visual impairment we have seen with this drug, we think that others using it should be aware of this serious, adverse reaction.

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Departments of Rheumatology, Ophthalmology, and Medical Physics, Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP
M J DODD, BSC, MRCP, senior registrar in rheumatology
I D GRIFFITHS, BSC, MRCP, consultant rheumatologist
J W HOWE, FRCS, consultant ophthalmologist
K W MITCHELL, BSC, senior physicist

Amenorrhoea, galactorrhoea, and hyperprolactinaemia induced by methyldopa

Among the side effects of methyldopa are decreased potency and failure of ejaculation in men and non-puerperal lactation in both premenopausal and postmenopausal women.[1 2] Steiner *et al*[3] found increased serum concentrations of prolactin after single doses of methyldopa during long-term treatment and suggested that this might be the mechanism of galactorrhoea, though they pointed out that no studies had been made of patients with this side effect. Hyperprolactinaemia of renal failure is enhanced by treatment with methyldopa.[4] Troublesome galactorrhoea and other side effects of hyperprolactinaemia might therefore be expected to be detected first in patients with renal disease treated with methyldopa.

We report on two patients with amenorrhoea, one of whom had galactorrhoea, due to methyldopa in whom hyperprolactinaemia was confirmed.

Case reports

CASE 1

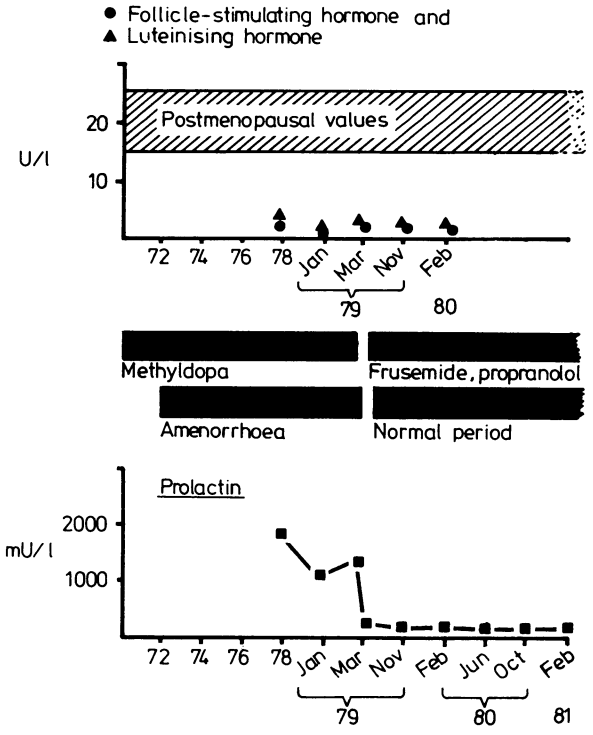
A 41-year-old hypertensive woman started taking methyldopa in 1972, increasing the dose gradually to 4 g/24 h at the beginning of 1978. In 1974 her periods stopped and this was interpreted as postmenopausal amenorrhoea. At the end of 1978 she developed prolonged irregular bleeding, which was erroneously regarded as postmenopausal. Concentrations of follicle-stimulating and luteinising hormones, however, were normal at 0·4 and 2·4 U/l respectively, and she had prolactinaemia of 1865 mU/l (figure). Two repeat samples over the next three months were also raised at 1069 and 1743 mU/l respectively. *X*-ray films of the skull and tomograms of the pituitary fossa were normal.

Methyldopa was gradually withdrawn; one month after it was stopped the serum prolactin concentration had fallen to 214 mU/l, and over the following three years she had normal, regular periods and serum prolactin concentrations within the normal range (figure).

CASE 2

A 17-year-old girl with proliferative glomerulonephritis developed severe hypertension requiring variable doses of methyldopa up to 750 mg daily to achieve normotension. Her periods became irregular with frequent episodes of amenorrhoea lasting for several months. At the age of 19, after 12 weeks of amenorrhoea, she was found to be pregnant. The pregnancy was terminated at 12 weeks and she developed persistent galactorrhoea, breast tenderness, and nodularity. The discharge of milk fluctuated with the dose of methyldopa. Serum prolactin concentration was 6364 mU/l when the dosage of methyldopa was 250 mg thrice daily, dropping to 3790 mU/l when the dosage was 125 mg daily. *X*-ray films of the skull and tomograms and a computed tomogram of the pituitary fossa were normal.

Methyldopa was stopped and bromocriptine started. One month later her galactorrhoea had stopped and her periods returned to normal; the prolactin concentration fell to 210 mU/l. Bromocriptine was stopped after six months; normal periods continued for a further three months and slight galactorrhoea recurred and persisted. Serum prolactin concentration rose again to 5319 mU/l and remained high. Continuous ambulatory peritoneal dialysis was started, and by the age of 23 years she had been receiving this for 12 months.



Serial concentrations of follicle-stimulating hormone, luteinising hormone, and prolactin in case 1. Hatched area represents postmenopausal values of the hormones; upper limit of normal for serum prolactin concentration is 450 mU/l.

Comment

In case 1 a clear-cut relation existed between hyperprolactinaemia, amenorrhoea, and administration of methyldopa, all abnormalities clearing up simultaneously when the drug was withdrawn.

In case 2 the pregnancy, terminated at 12 weeks, may have played some part in precipitating galactorrhoea. At that time the renal function (plasma creatinine concentration 125 μmol/l (1·4 mg/100 ml)) was not decreased to a degree that usually causes hyperprolactinaemia, and the extremely high prolactin concentrations found after the withdrawal of bromocriptine were well above those usually found in chronic renal failure. Probably she eventually developed a prolactinoma, though we have no confirmatory evidence for this. Whether the prolactinoma was the result of prolonged treatment with methyldopa in a patient with impaired renal function or whether the treatment merely drew to light a prolactinoma that would have declared itself later in any case remains speculative.

Galactorrhoea or menstrual abnormalities in patients receiving methyldopa are an indication for estimation of the serum prolactin concentration.

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Wellcome Research Laboratories, University Department of Medicine, Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP
R S ARZE, MD, research associate
J M RAMOS, MD, research associate
H U RASHID, MB, FCPS, research associate
D N S KERR, MSC, FRCP, professor of medicine