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# Comparison of the efficacy of University of Wisconsin solution and Newcastle organ perfusion fluid in the preservation of livers for transplantation

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**Abstract** University of Wisconsin solution (UW) is now used widely for the preservation of livers for transplantation. However, the use of commercial solutions has added considerably to the cost. We were able to produce a local version of organ perfusion fluid (NOPF) incorporating all the constituents of UW except for the hydroxyethyl starch and adenosine. We compared graft outcome using NOPF with imported grafts perfused with commercial UW solution. The two recipient groups (15 patients each) were similar with respect to age and sex distribution, urgency of transplantation, regraft status and patient and graft survival. Postoperative duration of ventilation, dialysis requirements, peak bilirubin, peak ALT and lowest unsupported prothrombin time were also similar in both groups. In conclusion, local perfusion fluids based on UW can be produced without detriment to graft outcome with considerable financial savings. At our institution, this represents a reduction of 33% in the cost of perfusion fluids.

**Key words** Liver transplantation · Ischaemia · Reperfusion · Organ preservation

## Introduction

The results of liver transplantation have improved considerably over the last few years. This has been demonstrated by better patient and graft survival. The reasons for this include improved immunosuppression, standardization of surgical technique and better organ preservation and sharing systems. One-year patient survival after first liver transplantation in the UK has improved between 1985 and 1992 and this improvement is particularly seen when transplantations carried out before and after 1988 are compared [7]. Although there are several possible reasons for this improvement, the introduction of University of Wisconsin perfusion fluid (UW) has probably made an important contribution by improving preservation of liver grafts.

In UW, lactobionate and raffinose are used as impermeants to prevent intracellular swelling, and a stable nontoxic colloid, hydroxyethyl starch (HES), is used to prevent expansion of the extracellular space. Adenine is used as a precursor for ATP synthesis. The use of UW, however, adds a significant amount to the cost of liver transplantation, and various simplified versions have been described. These include a high sodium variant and solutions from which hydroxyethyl starch and adenosine are omitted. Experimental studies have shown that the effectiveness of UW is maintained in these two variants [5].

Our institution has facilities for producing total parenteral nutrition, so we were able to produce a local version of organ perfusion fluid, incorporating all the constituents of commercial UW, except HES and adenine. The aim of this study was to analyse retrospectively the efficacy and safety of the Newcastle organ perfusion fluid (NOPF) in terms of early graft function, and to determine the potential cost benefit.

## Patients and methods

### Patients

Two groups of 15 patients were studied over a 2-year period. The first group consisted of 15 patients who received local donor livers perfused with NOPF. The second group of 15 patients received imported livers through the organ sharing scheme, and these were perfused with commercial UW.

### Local donor protocol

Aortic perfusion was carried out with 3–4 l of Marshall's solution (hyperosmolar citrate) and portal vein perfusion with 2 l of NOPF. Back table perfusion at the donor hospital was performed using 1 l of NOPF via the hepatic artery, portal vein and common bile duct. The liver was packed using 1 l of NOPF.

Statistical analysis was performed using nonparametric tests (Mann Whitney, Kruskall Wallis, Chi-squared, and Fisher's exact test).

The two groups were similar with respect to age, sex, cold ischaemia time (CIT), and cause of liver failure (Table 1). The mean follow-up period was 33 ± 11 months for the NOPF group (median 33 months) and 28 ± 10 months (median 29 months) for the UW group.

