein and with EC solution through the aorta, was used in the remaining 47 livers. Livers harvested using such a combined method showed substantially better postoperative function in terms of AST, ALT, and prothrombin activity than those harvested in EC solution alone. Although AST and ALT values were lower in patients whose livers were harvested using the combined method than with UW alone, differences were not significant. On the other hand, prothrombin activity was consistently better in the UW group. Bilirubin levels, platelet count, and bile output showed no difference among the three groups. We conclude that the combined use of UW and EC solutions for flushing and harvesting is not hazardous to human liver preservation and, in fact, may considerably reduce the amount of UW solution needed and, consequently, the costs.

Key words: UW solution, in liver transplantation – Euro-Collins solution, in liver transplantation – Preservation solutions, in liver transplantation

Since 1983, orthotopic liver transplantation (OLT) has become an effective therapeutic modality for end-stage liver disease [10]. Up until 1987, the mainstay of liver preservation was cold storage in Euro-Collins (EC) solution, which provides acceptable graft function within a preservation time of 9 h [3]. The University of Wisconsin (UW) solution subsequently proved to be a major advance in organ harvesting. Its safety and efficacy have been widely demonstrated for extended preservation of the human liver [1, 6–8, 11, 15–18]. Nevertheless, due to its numerous components, the cost of UW solution is generally quite high. Therefore, in June of 1989, we began using UW solution in combination with EC solution. The aim of this study was to retrospectively compare postoperative graft function in livers harvested either in EC solution alone, in UW solution alone, or in a combination of the two solutions.

Materials and methods

From June 1988 to October 1990, a total of 100 OLTs in 91 patients were performed at the Hospital Clinic of Barcelona. EC solution was used as the flush and storage solution in 29 livers and UW solution was used in 24. The remaining 47 livers were harvested using a combined method in which UW solution was flushed through the portal vein and EC solution through the aorta. Table 1 presents data on the graft recipients, including sex, age, and indication for transplantation. Donor groups (EC, UW, and combined) were similar with respect to age, sex, cause of death, length of hospitalization, and liver function (Table 2).

Table 1. Recipient data

<table>
<thead>
<tr>
<th>Group</th>
<th>EC</th>
<th>UW</th>
<th>Combined</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no. of grafts</td>
<td>29</td>
<td>24</td>
<td>47</td>
</tr>
<tr>
<td>Mean age ± SE</td>
<td>44.4 ± 11</td>
<td>42 ± 10</td>
<td>43.8 ± 9</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>16/13</td>
<td>12/12</td>
<td>26/21</td>
</tr>
<tr>
<td>Indications for OLT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Fulminant hepatic failure</td>
<td>3</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>2. Cirrhosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic active hepatitis</td>
<td>9</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Cryptogenic</td>
<td>5</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>Alcohol</td>
<td>2</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>3. Cholestatic diseases</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary biliary cirrhosis</td>
<td>5</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>Sclerosing cholangitis</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>4. Other diseases</td>
<td>3</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>5. Retransplants</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>immediate</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>late (chronic rejection)</td>
<td>0</td>
<td>1</td>
<td>5</td>
</tr>
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</table>

* Preliminary results from this study were presented at the First International Congress of the Society for Organ Sharing in Rome in June 1991 and will also appear in Transplantation Proceedings.

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Patients were managed in a similar way during the post-patent replacement was performed in all cases by the same surgeons. The previously described operative technique was used [2, 14]. Heparin or UW solution through the portal vein and the aorta. In the group formed until the liver was cooled. The liver was perfused with either steroids (triple therapy).

Prior to reperfusion of the liver, the hepatic graft was flushed with UW solution when procurement and harvesting were also performed on a multiorgan basis with kidneys in 100% of the cases, hearts in 60%, and pancreases in 20%. Livers were flushed and preserved totally in UW solution when procurement and harvesting were also performed for pancreases or when there were two organ donors.

Organ procurement

All livers were harvested in a similar fashion with dissection of the porta hepatitis and celiac axis. Mobilization of the liver was not performed until the liver was cooled. The liver was perfused with either EC or UW solution through the portal vein and the aorta. In the group using the combined method, two liters of UW solution was flushed through the portal vein, while EC solution was used through the aorta. Around 250 ml was left in the bag for a back table flush through the celiac axis. No precooling was done. All livers were obtained on a multiorgan basis with kidneys in 100% of the cases, hearts in 60%, and pancreases in 20%. Livers were flushed and preserved totally in UW solution when procurement and harvesting were also performed for pancreases or when there were two organ donors.

Recipient operation and perioperative care

The previously described operative technique was used [2, 14]. Hepatic replacement was performed in all cases by the same surgeons. Prior to reperfusion of the liver, the hepatic graft was flushed with HaemoC. Patients were managed in a similar way during the post-operative period, following a previously established protocol. Immunosuppression consisted of azathioprine, cyclosporin A, and steroids (triple therapy).

