Effect of Pretransplant Hemoglobin Blood Level on Kidney Transplant Outcome

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Abstract

Objectives: We investigated the effect of pretransplant hemoglobin level on the outcome of kidney transplant.

Patients and Methods: Patients were divided in 2 groups: group A < 10 g/dL (80 patients; PTHb < 10 g/dL), and group B > 10 g/dL (69 patients; PTHb ≥ 10 g/dL), and were matched regarding donor age, recipient sex, blood group, donor-recipient HLA, and Cytomegalovirus status.

Results: The frequency of acute rejection, together with the timing of rejection, treated antithymocyte globulin Fresenius rescue therapy, infection rate, and posttransplant surgical complications were comparable between both groups. While the 1-year actuarial patient and graft survival rates, delayed graft function, and slow graft function rates were comparable between both groups, longer hospital stay was required for group B (> 10 g/dL) patients (P = .005). Mean serum creatinine levels upon discharge (P = .02), at 6 months (P = .005), and 1 year (P = .02) after discharge were higher in group B (> 10 g/dL) patients. While posttransplant hemoglobin levels were lower than pretreatment levels, they were higher in group B (> 10 g/dL) compared with group A (< 10 g/dL), (P = .019).

Conclusions: Pretransplant hemoglobin level does not affect the outcome of kidney transplant, except for creatinine levels at 1 year.

Key words: Renal transplant, Transplant rejection

Introduction

Anemia is a potentially reversible cardiovascular risk factor, and a frequent complication of chronic renal disease, and renal transplant recipients (1, 2). It is reportedly caused by several factors including deficiency, gastrointestinal blood loss, immunosuppressive medications, and less frequently, by disorders such as hemolytic uremic syndrome or aplastic anemia (3). The prevalence of anemia in transplant recipients is high, especially during the early posttransplant period (4, 5), with rates of up to 40% being reported in some studies, which may increase with advanced kidney disease. Accordingly, a positive correlation between hemoglobin concentration and graft function (creatinine clearance) has been suggested (4), and appears to be associated with the extent of impaired renal function (5, 6) and also, with the immunosuppressive treatment including the anti-metabolites azathioprine, and mycophenolate mofetil (3, 4, 7).

While anemia represents an important posttransplant cardiovascular risk factor (3), its management after renal transplant has not been investigated well. Corrective measures should be undertaken when hemoglobin fails to normalize (less than 11 g/dL in premenopausal females, or less than 12 g/dL in males and postmenopausal females) by 3 months posttransplant (7). The aim of this study was to assess the usefulness of correcting anemia by reaching pretransplant hemoglobin blood (PTHb) levels of 10.0 or above (using erythropoietin or packed red blood cell transfusions) before the transplant, and to determine if this will result in better transplant outcomes.
Subjects and Methods

Patient demographics: Patients were divided into group A (n=80) with normal hemoglobin (< 10 g/dL) and group B (n=69) with high hemoglobin (≥ 10 g/dL). Recipients’ mean ages were 42.1 ± 3.3 years vs 36.1 ± 2.6 years (P = .006), donor sex (M:F) distribution was 52:17 vs 48:32; (P = .029), and donor-recipient relation (P < .001) were significantly different between group B (≥ 10 g/dL) and group A (< 10 g/dL), respectively. HLA matching, donor age, number of sensitized patients, and Cytomegalovirus (CMV) status were similar between group A (< 10 g/dL) and group B (≥ 10 g/dL) (P=NS). Indications for kidney transplant in group A (< 10 g/dL) and group B (≥ 10 g/dL) included chronic glomerulonephritis (7 vs 13), polycystic kidney disease (4 vs 6), chronic pyelonephritis (9 vs 7), interstitial nephritis (2 vs 3), arterial hypertension (3 vs 4), and others. The duration of pretransplant dialysis was 8.9 ± 2.9 months and 16.0 ± 3.8 months with pre-emptive dialysis done for 13 and 9 patients in group A (< 10 g/dL) and group B (≥ 10 g/dL), respectively. Higher pretransplant (11.48 ± 0.28 g/dL vs 7.95 ± 0.29 g/dL) (P = .005), posttransplant hemoglobin blood level (7.75 ± 0.45 g/dL vs 7.14 ± 0.34 g/dL) (P = .019), and hemoglobin blood level difference (3.8 ± 0.37 vs 1.2 ± 0.27) (P = .005) were seen in group B (≥ 10 g/dL) versus group A (< 10 g/dL) patients. Packed red blood cell transfusions were administered to 21 patients in group A (< 10 g/dL), and to 12 patients in group B (≥ 10 g/dL) after kidney transplant (P=NS) when the posttransplant hemoglobin levels dropped to below 5.0, or when symptoms had occurred.

