Carbimazole – resistant thyrotoxicosis

Sir, 
We read with interest the report of two cases of thyrotoxicosis apparently resistant to high doses of carbimazole.1 In searching for the cause of a poor therapeutic response to antithyroid drugs, several possibilities must be considered. As pointed out by Cooper,2 iodine does affect the thyroid stores and is the most probable cause of treatment failure. In his study, among nine patients referred for nonresponse to high doses of propylthiouracil, one only was finally considered as noncompliant. However, even if it is unusual, Li et al recently reported a case of true resistance to methimazole confirmed by the determination of serum and intrathyroidal methimazole concentration.3 An iodine test reported by Li et al in 15 of these patients showed low levels were not measured. However, the hypothesis of resistance to carbimazole could have been tested alternatively by performing a perchlorate discharge test four hours after taking iodine under antithyroid medical supervision; a negative perchlorate test indicating an inadequate blockade of iodine organification and thus a possible carbimazole resistance, a positive test indicating the possibility of some degree of iodine organification block and, therefore a possible lack of compliance.2

Regardless of the problem of compliance, iodine contamination should have been ruled out by measuring urinary iodine excretion. Iodine does affect the response of the thyroid to antithyroid drugs, directly altering its intrathyroidal metabolism of the drug and indirectly by increasing the thyroidal stores of propylthiouracil. Therefore, delaying the response to treatment.4 Such mechanisms are involved in the resistance to antithyroid drugs of amiodarone- or iodine-induced thyrotoxicosis which may persist for months. One might assume that iodine-contaminated drug patients partially or totally resistant to antithyroid drugs may show a dramatic response to glucocorticoids,5,6 as the two cases reported here show. Therefore, we think that an unsuspected iodine contamination may have played a role in the unresponsiveness of these two patients to high doses of carbimazole and should have been discussed.

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Reference

3 Li H, Olshen J, Akrizitu T, Mori T. A hyperthyroid patient with Graves’ disease who was strongly resistant to methimazole: investigation on possible mechanisms of resistance. Endocrine J 1995; 42: 697–704.

Gastrointestinal disorders in Parkinson’s disease

Sir, 
Gastrointestinal disorders are common in Parkinson’s disease. Although the underlying pathophysiology remains largely unknown, enteric nervous dysfunction and subsequent gastrointestinal failings of the small bowel bacterial overgrowth with malabsorption is an attractive hypothesis. Davies et al7 recently used the lactulose hydrogen breath test to study whether increased orocecal transit time and small bowel bacterial overgrowth could explain weight loss in Parkinson’s disease. None of their 15 patients showed an early rise in breath hydrogen, which led the authors to conclude that bacterial overgrowth was not a factor in this study. However, the lactulose hydrogen breath test is a questionable tool to diagnose small bowel bacterial overgrowth.8 The condits-sine-qua-non for this test is the presence of a hydrogen-donating flora, but in 15–20% of tested subjects the gut flora will not meet this condition.9 Therefore, the fact that none of the patients studied by Davies et al7 had an early rise of breath hydrogen excretion does not exclude small bowel bacterial overgrowth. Furthermore, the authors cited the study by Metz et al.9 as evidence that the lactulose hydrogen breath test has a rather poor sensitivity (approximately 67%).10 Preferentially, the authors should have followed the recommendation of Metz et al.9 to use a combination of breath tests to screen for small bowel bacterial overgrowth. Alternatively, the authors could have used the more innovative method of quantitative enteric bacterial overgrowth, jejunal or ileal aspirates, which remains the most accurate diagnostic tool to demonstrate small bowel bacterial overgrowth, especially when gastrointestinal motility disorders are suspected.11

Second, one would have expected to find small bowel bacterial overgrowth since orocecal transit time was increased in 10 of the 15 patients with Parkinson’s disease. Disturbance of small bowel motility is an important risk factor for small bowel bacterial overgrowth.6 Histological observations suggest that impaired gastrointestinal motility might be related to impairment of the gastrointestinal motoric plexus, which appears to be affected in Parkinson’s disease.7

Third, Davies et al7 found high lactulose/manitol ratios in their patients, suggesting a reduction in the absorptive surface area of the small intestine. This might indicate the existence of small bowel bacterial overgrowth, since it is a well-known cause of intestinal mucus loss, loss of brush border enzyme activity, and resultant malabsorption.4 In conclusion, the study of Davies et al7 does not exclude the possibility that small bowel bacterial overgrowth, due to disturbed small bowel motility, may at least partially explain weight loss, malabsorption and other gastrointestinal disorders in Parkinson’s disease.

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Reference


Oxidative haemolysis after spiramycin

Sir, 
I report a case of spiramycin-induced acute haemolysis in a glucose-6-phosphate dehydrogenase (G6PD)-deficient patient confirmed by rechallenge.

A 48-year-old woman was hospitalised with complaints of malaise, weakness, abdominal and lumbar pain 24 h after initiation of treatment with oral spiramycin (1 g bid) for fever and symptoms of an upper respiratory tract infection. Eight years previously, G6PD deficiency was diagnosed, when she suffered from several sulfonamide- and acetanilide-induced haemolytic episodes requiring blood transfusions. The laboratory data were: haemoglobin 7.7 g/dl, haematocrit 22.4%, reticulocyte count 4.5%, whole blood count 12.4 × 10^6/μl, platelet count 224 × 10^9/μl. The lactate dehydrogenase concentration was markedly elevated (1823 U/l), normal<300). Three days after the spiramycin therapy, she was afebrile but nauseated, icteric, and passing dark urine. The liver was 3 cm below the right costal margin and the spleen was not palpable. Serum bilirubin was 2.9 mg/dl (normal<1.0 mg/dl) with preponderantly unconjugated bilirubin fraction (2.8 mg/