Hydroxyurea, Sickle Cell Disease and Renal Transplantation

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Dear Sir,

The use of hydroxyurea to increase HbF production in patients with homozygous sickle cell disease is increasing, particularly after recent publication of data demonstrating a significant reduction in painful crises [1]. We here describe the successful use of hydroxyurea in a sickle cell patient with severe painful crises occurring after renal transplantation and an associated rise in haematocrit.

A 26-year-old Jamaican with homozygous sickle cell disease had a stable haemoglobin of 8-9 g/dl and painful crises once every 3 years. He developed proteinuria and renal impairment, and renal biopsy demonstrated mesangiocapillary glomerulonephritis. Renal function slowly declined with a parallel fall in haematocrit and he commenced haemodialysis in early 1994. At this point his haemoglobin was 4 g/dl but he failed to respond to subcutaneous erythro-poietin despite doses of up to 600 U/kg/week – higher doses were not tolerated because of pain on injection and the usual causes of erythropoietin resistance were excluded.

In December 1994 he received a cadaveric renal allograft after a 4-unit exchange transfusion, with standard triple immuno-suppression (cyclosporin 8 mg/kg b.d. initially, prednisolone 20 mg and azathioprine 1 mg/kg). Three further units of packed red blood cells were given peri-operatively. Cre-atinine fell to 159 µmol/l (1.8 mg/dl) and haemoglobin rose to 11 g/dl with HbS > 80% once the transfused blood had gone. The ele-

120-1

¾ 100

300 400

Time (days)

Fig. 1. Haemoglobin concentration and globin fractions in relation to renal transplantation and hydroxyurea therapy.

Renal transplantation in homozygous sickle cell patients with end-stage renal disease is well described with good graft and patient survival rates [2, 3]. The usual rise in haematocrit, seen when the graft functions well, is sometimes associated with the development of painful crises, ascribed to the concurrent rise in plasma viscosity [4, 5]. Previously these crises have been managed with analgesia and venesection or exchange trans-

vated haemoglobin heralded the onset of severe painful sickle crises requiring prolonged hospital admission for analgesia and venesection. Three months after transplantation he commenced hydroxyurea 500 mg b.d. (17 mg/kg/day) with rapid and complete cessation of painful episodes. Haemoglobin has fallen to around 10 g/dl and the hydroxyurea dose has been titrated to maintain this level and to allow for mild leucopenia.

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fusion to reduce viscosity or sickle percentage, respectively. This is the first description of hydroxyurea being used to control painful crises following renal transplantation and has resulted in both increased HbF production to nearly 20% and reduced haematocrit with excellent clinical response (fig. 1). Severe myelotoxicity has not occurred, but long-term hydroxyurea use in conjunction with transplant immunosuppression might be undesirable in view of possible increased carcinogenicity.

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