Benign intracranial hypertension associated with the withdrawal of a non-ergot dopamine agonist

S L Atkin, E A Masson, L D Blumhardt, M C White

Abstract
The cases are reported of two patients who developed benign intracranial hypertension after the withdrawal of the novel non-ergot derived dopamine agonist CV 205 502 (quinagolide).

Semisynthetic ergot-derived dopamine agonists were introduced in 1971 for the treatment of hyperprolactinaemia. Many studies have documented the efficacy of these drugs in decreasing serum prolactin levels, reducing pituitary prolactinoma size and the effects of pituitary compression, and in restoring gonadal function. The side effects of these drugs include nausea and orthostatic hypotension and, less commonly, headache, fatigue, nasal stuffiness, abdominal cramps, and constipation. CV 205 502 (quinagolide) is a novel non-ergot derived dopamine agonist (an octahydrobenzyl(L)quinolone compound) which has been available on a 'named patient' basis for the treatment of hyperprolactinaemia in patients intolerant of bromocriptine. We report the development of benign intracranial hypertension in two patients within two weeks of withdrawal from CV 205 502.

Case 1
A 32-year-old woman who had had transphenoidal surgery for a macroprolactinoma continued to have hyperprolactinaemia despite a radiological empty sella. She was intolerant of bromocriptine and treatment with 75 µg CV 205 502 restored menses and stopped galactorrhoea for 24 months. Two weeks after stopping CV 205 502 she developed morning headaches, visual disturbance, nausea, and vomiting, which continued with increasing severity over the next four weeks.

Case 2
A 25-year-old woman with hyperprolactinaemia due to a microprolactinoma was intolerant of bromocriptine. She was successfully treated with 75 µg CV 205 502 for 30 months. Two weeks after stopping treatment she developed morning headaches with nausea and blurred vision, which continued with increasing severity over the following two weeks. Her past history showed that identical, though less severe, symptoms had developed over a similar time course one year previously when she had stopped treatment with CV 205 502 for one month. The symptoms had resolved shortly after restarting treatment.

Correspondence to:
Dr S L Atkin, Department of Medicine, University of Hull, Kingston General Hospital, Beverley Road, Hull, HU3 1UR, UK.
Received 29 June 1993.
Accepted 28 July 1993
Discussion

Benign intracranial hypertension is a rare disorder of unknown aetiology and uncertain incidence. It is more common in obese women between the ages of 17 and 40 years and is associated with the menarche and pregnancy. It is unclear if an apparent association with menstrual irregularity is more than would occur by chance. Drugs associated with benign intracranial hypertension include tetracyclines, naladixic acid, nitrofurantoin, corticosteroids (oral and topical), ketamine, nitrous oxide, vitamin A (excess and deficiency), oral contraceptives, ketoprofen, and thyroxine. To date there have been no reports of any association between benign intracranial hypertension and dopamine agonists.

CV 205 502 is a quinolone compound with selective D2 receptor agonist activity, whereas the lysergic acid derivative bromocriptine has D1 and D2 agonist activity. The two drugs have been associated with psychiatric complications.

Our patients described identical symptoms occurring two weeks after stopping CV 205 502, though the symptoms and signs in patient two were less severe, possibly due to earlier presentation. The two patients had other features of benign intracranial hypertension. Patient 1 had an empty sella secondary to an operation and patient 2 was taking oral contraceptives. The similar time interval in the two patients between stopping CV 205 502 and the development of symptoms, and the history of identical symptoms one year earlier, strongly suggest a relation with the drug. The development of symptoms within two weeks of stopping CV 205 502 and the subsequent resolution of all symptoms within one month of restarting treatment suggests that benign intracranial hypertension may have been precipitated one year earlier. If this is true, it can be speculated that CV 205 502 was preventing the development of benign intracranial hypertension.

It is also notable that the two patients had vascular headaches characteristic of migraine which were reduced in frequency and increased in severity on treatment with CV 205 502. In both the patients the headaches increased in frequency and decreased in severity on stopping the drug. Migraine is common and may be a coincidental feature, but the temporal relation of CV 205 502 treatment to the alteration in the pattern of the migraine suggests that CV 205 502 was responsible for the reported modulation of the frequency and severity of the headaches. Bromocriptine may improve migrainous attacks in patients with menstrual migraine, though marked hypotension may complicate bromocriptine treatment in patients with migraine. Our observations and the vascular basis of migraine and benign intracranial hypertension suggest that CV 205 502 may have a direct action on the cerebral vasculature.

References