dose 54 units/day). All 10 patients had been issued with a further appointment. Three were subsequently admitted as emergencies, and seven returned to the clinic.

Eleven patients (eight men, three women; age range 40-71, mean 56) were under the supervision of their general practitioner, who did not know why they had ceased to attend. Seven patients were on a diet, all but one were also receiving tablets. The remaining four were being treated with insulin (mean dose 38 units/day); none were aged under 30 and three were in the range 30-50. Nine patients were issued with a further appointment. Four were contacted through the district nurse, who took blood samples for estimation of haemoglobin A₁ (HbA₁) (upper limit of normal 8.5 g/dl). One patient, whose HbA₁ concentration was 5.6 g/dl said he had been told by the doctor not to return to the clinic. Two patients (with HbA₁ concentrations of 9.9 g/dl and 7.5 g/dl) said they did not attend unless they felt unwell. The fourth patient (HbA₁ 14.9 g/dl) thought everything was under control.

The remaining three non-attenders (one man, two women; age range 36-55, mean 46) were under no supervision, and their general practitioner did not know why they had ceased to attend. One was on a diet and two were being treated with tablets. Two had been given another appointment.

Comment

The interval between visits for diabetic patients attending our clinic is very variable: some stable patients have annual appointments, while problem patients may be seen after intervals of two to three months, or even less. If patients fail to attend they automatically receive at least one further appointment by post. If a patient continues to default, the doctor at the clinic usually writes to the general practitioner. The clinic studied may have a lower drop-out rate than the diabetic clinic of other centres, but we have no hard evidence to confirm or refute this.

Some 5% of diabetics were lost from follow-up over the period studied. The true loss to hospital follow-up, however, was only 1.4%, as 0.2% had died, 1% returned subsequently to hospital care, and 1.9% moved to another area or clinic (assuming those who moved to another area establish hospital contact). Of the remainder, 1.1% were being seen by their GP and only 0.3% (none of whom were taking insulin) were under no supervision whatsoever. It is noteworthy that three patients required subsequent emergency admission (one with diabetic ketoacidosis and one with an ischiorectal abscess). Men seem more likely to stop attending than women. The mean age was similar for all groups except for those attending their GP, who were slightly older.

If a recall system such as we describe existed for patients who fail to reattend a diabetic clinic, surprisingly few patients would be under no sort of medical care whatsoever and most (67%) would return to hospital care somewhere. Our findings suggest that a more detailed system is probably unnecessary.

Requests for reprints should be addressed to: Dr I N Scobie, Department of Medicine, St Thomas's Hospital Medical School, London SE1 7EH. We thank Staff Nurse Eleanor Brown for visiting patients at home.

¹ Deckert T, Poulsen JE, Larsen M. Prognosis of diabetics with diabetes onset before the age of thirty-one. II. Factors influencing the prognosis. *Diabetologia* 1978;14:371-7.

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Valproic acid and fetal abnormality

Infants born to women with epilepsy have an increased incidence of fetal abnormality. There are several possible causes for this including inherited factors and the effects of convulsions during pregnancy. Some fetal abnormality, however, may be attributed to the teratogenic effects of anticonvulsants, and phenytoin and phenobarbitone are the drugs most commonly blamed for this. Valproic acid and carbamazepine have been recommended in preference to phenytoin and phenobarbitone as anticonvulsants for women of childbearing age.¹ We report two cases that may call into question the wisdom of this advice with respect to valproic acid.

Case reports

Case 1—The mother of this infant was a 20 year old primigravida with idiopathic epilepsy. During pregnancy she had taken valproic acid 400 mg twice daily and had no convulsions. Serum valproic acid concentration at 35 weeks' gestation was 340 mg/l. There was no family history of congenital abnormality, and the only other medication (apart from iron and folate) had been six tablets of Distalgesic (dextropropoxyphene hydrochloride 32.5 mg, paracetamol 325 mg) taken four weeks after the last menstrual period. The infant was male and born at term weighing 3000 g. He had bilateral finger-like thumbs. One thumb was triphalangeal. A rudimentary extra digit arose from the base of the right thumb. A median cleft of the left foot was present with syndactyly of the first and second toes. Subsequent investigation of failure to thrive showed bilateral renal hypoplasia.

Case 2—The mother of this infant was a 22 year old primiparous woman of subnormal intelligence who also suffered from idiopathic epilepsy. A previous pregnancy had ended in spontaneous abortion at eight weeks. In both pregnancies she had taken valproic acid 600 mg thrice daily. In the second pregnancy she had had four grand mal convulsions during the last trimester. Serum valproic acid concentration at 32 and 36 weeks' gestation was 540 mg/l and 140 mg/l respectively. There was no known family history of congenital malformations. The infant was male and born at 38 weeks' gestation weighing 2400 g. He had micrognathia, bilateral undescended testes, and glandular hypospadias. There was a flexion deformity on the left wrist with shortening of the forearm. The left fifth digit was elongated and proximally inserted. The thumb was finger like. He also had moderately severe valvular aortic stenosis. Intravenous pyelography and chromosome analysis yielded normal results.

Comment

In each of these two cases the mother had taken valproic acid throughout the pregnancy. There are few data on the outcome of pregnancies in which valproic acid was the sole drug taken, but facial, digital and skeletal abnormalities as well as developmental delay have been described.^{2,3} The manufacturers of the drug have collected data on 33 pregnancies in which valproic acid was the sole anticonvulsant (Labaz, personal communication). These pregnancies resulted in 25 normal babies, four spontaneous abortions, and four infants with congenital malformations (two with meningomyelocoeles, one with syndactyly, and one with a small ventricular septal defect). Recently eight participants in the International Clearinghouse for Birth Defects Monitoring Systems reported that valproic acid was associated with neural tube defects in about 1% of fetuses exposed in early pregnancy.⁴

In case 1 dextropropoxyphene as well as valproic acid had been taken at the critical period of differentiation of fetal limb buds. Abnormalities including skeletal and thoracic malformations have been recorded after the use of dextropropoxyphene, usually in combination with other drugs.⁵

We cannot be certain that valproic acid was responsible for the abnormalities in our two cases but wish to draw attention to the occurrence of appreciable congenital malformations in two infants born to mothers who took valproic acid throughout pregnancy and to the possibility that yet another drug is hazardous for women in their childbearing years.

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