Effect of dialyser biocompatibility on recovery from acute renal failure after cadaver renal transplantation

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Abstract

Background. It has been reported that patients with acute renal failure (ARF) requiring haemodialysis show an improved recovery of renal function when the dialysis treatment is performed using a biocompatible membrane rather than a bioincompatible membrane. However, most recent published human trials have not been able to confirm these findings.

Method. Over a 2-year period, we prospectively studied 53 patients with ARF after cadaver renal transplantation who required haemodialysis and randomized them into two treatment groups. One group underwent dialysis with a cuprophane membrane and the other group underwent haemodialysis with a more biocompatible membrane, polysulfone. All patients received an immunosuppressive regimen which included azathioprine, prednisone and cyclosporine.

Results. There was no difference by patient characteristics or immunosuppressive regimen before acute tubular necrosis (ATN) recovery. In both groups the number of haemodialysis sessions required prior to the recovery of renal function (6.57 ± 2.79 vs 6.05 ± 2.40), the number of oliguric days (16.25 ± 5.14 vs 14.40 ± 4.67) and the number of hospital days (33.38 ± 12.85 vs 30.10 ± 11.00), were not statistically different. There was also no difference in long-term allograft outcome.

Conclusion. Our data demonstrate that the use of a more biocompatible membrane had no influence on the recovery from acute renal failure after renal transplantation.

Key words: acute renal failure; biocompatibility; dialyser membrane; haemodialysis; renal recovery; renal transplantation

Introduction

Exposure to less biocompatible cellulosic dialysis membranes has been suggested to adversely affect the course of acute renal failure (ARF) [1–5]. Dialysis membranes have been found to activate a variety of humoral and cellular pro-inflammatory systems [6–9]. These processes are currently referred to as bio(in)compatibility-related problems [10], and these activated systems, in turn, produce or release a variety of inflammatory products which can be injurious to tissues [11]. For several years there has been concern in ARF as to whether these effects contribute to dialysis-related morbidity, and produce new insults to the injured kidney [10,12]. In addition, the slower recovery of renal function in haemodialyzed patients has been attributed to ongoing ischaemic insults to the injured kidneys due to hypotension during the dialytic procedure in the setting of impaired autoregulation of renal blood flow [13,14].

In 1994, two papers reported the results of prospective, randomized trials in which ARF patients received haemodialysis using membranes that had either low or high complement-activating potential [14,15]; the rate of recovery of renal function was more rapid and the mortality rate was less in patients dialysed with more biocompatible membranes. However, most recent published human trials have not been able to confirm these findings [16,17].

ARF after renal transplantation is a clinical example of ischaemic acute tubular necrosis (ATN) where morbidity–mortality factors (infection, sepsisemia, trauma or multi-organ failure) are rarely present, and as such could be used as a good example to analyse the effect of haemodialyser biocompatibility on recovery from ischaemic ARF. The aim of the current report was to verify the influence of dialyser biocompatibility in the outcome of ARF in renal transplant recipients, in a randomized and prospective study.

Material and methods

A cohort of 95 patients with end-stage renal failure on maintenance dialysis who had undergone cadaveric renal transplantation were prospectively studied over a 24-month period (from February 1995 to February 1997). Of these, 53 patients required supportive haemodialysis in the immediate
post-operative setting. The main criteria for initiating dialysis were fluid overload, hyperkalaemia and uraemia in anuric or oliguric patients. Once a decision had been made to initiate haemodialysis, the patients were randomized to receive supportive haemodialysis with either a bioincompatible membrane (cuprophone, CU) or a biocompatible membrane (polysulfone, PS). We used a polysulfone dialyser (Fresenius F6; Fresenius, Germany) as the biocompatible membrane and a cuprophane (Asahi AM-65H, Asahi Medical, Japan) as the bioincompatible membrane. The two membranes have low flux hollow-fiber and similar clearance and ultrafiltration characteristics, with an ultrafiltration coefficient under 6 ml/mmHg/h. The membranes were not reused. All treatments were performed using a volumetric-control dialysis machine (Fresenius A2008E, Fresenius, Germany), and water treated by reverse osmosis (non-filtered bicarbonate-based dialysate with less than 200 CFU/ml and endotoxin content <5EU/ml, in monthly analysis, as a part of the routine dialysis programme throughout the study).

Heparin was given as a systemic anticoagulant in all cases, except in patients at a high risk of bleeding [18]. All patients received 2.5–4.0 l of dialysis every other day or if required on clinical grounds. Blood-pump speed was set to ≥300 ml/min and dialysate to 500 ml/min. Informed consent was obtained from the patients. Transplant recipients received standard immunosuppressive protocol at our institution [19]: this consisted of azathioprine, prednisone and cyclosporine as maintenance therapy from the transplantation day onwards. Patients were followed for the length of time taken to recover allograft function (sustained urine output >1.2 l/day and a spontaneous fall in serum creatinine level).

Continuous variables are reported as the mean ± SD. Statistical analysis was performed using Student’s unpaired t-test, Fisher’s exact test and Kaplan–Meier analysis of the percentage of patients with recovery of renal function, as appropriate. Statistical significance was assumed at P<0.05.

Results

Fifty-three of the 95 patients required haemodialysis after renal transplantation. Nine patients were excluded from this study due to biopsy-confirmed acute vascular rejection (three patients), primary nonfunction (one patient), vascular thrombosis (two patients) and death prior to recovery from ARF (three patients; two were receiving conventional haemodialysis). These exclusions left 44 patients with ARF after renal transplantation for final analysis. Cellulosic membranes were used in 24 patients and more biocompatible polysulfone membranes for 20 patients. The main demographic characteristics of these subjects are shown in Table 1. The cuprophane group was older than polysulfone group (44.8 ± 11.0 vs 34.8 ± 10.9 years; P = 0.005). There were no significant differences between the two groups in terms of gender, time on dialysis before transplantation, retransplanted patients, panel-reactive antibodies, cold ischemia time and perfusion solution.

