Drug points

Worsening of symptoms of multiple sclerosis associated with carbamazepine

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Carbamazepine is widely used to treat paroxysmal neurological symptoms and pain. We report on five patients with multiple sclerosis in whom disability was seriously enhanced by treatment with carbamazepine at comparatively low dosages. It is possible to misinterpret worsening of symptoms as an exacerbation of multiple sclerosis.

Case 1

A 48 year old man had had symptoms of multiple sclerosis for three years, at first intermittent but eventually progressive, with mainly ataxia and spastic weakness of the legs. He also had disabling oscillopsia due to a multidirectional nystagmus. Two days after starting carbamazepine (100 mg three times daily) he was unable to walk because of increased weakness, but two days after stopping it he could walk unassisted. Carbamazepine (50 mg three times daily) was restarted one week later without any change in symptoms. When the dose was increased to 100 mg three times daily he developed a profound weakness of the legs, which disappeared two days after stopping treatment.

Case 2

A 67 year old woman with secondary progressive multiple sclerosis had a recurrence of right sided trigeminal neuralgia. Although she was severely disabled (ataxia of all limbs and spastic weakness of her legs), she could walk with a frame. Carbamazepine 100 mg three times daily was started. Two days later she could not stand owing to weakness of her legs. The sudden worsening was interpreted as an exacerbation, and she was treated with intravenous methylprednisolone 500 mg daily for five days, without benefit. Two weeks after discharge she was seen at the clinic. Carbamazepine was stopped, and two days later she could walk with a frame. She recalled a less severe effect from carbamazepine during the previous episode of trigeminal neuralgia.

Over the past year three further women with secondary progressive multiple sclerosis showed worsening of symptoms with carbamazepine, prescribed for trigeminal neuralgia. Each patient received comparatively low doses of carbamazepine (300-600 mg daily). Two had profound weakness of the legs and increased difficulties with micturition, whereas one, who was bedridden, lost the use of her upper limbs. Symptoms worsened within the first three days of starting carbamazepine and disappeared within two days of stopping it.

In multiple sclerosis there is a remodelling of the demyelinated axonal membrane so that it acquires more sodium channels than normal, which permits conduction of action potentials despite the loss of myelin.[1] Carbamazepine may counteract this compensatory mechanism by blocking sodium channels.

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Immune complex haemolytic anaemia associated with sulfasalazine

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A 79 year old woman was admitted because of a positive Coombs's test result for haemolytic anaemia (haemoglobin concentration 8.2 g/dl). She had been taking sulfasalazine for ulcerative colitis for five years.

The patient's medical history included a cerebrovascular accident and atrial fibrillation, which were treated with digoxin, verapamil, aspirin, and oxazepam. On admission, aspirin, sulfasalazine, and oxazepam were discontinued, and two units of blood were given. After sulfasalazine was reintroduced, the patient showed evidence of haemolysis: her haemoglobin concentration had decreased by 2.5 g/dl, lactate dehydrogenase concentration had increased from 494 to 2620 U/l, and total bilirubin concentration had increased from 0.4 to 1.4 mg/dl. Sulfasalazine was discontinued, and all biochemical parameters returned to normal. Haematological studies were performed according to published methods.[1]

The possibility of a drug dependent immune complex was assessed. Agglutination occurred when a mixture of sulfasalazine and the patient's serum was added to normal erythrocytes treated with the endopeptidase ficin. No reactivity was noted when control serum was used or when sulfasalazine was omitted. Preincubation of sulfasalazine with normal erythrocytes gave negative results on addition of the patient's serum, excluding the possibility of a penicillin-like reaction.

Sulfasalazine causes Heinz body anaemia in patients with abnormal haemoglobin and haemolysis in patients deficient in glucose-6-phosphate dehydrogenase. Our patient had a normal concentration of glucose-6-phosphate dehydrogenase, and no Heinz bodies were seen on a blood smear. A few patients with ulcerative colitis treated with sulfasalazine and who have immune haemolytic anaemia have been described, but in none was sulfasalazine clearly implicated.[2–4] The manufacturer (Pharmacia Upjohn) could provide no additional information about this side effect. Our report is important as 1.7% of patients with ulcerative colitis develop immune haemolytic anaemia even in the absence of treatment with sulfasalazine.[5]

1 Petz LD, Branch DR. Drug-induced immune hemolytic anemia. In: Chaplin H, ed. *Methods in hematology: immune hemolytic anemia*. New York: Churchill Livingstone, 1985:47-94.
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4 Balint JA, Hammack WJ, Patton TB. Association of ulcerative colitis and red blood cells coated with autoimmune antibody. *Am J Dig Dis* 1963;8:537-44.
5 Giannadaki E, Potamianos S, Roussomoustakaki M, Kyriakou D, Fragkiadakis N, Manousos ON. Autoimmune hemolytic anemia and positive Coomb's test associated with ulcerative colitis. *Am J Gastroenterol* 1997;92:1872-4.