Perioperative Erythropoietin Efficacy in Renal Transplantation


ABSTRACT

Background. There is no consensus on the usage of erythropoietin in the immediate postoperative period to prevent anemia and delayed graft function.

Methods. A retrospective case note audit of renal transplants included hemoglobin (Hb) and serum creatinine (Scr) values preoperatively as well as at days 7, 14, 30, 60, and 90. Patients were categorized as those receiving erythropoietin during the first 6 months posttransplant (Epo+ve) and those not receiving any erythropoietin (Epo-ve).

Results. Hb decreased from 12.4 ± 1.6 g/L preoperatively to 9.5 ± 1.5 g/L at day 14 and then rose to 10.5 ± 1.6 g/L at 1 month and 12.4 ± 1.7 g/L at 3 months. There was no difference in absolute Hb values in three transplant groups. Scr decreased from 597.0 ± 200.1 mmol/L preoperatively to 254.1 ± 196.9 mmol/L at day 14 and continued to fall to 163.8 ± 98.9 mmol/L at 1 month and 147.8 ± 66.9 mmol/L at 3 months. There was no difference in absolute Hb values and delayed graft function in the three transplant groups.

Conclusion. With respect to anemia and delayed graft function, the use of erythropoietin in the first 3 months had little impact. We suggest that such an expensive medication may be safely omitted in the immediate postoperative period.

Renal anemia may be corrected by the administration of recombinant erythropoietin (RhuEPO). There is no consensus on the usage of erythropoietin in the immediate posttransplant period to prevent anemia or to reduce the length of delayed graft function (DGF). In this environment of acute rejection, heavy immunosuppression, infection, hyperparathyroidism, blood loss from regular phlebotomy, iron deficiency, increased cardiovascular risk, and fluid overload, the efficacy of erythropoietin may be suspect.

Evidence from animal models using RhuEPO have shown a faster correction of ischemic acute tubular necrosis. Correction of anemia may also improve tissue perfusion and cellular hypoxia in the immediate posttransplant period. Therefore, a fast correction of anemia might be useful. In addition, this hypothesis raises the possibility that RhuEPO may positively influence the length of DGF after transplantation. Our aim was to investigate the influence of RhuEPO on the length of DGF and anemia correction post–renal transplant.

METHODS

A retrospective case note audit of renal transplants included hemoglobin (Hb) and serum creatinine preoperatively as well as at days 1, 7, 14, 30, 60, and 90. DGF was defined as any renal transplant patient requiring hemodialysis (HD) on more than one occasion postoperatively; patients requiring HD for isolated hyperkalemia were excluded. Three different transplant types were compared: living donor (LD), heart-beating donor (HBD), and non–heart-beating donor (NHBD). Patients were categorized into those receiving erythropoietin during the first 6 months posttransplant (Epo+ve) and those not receiving any erythropoietin (Epo-ve). All patients received RhuEPO prior to transplantation. There was no conscious effort to influence the prescribing of RhuEPO for any particular group of patients or clinical effect once patients were transplanted. The decision to continue or stop RhuEPO was left to the transplant teams discretion; however, those patients on RhuEPO continued on this therapy for at least 6 months or more. We also evaluated the length of DGF in the above groups.

Those patients on RhuEPO were kept on the same maintenance dose as prior to the transplant. The immunosuppressive regimen consisted of induction intravenous methylprednisolone 500 mg...
followed by maintenance azathioprine (1.5 mg/kg), calcineurin inhibitor, and prednisolone (20 mg). All statistical analyses were performed with SPSS11.1 for Windows (SPSS Inc, Chicago, Ill, USA). Continuous variables were compared using Student \( t \) test.

The baseline characteristics of the enrolled patients are shown in Table 1.