The following parameters were evaluated in the three groups (EC, UW, and combined): cold ischemia time, immediate graft function in terms of AST, ALT, prothrombin activity, bilirubin, platelet count, and bile output from day 1 to day 7. The probability of graft survival was also calculated, with a maximum follow-up of 12 months. In order to obtain a complete picture, early postoperative graft function was evaluated using a scoring system previously described [5]. In brief, a score was obtained from the peak ALT value, the mean 24-h bile output, and the lowest prothrombin activity measured during the first 72 h. For each patient, the score corresponded to the sum of the assigned value of each parameter, with a possible range from 3 to 9. Depending on their scores, patients were classified into three different groups: I (good early graft function) when the score was 3, or IV (intermediate early graft function) when the score was 5 or 6, and III (poor early graft function) when the score was 7–9 (Table 3).

Statistics

Statistical analysis was performed using the analysis of variance factorial and repeated measures. Actuarial survival curves were calculated according to the conditional probability of Kaplan and Meier. Curves were compared by means of the log-rank test. Figures are given in absolute values ± standard error (SE).

Results

Preservation time

The cold storage time, measured from the time of portal venous perfusion until the time of reperfusion in the recipient, once the portal vein anastomosis was completed, had a mean of 253.8 ± 16 min (range 180–430 min) in the EC group while it was 300.7 ± 13 min (range 216–720 min) in the combined group and 539 ± 50 min (range 310–1080 min) in the UW group. There was a significant difference between the UW and the other two groups (F = 28.137, P = 0.0001).

Postoperative liver function

There was one primary nonfunction in the combined group (preservation using the combined method again). One patient in the UW group was retransplanted after 10 days (this time with a graft preserved using the combined method) because of acute hepatic failure, with a rapid rise in ALT and a sharp decrease in prothrombin activity. Nevertheless, the pathology showed a normal or near-normal pattern of the liver tissue.

Figure 1 shows the AST postoperative levels in the three different groups. As can be seen, livers in the combined group fared better than those in either of the other groups. An analysis of variance (repeated measures) showed an F value of 6.79 (P = 0.0018). From day 1 to day 5, differences were significant only between the EC and combined groups (Dunnett t = 2.2–3.2, significant at 95%). UW values were not different from EC or combined group values on any of the postoperative days considered.

Postoperative ALT levels were also consistently better in the combined group (ANOVA F = 5.973, P = 0.0037). Again, the differences were significant only between the EC and combined groups on postoperative days 1–5. Values in the UW group did not differ from those in either of the other groups on any given day (Fig. 2).

With respect to postoperative prothrombin activity, levels through the 1st week were always better in the UW

<table>
<thead>
<tr>
<th>Table 2. Donor data</th>
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<tbody>
<tr>
<td>Group</td>
</tr>
<tr>
<td>Numbers of donors</td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Sex (male/female)</td>
</tr>
<tr>
<td>Mean number of days in hospital</td>
</tr>
<tr>
<td>Liver function (mean)</td>
</tr>
<tr>
<td>AST</td>
</tr>
<tr>
<td>ALT</td>
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<tr>
<td>Bilirubin (mg/dl)</td>
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<tr>
<th>Table 3. Score for early postoperative graft function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameter</td>
</tr>
<tr>
<td>Serum alanine aminotransferase (IU/l)</td>
</tr>
<tr>
<td>&lt; 1000</td>
</tr>
<tr>
<td>1000–2500</td>
</tr>
<tr>
<td>&gt; 2500</td>
</tr>
<tr>
<td>Bile output (ml/day)</td>
</tr>
<tr>
<td>&gt; 100</td>
</tr>
<tr>
<td>40–100</td>
</tr>
<tr>
<td>&lt; 40</td>
</tr>
<tr>
<td>Prothrombin activity</td>
</tr>
<tr>
<td>&gt; 60% (spontaneously)</td>
</tr>
<tr>
<td>&gt; 60% (with fresh frozen plasma administration)</td>
</tr>
<tr>
<td>&lt; 60% (despite fresh frozen plasma administration)</td>
</tr>
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</table>

*Highest value within the first 72 h after transplantation. Normal values in our laboratory < 40 IU/l.

*Mean value during the first 72 h after transplantation.

*Lowest value within the first 72 h after transplantation.

<table>
<thead>
<tr>
<th>Table 4. Early graft function and type of organ harvesting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group</td>
</tr>
<tr>
<td>Score: I and II (good, intermediate)</td>
</tr>
<tr>
<td>Score: III (poor)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Organ procurement</th>
</tr>
</thead>
</table>

| Parameter | Assigned value |
|---------------------|
| Serum alanine aminotransferase (IU/l) | |
| < 1000 | 1 |
| 1000–2500 | 2 |
| > 2500 | 3 |
| Bile output (ml/day) | |
| > 100 | 1 |
| 40–100 | 2 |
| < 40 | 3 |
| Prothrombin activity | |
| > 60% (spontaneously) | 1 |
| > 60% (with fresh frozen plasma administration) | 2 |
| < 60% (despite fresh frozen plasma administration) | 3 |

<table>
<thead>
<tr>
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<td>Curve was compared by means of the log-rank test. Figures are given in absolute values ± standard error (SE).</td>
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