formulation as blue-coloured, sweet-tasting tablets, and in the fact that it is prescribed for migraine, a relatively non-serious disease. Diazepam is probably regarded as a non-dangerous drug, being stored in places accessible to children, while, by contrast, the antihypertensive Catapres is treated with appropriate respect. We hope that this article will alert doctors prescribing Diazepam so that they can issue appropriate warnings to parents to keep this drug out of the reach of young children.

When the size of this problem became known, the manufacturers alerted pharmacists through a letter published in the *Pharmaceutical Journal,* and, more recently, a warning has been incorporated in the label on the standard package for Diazepam. As yet, we have detected no decline in the rate of new cases, possibly because the new potentials did not reach all retailers until late 1977. Probably, however, further measures will be needed, and safety packaging is being considered.

We thank those doctors who replied to our questionnaire and thus made possible this survey. We are also grateful to Dr J W Bell and Dr D Segal of Boehringer Ingelheim Ltd Bracknell, UK for their advice and co-operation.


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Myositis and acute respiratory infection

Acute viral infections are commonly accompanied by myalgia. Electromyographic examinations in these cases have failed to show pathological findings. We describe one patient with positive EMG findings in association with acute viral infection.

Case report

The patient was a 31-year-old man, who one week after the onset of non-productive cough, mild fever, and tiredness developed coarse muscle twitching in his fingers. Within one week the twitches had affected several other muscles in the fingers and toes, and he also complained of paraesthesiae in the thenar eminences and mild muscle pains in the hands and feet. His respiratory symptoms subsided after two weeks and the mild fever after three weeks, although muscle twitches persisted for four months. No abnormal signs whatsoever were found on neurological examination. During the first three weeks after the onset of the disease the blood sedimentation rate was 2-4 mm in the first hour, and the blood leucocyte count 3-4-3.8×10⁹/l. There was an insignificant rise in the serum antibody titre of adenoviruses (1/16-1/64) but no other changes in the tested viral antibody titres. The serum electrolytes and transaminase concentrations were normal. Three and four weeks after the start of the disease the serum creatine kinase concentrations were 140 and 41 U/l (at 37°C) respectively. Two months from the onset the blood sedimentation rate was 2 mm in first hour, and the blood leucocyte count 7-6×10⁹/l. The ECG and chest x-ray appearances were normal.

Electromyographic findings—The first EMG (taken three weeks after the initial symptoms) was abnormal. The proximal muscles of the arms, predominantly the biceps, showed insertional and abundant abnormal spontaneous activity as fibrillation potentials and positive sharp waves. Bizarre high-frequency potentials were also present. The motor unit action potentials were normal. A normal interference pattern was detectable with maximal effort. The distal muscles of the arms showed less spontaneous activity, and in the legs only the extensor digitorum brevis showed a few fibrillation potentials. The motor conduction velocities in the median and peroneal nerves were normal, and no fasciculation potentials were found. On repeat EMG examination one month later the pathological findings were fewer: prolonged insertion activity persisted, but spontaneous activity had diminished appreciably. The motor unit action potentials remained normal.

Digoxin prescribing: an evaluation of clinical judgment

When prescribing digoxin most doctors rely on intuition. We report the variation in mean steady state serum digoxin concentration after intutive dosing in a large group of patients. Comparison is made with the expected outcome had other prescribing methods been used.

Patients, methods, and results

A total of 129 patients in the Manchester region (67 men, 62 women; mean ± 1 SD age 59 ± 12 years, 62 ± 13 kg, creatinine clearance 60 ± 23 ml/min) receiving maintenance digoxin were studied. Of these, 110 were outpatients and 19 were acute medical admissions. The daily dose (0.27 ± 0.11 mg) had been selected previously by a general practitioner or a hospital doctor. We prescribed this as Lanoxin (Wellcome Medical Division Ltd, UK and Ireland Region), to be taken at 1000 and made every effort to encourage compliance. After allowing three weeks to attain "steady state" conditions blood samples for digoxin inmmunnoassay were taken on an average of four visits per patient. Results were expressed as estimated mean steady state concentration.

