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LETTER TO THE EDITORS

Severe anemia caused by the angiotensin receptor blocker irbesartan after renal transplantation

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Renal transplant recipients are often anemic in the early post-engraftment period because of preexisting anemia exacerbated by perioperative blood loss [1]. Six or more months after transplantation, anemia is slightly less common, and mostly occurs in the setting of chronic allograft nephropathy associated with reduced glomerular filtration rate [1]. We report the first pediatric case of anemia after renal transplantation caused by the use of irbesartan, a drug that inhibits the renin-angiotensin II-aldosterone system by blocking the type 1 of angiotensin II receptors [2–5].

A 12-year-old boy with a history of congenital nephrotic syndrome of the Finnish type and poor renal function (GFR estimated 25 ml/min/1.73 m^2, urinary protein/creatinine ratio 48 mg/mmol) 7 years after a cadaveric transplantation was on treatment with the immunosuppressants mycophenolate and sirolimus. This rather unusual immunosuppressive regimen had been started 2 years earlier because of resistant arterial hypertension and chronic nephropathy while on therapy with cyclosporine A, azathioprine and prednisone. The chronic antihypertensive regimen included the calcium-channel blocker amlodipine (0.16 mg/kg body weight once a day), the β-blocker metoprolol (1.7 mg/kg body weight once a day) and irbesartan (up to 10 mg/kg body weight once a day). An important hyporegenerative normocytic anemia (hemoglobin 63 g/l) was noted, which was not associated with either acute or chronic infections, including testing for Parvovirus B19 infection, and failed to improve on parenteral iron and recombinant human erythropoietin (at the beginning 170 IU/kg weekly, increased during anemia up to 230 IU/kg weekly). Finally, hemoglobin increased up to 119 g/l within 4 weeks after withdrawing irbesartan (Fig. 1).

Drugs that inhibit the renin-angiotensin II-aldosterone system modestly decrease hemoglobin and circulating erythropoietin [1]. Like converting enzyme inhibitors, angiotensin II receptors blockers may produce anemia either by direct inhibition of erythropoietin or insulin-like growth factor-1 production, or via an indirect mechanism that improves renal perfusion and subsequently decreases oxygen consumption. Furthermore, a negative effect on hematopoiesis at the bone-marrow level has also been suggested, since angiotensin II type 1 receptors have been identified on erythroid progenitors [6].

The effect on hemoglobin is usually of limited clinical relevance, and should not stand in the way of use of these agents for their cardioprotective and renoprotective effects [1, 2]. The present report confirms that there may be "susceptible" patients for whom hemoglobin levels decrease significantly on drugs that inhibit the renin-angiotensin II-aldosterone system [1]. Thus, in selected cases, some thought could be given to engineering a "drug holiday" to test whether hemoglobin level increases after discontinuation, as previously reported in a child with nephrotic syndrome on treatment with the converting enzyme inhibitor enalapril [7].

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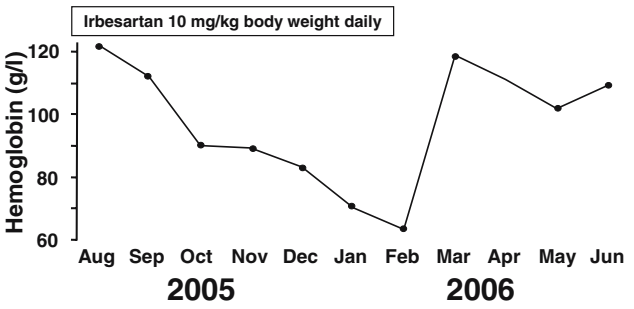

Fig. 1 Hemoglobin levels with and without irbesartan, a drug that inhibits the renin-angiotensin II-aldosterone system by blocking the type 1 of angiotensin II receptors

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