**Table 1** Recipient demographic data

| | Group 1 | Group 2 | *p*-value |
|---|---|---|---|
| Age (years) | | | |
| Mean ± SD Median | 48 ± 12 (46) | 45 ± 11 (46) | 0.44 |
| Sex (male/female) | 7/8 | 9/6 | 0.5 |
| Cold ischaemia time (min) | | | |
| Mean ± SD | 780 ± 137 | 563 ± 175 | 0.002* |
| Median | 795 | 508 | |
| Fulminant liver failure | 3 | 5 | |
| Cholestatic cirrhosis | 6 | 4 | |
| Postnecrotic cirrhosis | 6 | 4 | |
| Regrafts | 2 | 1 | |

* $p < 0.05$

**Table 2** Early graft function parameters (day 1–5). Values are means ± SD. Figures in parentheses are median values

| | Group 1 | Group 2 | *p*-value |
|---|---|---|---|
| Primary nonfunction | 1 | 0 | |
| ICU stay (days) | 2 ± 2 (1) | 2 ± 2 (1) | 0.5 |
| Peak bilirubin (mmol/l) | 107 ± 112 (50) | 99 ± 59 (93) | 0.6 |
| Day 1 ALT (mmol/l) | 854 ± 861 (462) | 556 ± 461 (439) | 0.7 |
| Peak ALT (mmol/l) | 546 ± 582 (477) | 661 ± 676 (453) | 0.6 |
| Lowest prothrombin time (s) | 16 ± 3 (15) | 16 ± 2 (16) | 0.8 |

**Table 3** Patient and graft survival

| | NOPF | UW |
|---|---|---|
| Patient survival 1 month | 13 (87%) | 15 (100%) |
| Graft survival 1 month | 13 (87%) | 15 (100%) |
| Patient survival 1 year | 12 (80%) | 11 (73%) |
| Graft survival 1 year | 12 (80%) | 11 (73%) |

## Results

All patients were admitted to the intensive care unit (ICU) as per protocol and electively ventilated. The mean duration of stay in the ICU was 2 ± 2 days (median 1 day) for the NOPF group and the UW group. Two patients in the NOPF group and one in the UW group had regrafts.

The peak bilirubin levels in group 1 and 2, respectively, were 107 ± 112 (median 50) mmol/l and 99 ± 59 (median 93) mmol/l ($p = 0.6$ Kruskall Wallis test). The ALT levels on day 1 were 854 ± 861 (median 462) mmol/l and 556 ± 461 (median 439), respectively ($p = 0.7$, Kruskall Wallis test). Peak ALT levels in the two groups were 546 ± 582 (median 477) mmol/l and 661 ± 676 (median 453) mmol/l ($p = 0.6$ Kruskall Wallis). The lowest unsupported prothrombin time was 16 ± 3 (median 15) s and 16 ± 2 (median 16) s ($p = 0.4$ Kruskall Wallis test), respectively. These results are summarized in Table 2. Patient and graft survival were similar in both groups, as shown in Table 3.

The cost per litre of UW to our unit is £ 139.90 and of NOPF is £ 93.50. As 4 l of perfusion fluid are used for each liver transplant, there was a saving of £ 183.20 for each liver transplant procedure.

## Discussion

Orthotopic liver transplantation (OLT) is now well established as standard treatment for end-stage liver failure. The technical aspects of OLT have now been standardized and the introduction of UW has extended preservation times, enabling the operation to be performed as a planned procedure. Preservation times have been extended to almost 20 h with UW [6]. Primary nonfunction and damage from ischaemia-reperfusion injury are issues that still need to be resolved. Many risk factors for primary nonfunction and dysfunction have been identified and these include fatty donor livers, older donors and prolonged cold ischaemic periods [4].

Ischaemia-reperfusion injury has been extensively reviewed [1] and various constituents have been added to perfusion fluids to minimize these problems and their roles still need to be defined more clearly. This complexity of perfusion fluids adds considerably to the costs of OLT and simplified perfusion fluids have been shown to be effective [5] in experimental studies. We have studied the effects of one such locally produced organ

perfusion fluid. Various indicators of early graft function were analysed, and liver preservation appeared to be at least as satisfactory as with the widely used perfusion fluid UW.

Markers of early graft function such as lowest unsupported prothrombin time, peak ALT and peak bilirubin were shown to be comparable using NOPF and UW. Patient and graft survival were also satisfactory using NOPF. There was also a significant cost benefit from using NOPF as represented by a saving of 33 % in the cost of perfusion fluids.

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