The above results were compared with those expected had alternative prescribing methods been used. The alternatives considered were a fixed daily dose of 0.25 mg (method A); a one-compartment model (method B), whose predictive value ranked higher than that of other pharmacokinetic models studied; and the score shown in the figure (method C). The expected concentrations were calculated on the assumption that a proportional relationship exists between the dose given to an individual and the digoxin concentration he achieves. Excluded from the comparison were five patients who had not been receiving Lanoxin and ten who were found to be intolerant of digoxin at serum concentrations below 1.28 nmol/l (1.0 μg/l). The mean serum digoxin concentration achieved by intuitive dosing (1.94 nmol/l ± 1.52 μg/l) was similar to that expected for method A (2.05 nmol/l ± 1.6 μg/l), method B (1.73 nmol/l ± 1.4 μg/l), and method C (1.78 nmol/l ± 1.4 μg/l). The variance in the logarithm of the concentrations achieved, 4.62×10⁻¹⁵ (a log₂ transformation being used to approach a normal distribution), was not different (P > 0.7) from that expected using A: 4.33×10⁻², but differed (P < 0.0001) from that expected using B: 2.38 ×
Management of embolised central venous catheters

The infraclavicular subclavian vein has become the favoured site for inserting central venous lines for pressure monitoring, drug administration, and parenteral feeding since its introduction in 1952. With the increasing use of central lines has developed the problem of polyethylene catheter embolism.\(^2\)\(^-\)\(^3\) The infraclavicular approach is easy to learn and quick to perform because of the constancy of the subclavian vein anatomy. Operators should be aware of the potential for catheter embolism especially when polyethylene catheters are inserted infraclavicularly through a metal needle. This report follows the referral of five patients to this department in a period of six months with catheter fracture or embolism and describes the commonest technique of removal.

Patients and management

Three patients were referred within a week of open heart surgery. Each had an infraclavicular subclavian venous catheter inserted preoperatively. Two patients had catheters inserted after major abdominal surgery. A standard approach between the clavicle and the first rib was employed in each case. A needle catheter intravenous placement unit\(^*\) was used in which, after percutaneous insertion of a 14 gauge needle into the vein, a polyethylene catheter was passed through the needle which was then withdrawn leaving the catheter in situ. At the time of removal some three to ten days later the catheters had fractured and either embolised (2) or remained fixed in the subclavian vein (3).

A Seldinger puncture of the femoral vein was performed under local anaesthetic. The venotomy was dilated through a 8 mm skin incision with a 9F gauge dilator. A 9F gauge grey Kifa catheter\(^\dagger\) (110 cm long, internal diameter 2.80 mm) was then advanced under fluoroscopic control over a Teflon guide wire to the inferior vena cava. The catheter was manufactured without a tapered tip. A 260 cm long spring guide wire (0.635 mm diameter) was then doubled over and preshaped so that on insertion through the distal end of the catheter a snare would unfold\(^\ddagger\) (figure). The snare was then manipulated over the distal catheter fragment and drawn tight. The Kifa catheter, snare, and catheter fragment were then withdrawn as an entity through the puncture site and pressure applied for ten minutes. All fragments were easily removed with less than 15 minutes of snare manipulation required.

Comment

We have presumed that no doctor intended to exceed a mean steady state serum digoxin concentration of 2.56 nmol/l (1.2 μg/l).\(^4\) If heart failure or atrial fibrillation remains uncontrolled at this concentration, a diuretic in the first case or a beta-blocker in the second should be added rather than risk cardiotoxicity by increasing the dose of digoxin. Concentrations below 1.28 nmol/l (1.1 μg/l) may be beneficial in heart failure and are indicated in those with slow heart rates or symptoms of toxicity at higher concentrations.\(^5\) Such patients were excluded from the comparison.

Our results show that doctors with access to patients and their case records were unable to select a dose to give a concentration between 1.28 and 2.56 nmol/l (1.1-2 μg/l) any more frequently than if they had simply prescribed 0.25 mg daily to all. The relative value of a conventional pharmacokinetic model in prescribing digoxin and the potential of an empirically derived score are shown. A multicentre trial to evaluate the score in other groups of patients is in progress.

SMD carried out the clinical work at the University of Manchester as a Wellcome Research Fellow.


\(^{2}\) Mawer, G E, Clinical Pharmacokinetics, 1976, 1, 67.


\(^{4}\) Iowa, Iowa State University Press, 1967.


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Start with a score of zero

The table shows the maintenance dose corresponding to a given score

<table>
<thead>
<tr>
<th>Total score</th>
<th>Tablets prescribed</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-13</td>
<td>One 0.0625 mg daily</td>
</tr>
<tr>
<td>14-24</td>
<td>Two 0.0625 mg daily</td>
</tr>
<tr>
<td>25-37</td>
<td>Three 0.0625 mg daily</td>
</tr>
<tr>
<td>38-49</td>
<td>Four 0.0625 mg daily</td>
</tr>
<tr>
<td>50-61</td>
<td>Five 0.0625 mg daily</td>
</tr>
<tr>
<td>62-73</td>
<td>Six 0.0625 mg daily</td>
</tr>
<tr>
<td>74-95</td>
<td>Seven 0.0625 mg daily</td>
</tr>
<tr>
<td>96-100</td>
<td>Eight 0.0625 mg daily</td>
</tr>
</tbody>
</table>

A score for prescribing digoxin. This was derived\(^1\) from data on the 129 patients described.

Comment

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