Immunosuppressive regimen: Induction therapy was instituted for 31 patients (38.8%) in group A (< 10 g/dL) and for 54 patients (78.3%) in group B (≥ 10 g/dL) (P < .001). This consisted of daclizumab (13/31 vs 15/54) administered as 2 dosages (3 and 2) or 1 dose (10 and 13), or as an intraoperative bolus of antithymocyte globulin Fresenius (ATG-F; 18/31 vs 39/54) given as bolus (15 and 24) or extended regimen (3 and 15) in group A (< 10 g/dL) and group B (≥ 10 g/dL). Maintenance immunosuppression comprised of triple therapy in which cyclosporine (cyclosporine [N] or FK506 [F]) was combined with an antimetabolite (mycophenolate mofetil [C] or azathioprine [A]) and prednisolone [P]). These consisted of FCP (31 and 24), FAP (1 and 0), NCP (41 and 40), and NAP (7 and 5) given to group A (< 10 g/dL) and group B (≥ 10 g/dL) patients (P=NS).

Results

Main transplant outcomes: The main outcomes are summarized in Table 1. Acute rejection (AR) occurred in 12 patients in group A (< 10 g/dL) (15.0%) and in 15 patients in group B (≥ 10 g/dL) (21.7%) (P=NS). In addition, the timing of rejection, and the need for ATG-F rescue therapy were comparable between both groups. Hospital stay rate was similar between the 2 groups. Complications of 28 infectious episodes in 23 patients in group B (≥ 10 g/dL) as compared to 28 infectious episodes in 22 patients in group A (< 10 g/dL), each comprised bacterial (18 vs 22), viral (6 vs 5), and fungal (2 vs 2) infections in group A (< 10 g/dL) vs group B (≥ 10 g/dL) patients. The 1-year actuarial patient (96.3% vs 95.7%) and graft (96.3% vs 94.3%) survival rates, together with delayed graft function (DGF; 2.5% vs 5.8%) and slow graft function (SGF; 5.0% vs 8.7%) rates were comparable between both groups. Longer hospital stays were recorded for group B (≥ 10 g/dL) than group A (< 10 g/dL) patients (12.55 ± 1.39 vs 9.01 ± 0.69 days) (P = .005).

Biochemical profile: Mean serum creatinine levels upon discharge (1.61 ± 0.10 vs 1.37 ± 0.12 mg/dL) (P = .02), at 6 months (1.37 ± 0.10 vs 1.26 ± 0.06 mg/dL) (P = .05), and 1 year (1.29 ± 0.07 vs 1.18 ± 0.06 mg/dL) (P = .02), but not at

Table 1. Main outcomes.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Category</th>
<th>Group A hemoglobin &lt; 10 g/dL</th>
<th>Group B hemoglobin ≥ 10 g/dL</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survival</td>
<td>Patient</td>
<td>96.3%</td>
<td>94.3%</td>
<td>NS</td>
</tr>
<tr>
<td>(1 y)</td>
<td>Graft</td>
<td>96.3%</td>
<td>95.7%</td>
<td>NS</td>
</tr>
<tr>
<td>Graft function</td>
<td>Slow</td>
<td>4/80</td>
<td>4/69</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Delayed</td>
<td>2/80</td>
<td>4/69</td>
<td>NS</td>
</tr>
<tr>
<td>Acute rejection</td>
<td>Incidence</td>
<td>12/80</td>
<td>15/69</td>
<td>NS</td>
</tr>
<tr>
<td>Timing (d)</td>
<td>3±28</td>
<td>3±11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospital stay (days)</td>
<td></td>
<td>9.01 ± 0.69</td>
<td>12.55 ± 1.39</td>
<td>.005</td>
</tr>
<tr>
<td>Infection episodes</td>
<td>Patients</td>
<td>22 (30)</td>
<td>23 (28)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bacterial</td>
<td>18 (60.0%)</td>
<td>22 (78.5%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Viral</td>
<td>10 (33.3%)</td>
<td>4 (14.5%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fungal</td>
<td>2 (6.7%)</td>
<td>2 (7.0%)</td>
<td></td>
</tr>
</tbody>
</table>

