Deferasirox and renal dysfunction in children

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Received: 12 May 2012 / Accepted: 25 May 2012 / Published online: 15 August 2012
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Dear Sir,

We read with great interest the recent article of Dubourg et al. published in *Pediatric Nephrology* [1]. In this timely article, the authors report their assessment of glomerular function, based on inulin clearance (20 % fall), estimated glomerular filtration rate (eGFR; 17 % fall), and serum creatinine (30 % rise), in a cohort of ten pediatric thalassemia major patients (mean age 12.4 ± 3.9 years) exposed to a mean dose of deferasirox therapy of 24.8 ± 9.6 mg/kg over a period of 17.2 ± 8.9 months. In Oman, we have also reviewed the effects of initiating deferasirox therapy to pediatric thalassemia major patients (25 patients: 11 female, 14 male; mean age 11.8 years ± 3.8 years). Deferasirox therapy was introduced for various reasons, including several cases of non-compliance with and intolerance to deferrioxamine or deferiprone. We also found that the introduction of deferasirox therapy at a dose of 20–30 mg/kg had a significant impact on renal function. The mean serum creatinine ($\pm$ standard deviation) increased from 34.3 ± 8.9 $\mu\text{mol/L}$ to a peak concentration of 57.6 ± 27 $\mu\text{mol/L}$ ($p < 0.01$), and after a mean of 19 ± 3.9 months of therapy, it remained elevated at 46 ± 29 $\mu\text{mol/L}$ (34 % rise; $p = 0.02$). The eGFR, calculated using the Schwartz equation (using

estimated height), was 151, 86.4, and 121 mL/min/1.73 m² at various times. On further examination, 24 and 20 patients had a >33 and >50 % rise in serum creatinine, respectively; three had recurrent rises in serum creatinine with deferasirox re-challenge. We also noted that there was only a modest change in serum ferritin level by the end of the follow-up period [2,192 (baseline) vs. 2,331 $\mu\text{g/L}$ (end of follow up)].

Our additional data clearly supplement the accumulating evidence of a potential safety issue which needs further long-term evaluation in the population of thalassemia patients as their life expectancy increases. We agree that eGFR should, as a minimum measure, be calculated in this population. The mechanism of glomerular damage remains unknown, as the hemodynamic changes would not seem to correlate with the longer term persistence of renal impairment. Effects on intracellular iron and oxidative stress leading to glomerular and tubular damage are perhaps more likely and may have long-term consequences on kidney function. In the interim, it may be that a more flexible use of chelators in combination, or alternating chelators, represents a way forward to maximize the obvious beneficial effects of chelator therapy while minimizing potential short-term and longer term adverse effects [2].

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