Generalized choreiform movements as a complication of methyldopa therapy in chronic renal failure

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Summary

A patient who developed bilateral choreiform movements in association with methyldopa therapy and deteriorating renal function without evidence of cerebrovascular disease is reported.

Introduction

Although methyldopa has been widely used in the treatment of hypertension for many years there is only a single case report (Yamadori and Albert, 1972) of bilateral choreoathetotic movements possibly related to treatment with this drug. That isolated case report was of a patient with concomitant severe bilateral cerebrovascular disease. The authors report here a similar case but in association with deteriorating renal function.

Case report

A 59-year-old Caucasian male was first seen in 1970 with maturity onset-type diabetes which was controlled by diet and chlorpropamide 250 mg daily. In 1973, proteinuria was noted and blood urea was 11.8 mmol/l. One year later, methyldopa 250 mg thrice daily was commenced for hypertension (blood pressure 200/110 mmHg) with the subsequent addition of chlorthalidone. Renal function gradually deteriorated but the patient remained otherwise well. In August 1980, blood urea was 34.8 mmol/l and creatinine was 600 μ mol/l.

In October 1980, he was admitted with a 3-week history of involuntary jerking movements which had initially been worse in the evenings. The movements had gradually increased in severity until coarse jerking movements were present throughout the day being exacerbated by an attempt at voluntary movement. They disappeared completely during sleep. On examination, bilateral purposeless coarse twitching movements involving different muscle groups in the trunk, shoulder girdle and arms were observed.

There was no tremor, ataxia nor nystagmus.

Cranial nerves were intact and intellectual function was preserved. Power and tone were normal and symmetrically equal. Ankle reflexes were absent bilaterally but other tendon reflexes were normal and plantar responses were flexor. Sensation was intact apart from absent vibration sense below both knees. Chvostek's and Trousseau's signs were negative. BP was 160/90 mmHg and he was anaemic. Investigations showed blood urea 44 mmol/l, creatinine 963 μ mol/l, sodium 142 mmol/l, potassium 4.4 mmol/l, chloride 110 mmol/l, bicarbonate 14 mmol/l, creatinine clearance 4.8 ml/min., calcium 1.54 mmol/l, phosphate 3.23 mmol/l, alkaline phosphatase 14 K.A.u./l, albumin 43 g/l, liver function tests normal, Hb 8.6 g/dl, MCH 26.8 pg, MCV 85 fl, white cell count $7.9 \times 10^9/l$, blood glucose 5 mmol/l.

Methyldopa was discontinued 24 hr after admission, and 12 hr later the abnormal movements were diminishing in frequency and severity. After a further 24 hr the abnormal movements had disappeared completely. All haematological and biochemical investigations were unchanged and he remained alert. A week later he developed oliguria with rapidly rising blood urea and died. There had been no recurrence of his abnormal movements.

Discussion

The only previously reported case of involuntary movements associated with methyldopa therapy occurred in a patient with severe bilateral cerebrovascular disease after the dose had been increased from one g/day to 1.5 g/day (Yamadori and Albert, 1972). The case reported here is of interest in that the patient had no history or clinical evidence of cerebrovascular disease and had been on the same dose of methyldopa for 7 years. The development of the abnormal movements coincided with deterioration in renal function.

As methyldopa is mainly excreted *via* the kidney, renal failure would be expected to lead to a rise in serum drug concentration. This increase may have

been sufficient biochemically to trigger an abnormal movement pattern. In the presence of normal renal function a single oral dose of methyldopa produces a peak serum concentration after 3 to 6 hr and 80–90% of the drug is eliminated after 48 hr (Wade, 1977). In the absence of an alternative explanation, the disappearance of the abnormal movements within 36 hr of stopping the methyldopa supports

the implication of methyldopa in the aetiology of these movements.

References

- WADE, A. (Ed.) (1977) Martindale. *The Extra Pharmacopoeia* p. 667–669. The Pharmaceutical Press, London.
- YAMADORI, A. & ALBERT, M.L. (1972) Involuntary movement disorder caused by methyldopa. *New England Journal of Medicine*, **286**, 620.