1Two-tailed t test for continuous variables; Fisher exact test for categoric variables.
2Percentage of total number of episodes.
3Abbreviations: NS, not significant.
1 month (1.44 ± 0.10 vs 1.39 ± 0.08 mg/dL) (P = NS), or 3 months (1.38 ± 0.10 vs 1.36 ± 0.09 mg/dL) (P = NS), were significantly higher in group B (> 10 g/dL) vs group A (< 10 g/dL) patients (Table 2). While posttransplant hemoglobin levels were lower in group A (< 10 g/dL) (7.14 ± 0.34 vs 7.95 ± 0.29 g/dL) and in group B (> 10 g/dL) (7.75 ± 0.45 vs 11.48 ± 0.28 g/dL) compared with pretransplant levels, they were still significantly higher in group B (> 10 g/dL) compared to group A (< 10 g/dL) patients (P = .019) (Table 2). Posttransplant surgical complications comprising ureteral stenosis (2 vs 0), bleeding (1 vs 0), renal artery stenosis (1 vs 3), and septic shock (1 vs 0) were comparable between the 2 groups.

Table 2. Biochemical profile.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Category</th>
<th>Group A hemoglobin &lt; 10</th>
<th>Group B hemoglobin ≥ 10</th>
<th>P1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin levels</td>
<td>Pretransplant</td>
<td>7.95 ± 0.29</td>
<td>11.48 ± 0.28</td>
<td>.005</td>
</tr>
<tr>
<td></td>
<td>Posttransplant</td>
<td>7.14 ± 0.34</td>
<td>7.75 ± 0.45</td>
<td>.019</td>
</tr>
<tr>
<td>Posttransplant transfusion</td>
<td></td>
<td>21 (0.45 ± 0.06)</td>
<td>20 (0.46 ± 0.07)</td>
<td>NS</td>
</tr>
</tbody>
</table>

1:2-tailed t test
2:Concentration in mg/dL
3:Concentration in g/dL

Discussion

Pretransplant hemoglobin level has no effect on the outcomes of the kidney transplant, except for the mortality rate noted at 1 year. Previous studies have shown hematologic adverse events, including an increase in hemoglobin levels, demonstrated dynamic changes in hemoglobin levels following kidney transplantation. Significant, negative correlations were noted between decreases in hemoglobin levels before and after conversion from 1 immuno-suppressive agent to another (3, 4, 7), and increased hemoglobin was associated with increasing dialysis duration (8). Others suggested that physiologic hemoglobin may be advantageous for hemodialysis patients, as evidenced by progressive improvement in echocardiographic parameters upon hemoglobin normalization, with a special reference to hypertension, which was not aggravated at higher target hemoglobin (9).

Our study confirms that graft and patient survival are independent of pretransplant hemoglobin levels. This is in agreement with some (10), but not other studies (11), which demonstrate that maintaining hemoglobin between 11 g/dL and 12 g/dL (and hematocrit between 33% and 36%) before kidney transplant does not have any significant impact on graft or patient survival after kidney transplant. In addition, delayed graft function and slow graft function were not different between groups A (< 10 g/dL) and B (> 10 g/dL) (which is reminiscent of a previous study, which noted a similar rate of delayed graft function among patients with different pretransplant hemoglobin levels (12). The exact mechanisms underlying the effect of PTHb levels in transplant patients remains to be determined, as was previously suggested to involve interaction with (inhibition of) angiotensin-I-converting enzyme. While this remains to be seen, other studies argued against (eg, a possibility of angiotensin-converting enzyme inhibitor therapy on maintaining hemoglobin levels) among kidney transplant patients with normal hemoglobin levels (12). Continued follow-up is needed to evaluate its effect on the long term.

References


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