**RESULTS**

From December 2001 to July 2004, 207 case notes were analyzed including a mean overall age \( \pm \) SD of 49 years \( \pm \) 14 and a male:female ratio of 120:87. Twenty-five case notes were not analyzed due to incomplete data, or the patient died with a functioning transplant, or underwent a transplant nephrectomy. The Hb decreased from 12.4 \( \pm \) 1.6 g/L preoperatively to 9.5 \( \pm \) 1.5 g/L at day 14 and then started to rise to 10.5 \( \pm \) 1.6 g/L at 1 month and at 3 months had reached 12.4 \( \pm \) 1.7 g/L.

There was no difference in absolute Hb values in the three transplant groups (Fig 1). Serum creatinine (Scr) decreased from 597.0 \( \pm \) 200.1 mmol/L preoperatively to 254.1 \( \pm \) 196.9 mmol/L at day 14 and continued to fall to 163.8 \( \pm \) 98.9 mmol/L at 1 month and at 3 months had decreased to 147.8 \( \pm \) 66.9 mmol/L (Fig 2). The mean DGF was 4.0 \( \pm \) 5.9 (mean \( \pm \) SD) days. As expected the LD showed the lowest DGF rate at 0.6 \( \pm \) 2.3 days, which was significantly different compared to the total (\( P = .0003 \)) group and also the HBD group (4.3 \( \pm \) 5.7 vs 0.6 \( \pm \) 2.3, \( P < .0001 \)) and NHBD group (5.9 \( \pm \) 6.0 vs 0.6 \( \pm \) 2.3, \( P < .0001 \); Table 1). There was no significant difference in DGF between the subgroups with and without the maintenance administration of RhuEPO. There was no significant change in parathyroid hormone or ferritin levels from prior to transplantation to 6 months posttransplantation in the groups.

**DISCUSSION**

This retrospective study revealed no difference in the levels of anemia and DGF in the presence or absence of RhuEPO use in the immediate postoperative period. Hemaglobin seemed to follow the rule of threes: on average the Hb, dropped by 3 g postoperatively and returned to the preoperative level by 3 months. Administration of RhuEPO had no influence on DGF in each group (HBD, LD, NHBD).

All groups had equal number of hemodialysis and peritoneal dialysis (PD) patients, thus negating any protective effect of PD on DGF.\(^4\) Also, historically the biggest influence on DGF rates has been the length of cold ischemic time. Cold ischemic times have gradually become shorter and therefore we would expect RhuEPO to have little or no further impact on reducing DGF rates.\(^5\)

In the immediate postoperative period we suggest that it may make economic sense that RhuEPO is discontinued, as its efficacy is severely reduced in this environment of acute rejection, heavy immunosuppression, infection, hyperparathyroidism, blood loss from regular phlebotomy, iron deficiency, and fluid overload. Further randomized prospective

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**Table 1. DGF in Different Transplant Groups With and Without Erythropoietin**

<table>
<thead>
<tr>
<th></th>
<th>Median (range/d)</th>
<th>( P ) Value, Epo-ve vs Epo+ve</th>
</tr>
</thead>
<tbody>
<tr>
<td>T/Epo+</td>
<td>1.0 (0–28)</td>
<td>&gt;.05</td>
</tr>
<tr>
<td>T/Epo−</td>
<td>0.0 (0–23)</td>
<td></td>
</tr>
<tr>
<td>LD/Epo+</td>
<td>0.0 (0–28)</td>
<td>&gt;.05</td>
</tr>
<tr>
<td>LD/Epo−</td>
<td>0.0 (0–20)</td>
<td></td>
</tr>
<tr>
<td>NHBD/Epo+</td>
<td>4.5 (0–12)</td>
<td>&gt;.05</td>
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<tr>
<td>NHBD/Epo−</td>
<td>5.0 (0–23)</td>
<td></td>
</tr>
<tr>
<td>HBD/Epo+</td>
<td>2.0 (0–21)</td>
<td>&gt;.05</td>
</tr>
<tr>
<td>HBD/Epo−</td>
<td>1.0 (0–16)</td>
<td></td>
</tr>
</tbody>
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Fig 1. Hb versus time post-transplant in all groups.
studies will be needed to provide corroborating evidence for our findings.

REFERENCES