PostScript

LETTERS

Iron deficiency anaemia: further education regarding the British Society of Gastroenterology guidelines is required

The publication of the iron deficiency guidelines in 2005¹ and the adoption of iron deficiency anaemia (IDA) as a 2-week referral criterion by the National Institute for Clinical Excellence lower gastrointestinal (GI) cancer guidelines² should have focused attention on this historically poorly managed condition. There is evidence from the primary care literature of poor adherence to previous IDA guidelines.³ In order to evaluate adherence to the new IDA guidelines in our trust, we undertook a short prospective audit of all patients admitted in 1 month through the medical admissions unit of a large teaching hospital in central England.

The initial phase of this study focused on two questions with regard to diagnosis of anaemia: (1) was serum ferritin measured in patients with microcytic anaemia and (2) were all patients with unexplained IDA assessed serologically for coeliac disease?

We evaluated 995 medical patients admitted during October 2006. Using a haemoglobin cut-off of 13 g/dl for men and 12 g/dl for women, 395 (36%) patients were found to be anaemic, of whom 46 (5%) had microcytosis (<80 fl). Of these, 13 (28%) patients had serum ferritin level measured on the second blood test during hospital stay, and in total 19 (41%) patients with a microcytic anaemia underwent ferritin level estimation during their current admission to hospital. All patients with a low serum ferritin level subsequently proceeded to further GI investigations. Pertinently, none of the patients with microcytic anaemia had blood taken for coeliac disease serology.

We believe that the results of this audit may well be representative of the investigation of anaemia, not just in our trust but also in the secondary care sector generally. The prevalence of adult coeliac disease in western European populations is thought to be about 1 per 100–300 people, based on epidemiological studies in which cohorts of healthy volunteers were screened. Previous case finding studies in primary care⁴ have demonstrated that coeliac disease commonly presents with IDA, and, even with the advent of serological testing, is considerably underdiagnosed. Patients presenting for secondary care to different medical and surgical specialties⁵ would seem to be at an even higher risk, underlining the importance of education regarding this entity.

Anaemia is an important public health problem, with an estimated prevalence of 2–10%,⁶ and although IDA may indicate underlying GI cancer and is associated with seriously detrimental effects on the quality of life,⁷ it seems to be poorly managed across the spectrum of healthcare. We believe it is important to raise awareness of the British Society of Gastroenterology IDA guidelines to promote better diagnosis, investigation and management of this common public health problem.

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Association of *BclI* polymorphism of the glucocorticoid receptor gene locus with response to glucocorticoids in inflammatory bowel disease

Glucocorticoids (GCs) are immunosuppressive drugs used for the acute treatment of patients with moderate to severe inflammatory bowel disease (IBD),¹ but interindividual variability in the response to these agents is frequently observed.² GCs diffuse freely into cells and bind to an intracellular receptor (hGR/NR3C1), so the sensitivity to these drugs may depend on the receptor number and affinity or on their availability to the receptors, and transport proteins (including P-glycoprotein (Pgp) encoded by the MDR1/ABCB1 gene) can modify their intracellular concentration.^{3,4} Polymorphisms in the hGR and MDR1 genes have been described in different populations and may contribute to the variability in sensitivity to GCs observed in the clinical setting.^{3,4}

A study was conducted to estimate the impact of genetic variations in hGR and MDR1 genes on the efficacy and individual response to GCs in young patients with IBD. Polymorphisms of the hGR gene (*BclI* and N363S which are related to GC hypersensitivity

and ER22/23EK which is associated with relative resistance to GCs⁵) and the MDR1 gene (C3435T and G2677T which are associated with changes in Pgp expression and activity⁶) were studied in 119 young patients (58 female) with IBD (64 with Crohn's disease and 55 with ulcerative colitis) of mean (SD) age 11.7 (5.94) years at the onset of the disease and 100 consecutive healthy blood donors from the same geographical area using PCR-RFLP.^{6–8}

Patients were enrolled between July 2000 and March 2005 in the gastroenterology units of the Children's Hospitals of Trieste, Firenze and Genoa, Italy. The study included all consecutive patients with IBD who had been treated with GCs for at least 30 days (prednisone 1–2 mg/kg/day for 2–4 weeks and subsequent dose tapering by 5 mg/week to a dose of 20 mg and then by 2.5 mg/week below 20 mg) and had a minimum follow-up period of 1 year. They were divided into two groups based on their response to GC treatment: GC-dependence (n = 45 patients) was defined by an initial response to prednisone with relapse on dose reduction, not allowing steroid discontinuation,⁹ and GC-responsiveness (n = 67 patients), equivalent to therapeutic success, was defined as GC withdrawal without the need for steroids for at least 1 year.¹⁰ Six patients (5.0%) initially had a partial response to GCs but steroid treatment was continued with the addition of azathioprine and aminosalicylates, so these patients were included in the study. Seven patients (5.9%) exhibited complete resistance to GCs and required colectomy; genetic analysis was also performed on this group and is reported in table 1. These patients were not considered in the statistical analysis; however, their number was very low, similar to that described by other authors in children,¹¹ and, in addition, they did not complete the scheduled observation period.

The genotype frequencies for all tested polymorphisms were consistent with the Hardy-Weinberg equilibrium in both the study and control groups. A significantly higher frequency of *BclI* mutated genotype, associated with GC hypersensitivity, was observed in the GC-responsive patients than in the GC-dependent group (OR 0.15, 95% CI 0.03 to 0.68, p = 0.0075/multiple testing corrected p = 0.0375) or controls (OR 3.61, 95% CI 1.44 to 9.01, p = 0.006/0.030). The significance was lost when the association was studied separately in patients with Crohn's disease (OR 0.23, 95% CI 0.045 to 1.13, p = 0.10/0.5) and ulcerative colitis (OR 0.10, 95% CI 0.005 to 1.97, p = 0.065/0.33) because of the small patient sample. No differences were observed for the other polymorphisms considered (table 1). A significantly higher frequency of the *BclI* polymorphism was also evident in patients with Crohn's disease than in healthy volunteers (OR 2.93, 95% CI 1.14 to 7.54, p = 0.03/0.06), confirming a previous observation in a smaller number of subjects (table 1).¹²

A logistic regression model, in which the response to GCs was the dependent variable and patients' age, sex, type of IBD and the considered genotypes were the independent variables, confirmed an independent significant association between the response to GCs and the variable *BclI* genotype (table 2).