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Post-transplant haemoglobin levels and host kidney status

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Abstract. Erythrocytosis after renal transplantation has been ascribed to inappropriate production of erythropoietin by the recipient's native kidneys. In a retrospective analysis we examined the effect of pre-transplant bilateral nephrectomy on post-transplant haemoglobin level (Hb) and haematocrit (Ht) in 370 renal transplant patients. Hb and Ht were significantly higher in the 341 patients with host kidneys in situ compared with the 29 patients who had undergone bilateral nephrectomy (Hb, 8.5 ± 1.2 mmol/l vs 7.8 ± 1.3 mmol/l, $P = 0.005$; Ht, $41 \pm 6\%$ vs $38 \pm 7\%$, $P = 0.02$). Moreover, a very high Hb and/or Ht (defined as a value above the 80th percentile of the whole group) occurred more frequently in patients with host kidneys in situ (20.5 % vs 3.5 %, $P = 0.02$). It thus appears that host kidneys significantly contribute to the unexpectedly high haemoglobin levels occurring after renal transplantation.

Key words: Erythrocytosis – Renal transplantation – Nephrectomy

Erythrocytosis is a well-recognized phenomenon in renal transplant recipients. The incidence has been reported to be 6–17 % [3, 7, 10], the condition probably being more common in cyclosporine-treated patients than in those treated with azathioprine [5, 8]. Several pathophysiological mechanisms have been proposed, including inappropriate production of erythropoietin (EPO) by the recipient's native kidneys [1, 3, 9]. We investigated retrospectively the effect of pre-transplant bilateral nephrectomy on post-transplant haemoglobin level and haematocrit in a large group of renal transplant patients.

Methods

The study population consisted of all adult patients who had undergone a renal transplantation in our centre from 1 to 10 years previously, and who currently had a functioning graft. Patients with polycystic kidney disease, an established cause of erythrocytosis, were excluded. Long-term immunosuppression consisted mostly of azathioprine and prednisone, but a minority of the patients received cyclosporine, usually in combination with prednisone.

The following data were obtained for each patient: sex, age, haemoglobin level (Hb), haematocrit (Ht), serum creatinine concentration, time after transplantation, use of cyclosporine, systolic and diastolic blood pressure, and current number of antihypertensive drugs. The last recorded Hb and Ht were used for analysis. If one or more therapeutic phlebotomies had been performed, the last recorded Hb and Ht preceding the start of phlebotomies were taken. For definition of a very high Hb and/or Ht we arbitrarily chose a limit at the sexspecific 80th percentile (P_{80}) of the whole group.

Statistical analysis was performed with Wilcoxon's test for unpaired data and the chi-squared test where appropriate. A P value smaller than 0.05 was considered statistically significant.

Results

Of the 370 patients who fulfilled the inclusion criteria, 29 had undergone bilateral nephrectomy (BN) for various reasons, and 341 had one or both host kidneys still in situ (HK). The values of the assessed parameters in both groups are summarized in Table 1. Since the use of antihypertensive medication differed significantly in both groups, we reanalysed the data after exclusion of 209 patients who used any kind of antihypertensive drug. Again, both groups did not differ significantly with respect to sex, age, serum creatinine, blood pressure, time after transplantation, and use of cyclosporine (data not shown). Hb, Ht and number of patients with Hb and/or Ht above the P_{80} in this subgroup are given in Table 2.

Discussion

The results clearly show that Hb and Ht were higher in renal transplant patients with host kidneys in situ than in patients who had undergone bilateral nephrectomy before transplantation. In addition, a very high Hb and/or Ht occurred more frequently in HK group.

Since diuretic therapy for hypertension has been associated with higher Hb and Ht levels [6, 7], and patients in

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Table 1. Data of patients in the BN (bilateral nephrectomy) and HK (host kidneys in situ) groups

	BN ($n = 29$)	HK ($n = 341$)	P
Males/females	17/12	207/134	NS
Age (years)[a]	42 ± 12	46 ± 13	NS
Time after transplantation (years)[a]	4.8 ± 3.1	4.3 ± 2.6	NS
Serum creatinine (μmol/l)[a]	110 ± 35	129 ± 59	NS
Use of cyclosporine (%)	14	19	NS
Systolic BP (mm Hg)[a]	138 ± 21	144 ± 22	NS
Diastolic BP (mm Hg)[a]	83 ± 10	85 ± 10	NS
Number of antihypertensive drugs[a]	0.4 ± 0.8	1.0 ± 1.1	0.004
Hb (mmol/l)[a]	7.8 ± 1.3	8.5 ± 1.2	0.005
Ht (%)[a]	38 ± 7	41 ± 6	0.02
Hb and/or Ht above P_{80}[b] (%)	3.5	20.5	0.025

[a] Data shown as mean ± SD.
[b] For males Hb > 9.5 mmol/l, Ht > 46%; for females Hb > 8.9 mmol/l, Ht > 45%.

Table 2. Data of patients in the BN (bilateral nephrectomy) and HK (host kidneys in situ) groups after exclusion of patients using antihypertensive medication

	BN ($n = 18$)	HK ($n = 143$)	P
Hb (mmol/l)[a]	8.0 ± 0.9	8.5 ± 1.1	NS
Ht (%)[a]	39 ± 4	41 ± 5	NS
Hb and/or Ht above P_{80}[b] (%)	5.6	27.6	0.05

[a] Data shown as mean ± SD.
[b] For males Hb > 9.4 mmol/l, Ht > 45%; for females Hb > 9.0 mmol/l, Ht > 44%.

the HK group used more antihypertensive drugs, we reanalysed the data after exclusion of all patients who used antihypertensive medication. Although the numbers probably were too small to reach statistical significance for all differences, a trend in the same direction was apparent. Somewhat unexpectedly, no fall in mean Hb and Ht levels was observed after exclusion of patients using antihypertensive medication. It should be stressed however, that the structure of our database did not allow selective exclusion of patients using diuretics instead of all patients using antihypertensive drugs. Other factors that might affect the incidence of post-transplant erythrocytosis were equally distributed between the BN and HK groups.

Our data suggest that host kidneys significantly contribute to the unexpectedly high haemoglobin levels that can occur after renal transplantation. In accordance with our findings, Pollak et al. demonstrated a lower prevalence of bilateral nephrectomy in patients with post-transplant erythrocytosis compared with a control population [7]. It has been postulated that the host kidneys exert their effect on haemoglobin level by inappropriate EPO production. Indeed, selective venous catheterization of transplanted and native kidneys in patients with post-transplant erythrocytosis, revealed that the native kidneys were responsible for the elevated systemic EPO levels occurring in this setting [1, 3, 9].

Because erythrocytosis is associated with an increased risk of thromboembolic events [10], treatment is generally advocated. In addition to repeated phlebotomies, administration of theophylline has recently been shown to be useful by reducing serum EPO levels [2]. Finally, the experience of normalization of haemoglobin levels after bilateral native nephrectomy in 20 out of 22 patients with post-transplant erythrocytosis [4], forms additional evidence for the pathogenetic role of EPO from the host kidneys in this condition.

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