



## Kidney Transplantation With Belzer or Custodiol Solution: A Randomized Prospective Study

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### ABSTRACT

**Purpose.** The purpose of this study was to compare the Belzer vs Custodiol solutions for cadaveric kidney perfusion in relation to delayed graft function, renal function, acute rejection episodes, and patient and graft survivals.

**Methods.** This randomized prospective study included 42 kidneys and 9 simultaneous kidney and pancreas recipients from December 2002 to February 2004, namely 24 in the Custodiol arm and 27 in the Belzer arm. We analyzed delayed graft function frequency, acute rejection episodes (biopsy proven), renal function (creatinine at 1, 6, and 12 months), as well as graft and patient survivals. Categorical and continuous variables were evaluated as appropriate.

**Results.** We failed to observe a difference in the immunosuppressant drug protocol, cold ischemia time, or mean recipient or donor age. The prevalence of delayed graft function was 63% among the Belzer arm, and 50% among the Custodiol arm ( $P = NS$ ). The renal function was the same in both arms at 1, 6, and 12 months. The graft survival after 3 months was 94% among the Belzer group (death from sepsis), and 95% among the Custodiol group (nonfunctioning graft). At 1 year, the results were 78% among the Belzer group (4 deaths from cardiovascular or infectious complications and 2 graft losses), and 79% among the Custodiol group (3 deaths, 1 primary nonfunctioning graft, and 1 graft loss;  $P = NS$ ). After 12 months follow-up, patient survival was 84% among the Belzer group, and 86% among the Custodiol group. In the first year, the incidences of biopsy-proven acute rejection episodes were 37% among the Belzer group, and 33% among the Custodiol group.

**Conclusion.** Custodiol solution achieved similar results compared with Belzer solution.

**D**URING ORGAN PRESERVATION for transplantation, the focus is to maintain the cells' biochemical and structural characteristics for graft viability from the time of removal to the time of implantation the recipient.<sup>1</sup> Hypothermia during use of various preservation solutions decreases the metabolic consumption during anaerobic conditions helping to maintain the structural and functional characteristics of the organ. Different preservation solutions with variable compositions have been studied during the last years. In parallel, new immunosuppressant drugs and modified surgical techniques have improved graft and patient survivals.<sup>2,3</sup> We compared the results of deceased donor kidney transplants using the Belzer solution (University of Wisconsin [UW], group 1), the gold standard for solid organ transplantation, and the

Custodiol solution (histidine-tryptophan ketoglutarate [HTK], group 2).

### METHODS

This randomized prospective study evaluated renal graft function in isolated kidney and combined pancreas recipients, using grafts from multiple organ donors. Data were randomized according to the preservation solution used by the hepatic transplant group in

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**Table 1. Results of the 2 Groups, Belzer and Custodiol**

	Belzer	Custodiol
Recipient mean age (y)	43 ± 13	46 ± 14
Donor mean age (y)	46 ± 13.5	43 ± 14.4
Cold ischemia time (h)	19.7 ± 4.87	19.8 ± 5.23
Mean creatinine at 1 month (mg/dL)	2.39 ± 1.12	2.44 ± 1.67
Mean creatinine at 6 months (mg/dL)	1.83 ± 0.77	1.84 ± 0.80
Mean creatinine at 1 year (mg/dL)	1.73 ± 0.60	1.72 ± 0.95
Graft survival at 3 months (%)	94	95
Graft survival at 1 year (%)	78	79
Patient survival at 1 year (%)	84	86
Incidence of delayed graft function (%)	63	50
Incidence of biopsy-proven acute rejection at first year (%)	37	33
Hospitalization more than 14 days (%)*	96.2	70.8

Note: other variables,  $P < .05$ .

\* $P = .021$ .

our institution. From December 2002 to February 2004, we selected 51 patients according to the compatibility criteria supplied by the State Transplant Coordination Center,<sup>4</sup> yielding 42 isolated kidney and 9 combined pancreas and kidney transplant recipients. There were 27 patients in the Belzer group and 24 patients in the Custodiol group. We analyzed the acute tubular necrosis prevalence, defined by the need for 2 or more dialysis sessions during the first week of transplantation. In addition, we examined the rate of biopsy-proven acute rejection episodes, renal function determined by serum creatinine (mg/dL) at 1, 6, and 12 months, length of hospitalization, as well as graft and patient survivals.

## RESULTS

Among 51 evaluated patients, 25 were female, 14 in group 1 and 11 in group 2. There was no difference in immunosuppressant drug protocol, cold ischemia time, as well as mean recipient and donor ages (Table 1). We observed no significant difference in acute tubular necrosis incidence ( $P = .87$ ) or acute rejection incidence ( $P = .52$ ) between the Belzer and the Custodiol groups. Renal function was similar among subjects in both arms at 1, 6, and 12 months. The mean creatinine at 1 year was 1.73 mg/dL among the Belzer arm, and 1.72 mg/dL among the Custodiol arm. The graft survival at 3 months was 94% among the Belzer group (death from sepsis), and 95% among the Custodiol group (nonfunctioning graft). At 1 year it was 78% among the Belzer group (4 deaths from cardiovascular or infectious complications and 2 graft losses), and 79% among the Custodiol group (3 deaths, 1 primary nonfunctioning graft, and 1 graft loss;  $P = NS$ ). After 12 months follow-up, patient survival was 84% among the Belzer group, and 86% among the Custodiol group. Two kidney plus pancreas recipients died; 1 in each group. For the hospitalization time, 96.2% of the Belzer group recipients stayed more than 14 days compared with only 70.8% of the Custodiol group recipients ( $P = .021$ ).

## DISCUSSION

Various preservation solutions have been studied in the last few years, seeking to physiologically improve the cold ischemia process. The Belzer solution has been used safely for a long time compared with Custodiol, a new solution that has shown good results in clinical trials. Even including combined kidney plus pancreas recipients, only renal function was assessed. The acute tubular necrosis prevalence was high in both groups. Cold ischemia periods greater than 24 hours interval separation were not analyzed, but the above percentage was higher than that reported in the literature, possibly due to donor management and the organ retrieval procedures and allocation criteria used in Brazil.<sup>4-8</sup> The acute rejection incidence at 1 year was similar to that in the literature. Renal function was similar during follow-up, and graft survivals were also similar.

We observed only 1 primary nonfunctioning graft (Custodiol group), but considering the number of patients, it was impossible to correlate the Custodiol solution with primary nonfunction. The shorter hospitalization period observed among the Custodiol group could be related to faster surgical recovery. Patient survival was lower than published data, probably because high-risk patients were included, some of whom underwent simultaneous kidney-pancreas transplantation.<sup>5-8</sup> From these results, we concluded that Custodiol was effective for organ preservation, and could be used safely to lower the costs in solid organ preservation for transplantation.<sup>9</sup>

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