Comment

The methods used in this study were reasonably satisfactory, although the response rate from the general practitioners (52%) was rather disappointing.

In common with most other studies,[1 2] our results provide no evidence of an increase in the risk of cardiovascular disease in women receiving hormone replacement treatment. Nevertheless, few subjects were studied and the use of hormone replacement treatment (especially current use) was generally infrequent. This finding was not unexpected since general practice prescribing data suggest that only about 3% of women aged 45-69 years were using hormone replacement treatment at any given time during the year 1978 (unpublished observations, G T Bungay). It seems doubtful whether a full-scale study of the type we have described would be rewarding unless hormone replacement treatment becomes more widely used.

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Impact of therapeutic audit on phenytoin prescribing

Phenytoin is difficult to use because of its low therapeutic ratio and non-linear kinetics (serum phenytoin concentration increases disproportionately with dose). These problems heighten the risk to epileptic patients, for whom the quality of care is known to be poor.[1] We assessed the effect of a therapeutic audit on the prescribing of phenytoin in one hospital and detected a rapid improvement in prescribing habits.

Methods and results

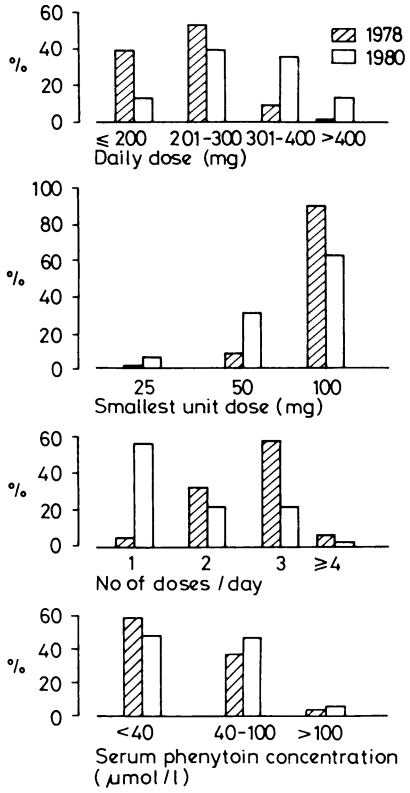
All adult outpatient prescriptions for phenytoin at this hospital were inspected in 1978 and again in 1980. Information regarding the dose, dosage interval, and incidence of polypharmacy was noted. In 1978 there were 189 scripts for phenytoin; 40% of patients receiving phenytoin were prescribed additional anticonvulsants. There was evidence of underdosing, little fine adjustment of dose, and complicated divided dosage regimens (figure).

In a further study of 229 outpatients in whom phenytoin concentrations were measured between October 1977 and April 1979 evidence of underdosing was supported by low serum concentrations. Frequency of fits was assessed by inspecting the case notes of a representative proportion of these subjects. Fifty out of 81 medical outpatients (62%) reported having had fits since their previous visit, and chronic recurrent seizures were clearly "clinically acceptable."[2] The implications of these findings were discussed at local clinical meetings and communicated to medical staff.

In 1980 (183 prescriptions) the incidence of polypharmacy was the same (41%). There was a significant increase, however, in phenytoin dosage ($\chi^2=80{\cdot}02$; $p<0{\cdot}0001$) and significantly greater use of 25 and 50 mg capsules for fine dosage adjustment ($\chi^2=39{\cdot}62$; $p<0{\cdot}0001$). In addition, once- or twice-daily dosing was the rule ($\chi^2=139{\cdot}48$; $p<0{\cdot}0001$) rather than the exception. Compared with 1978, serum phenytoin concentrations were more often in the therapeutic range than below it ($n=147$, $\chi^2=3{\cdot}97$, $p<0{\cdot}05$). The proportion of medical outpatients reporting seizures had fallen to 47% ($n=70$, $\chi^2=4{\cdot}42$, $p<0{\cdot}05$).

Comment

The average daily dose required to achieve therapeutic serum phenytoin concentrations of 40-100 μmol/l (10-25 mg/l) is 350-400 mg.[3] In an attempt to avoid toxicity underdosing is common and may be associated with poor seizure control,[1 2] sometimes with disastrous consequences. Small dosage adjustments (25-50 mg) may avoid the risks of toxicity[4] and may be accompanied by better control, while a simple once-daily regimen[5] will improve compliance, which is often poor among epileptics. The improvement in seizure control was unassociated with an increase in serum phenytoin monitoring, suggesting that better prescribing, titrated against the frequency of



Percentage of prescriptions for phenytoin related to daily dose, smallest unit dose, and dose interval; and to serum phenytoin concentration.

fits, was largely responsible. Unfortunately, the incidence of polypharmacy did not decline. This is not surprising in view of the difficulty of withdrawing anticonvulsants, the selective nature of the hospital population, and the short time between the two studies. It is important, however, to note the rapid impact of local audit in contrast to the poor response to the glut of publications in this field over the past 20 years.

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