The immunosuppression regime after renal transplantation and before ATN recovery is shown in Table 2. There was no significant difference in mean patients’ weight, mean immunosuppressive drugs and mean cyclosporine blood level between cuprophane group and polysulfone group. With regard to the haemodialysis treatment and recovery from ATN, the two groups were not statistically different (Table 3); the number of oliguric/anuric patients (80% vs 75%), the postoperative day at which the first haemodialysis session was performed, the number of haemodialysis sessions required prior to the recovery of renal function (6.67 ± 2.79 vs 6.05 ± 2.40), the number of oliguric days (16.25 ± 5.14 vs 14.40 ± 4.57) and the number of hospital days (33.38 ± 12.85 vs 30.10 ± 11.00) in each of

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<th>Table 2. Immunosuppressive regimen before acute renal failure recovery</th>
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<td>Patient weight (kg)</td>
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<th>Table 3. Haemodialysis treatment and recovery from acute tubular necrosis</th>
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<td>Oliguric/anuric patients – n (%)</td>
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<td>First dialysis session (PO day)</td>
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<td>No. of dialysis treatments (mean)</td>
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HD, haemodialysis.
the two groups of patients were similar. There was also no difference in long-term allograft outcome, and in cumulative percent of patients with recovery from acute renal failure along post-transplant days (Figure 1).

**Discussion**

Very recently, two reports and one abstract stressed an animated debate, so far unresolved, within the nephrological community [15,20]. The authors reported on the identification of one factor to account for morbidity/mortality in patients dialysed for acute renal failure, namely the biocompatibility of dialysis membranes. Among patients with ARF requiring haemodialysis, the use of a biocompatible membrane (polymethylmethacrylate, PMMA and polyacrylonitrile, PAN), as compared with the cuprophane membrane, resulted in an improved recovery of renal function, and had a higher rate of patient survival. In addition, patients treated with biocompatible membranes were reported as suffering a significantly lower incidence of bacterial infections, as well as a lower relative and absolute mortality rate due to sepsis [16,18]. Furthermore, most recent trials, including patients in ICU and cadaveric renal transplant recipients, have not been able to confirm these findings [17,21,22].

Our results demonstrate that the use of a more biocompatible membrane had no influence on the course of ARF (post-operative ischaemic acute tubular necrosis) in patients receiving a cadaveric renal transplant requiring supportive haemodialysis in the immediate post-transplant setting. In addition, the mean dialytic time after transplantation, and the number of dialysis treatments needed before recovery of renal function occurred was not influenced by the membrane applied. Our data are therefore in contrast to the earlier publications [14,15,20]; they reported that the application of a biocompatible membrane significantly reduced the number of dialysis sessions necessary to regain renal function in patients with ARF in intensive care units. However, the results reported in our patients are in agreement with Kurtal et al. [16] and Gastaldello et al. [17] (in ICU patients), and Valeri et al. (with renal transplant recipients) [21,22]. Kurtal et al. analysed 57 patients with ARF in an ICU requiring haemodialysis [16]: patients were divided into two groups according to the dialysate membrane used, (polyamide or cuprophane), and the study did not find any difference between membranes with regard to survival, the number of dialysis sessions and general morbidity.

Gastaldello et al. [17] designed a trial to evaluate the use of an incompatible membrane (cuprophane), a biocompatible low-flux membrane (polysulfone) and a more biocompatible high-flux membrane (polysulfone) in patients with ARF; the recovery of renal function and survival rate did not differ significantly between the three groups. Valeri performed a 2-year randomized study to analyse the effects of dialysis membrane type in 30 patients who suffered ARF post cadaveric renal transplant [21]. No differences were found between the 16 patients dialysed with cuprophane membranes and the 14 patients dialysed with PMMA dialysers with regard to the mean time before recovery from ARF (9.1 days vs 8.8 days, \(P=n.s.\)) or the mean number of dialysis sessions required (3.7 vs 3.4, \(P=n.s.\)). Moreover, no difference was reported between the two groups of patients concerning the long-term outcome of the allograft in terms of nadir serum creatinine concentration, number of episodes of acute rejection or number of cases with rejection. Recently, the same group has also reported similar results in 53 patients randomized to cuprophane, Hemophan (a membrane of intermediate biocompatibility) or PMMA hollow-fibre dialysers [22].

It is, of course, a difficult task to put forward any explanations for the different results of these studies. Important questions refer to stratifying patients by the severity of illness, the faster recovery of renal function in ARF after renal transplantation, which is of shorter duration than the average recovery time reported in other ARF trials, the small number of oliguric cases among ARF in renal transplant recipients, the effect of immunossuppressive drugs which could attenuate some of the end organ inflammatory effects of complement and leukocyte activation on the injured kidneys, and the systemic toxic deleterious effect of bioincompatible membranes on other injured target organs as lung, heart and immune system, in critically ill patients with multi-organ failure [22]. Therefore, further studies are necessary to clearly determine the relationship between biocompatibility issues and the course of ARF.

In conclusion, our data refute the hypothesis that exposure to cellulosic dialysis membranes of poor biocompatibility has a detrimental effect on the course

**Fig. 1.** Cumulative percent of patients with recovery from ATN vs post-transplant days (PS = polysulfone vs CF = cuprophane).
of ischaemic acute renal failure after renal transplantation.

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