Fluconazole in neonatal disseminated candidiasis

Sir.—We report the case of an infant, born at 28 weeks' gestation weighing 900 g, who on the 22nd day of life had thrombocytopenia and leukocytosis. Urine and blood cultures yielded *Candida albicans*. Amphotericin B was started at 1.0 mg/kg/day by day 4 and on day 5, fluconazole 25 mg/kg every six hours was added and a broviac catheter inserted. Peripheral and central blood cultures on the 7th, 14th, and 18th days of treatment with amphotericin B continued to yield *C. albicans*, and cultures of abscesses on the forehead and arm yielded *C. albicans* on day 5 of fluconazole, peripheral and central blood cultures were negative for *C. albicans*. Fluconazole was discontinued after 20 days with cultures remaining negative during four months of follow up.

Fluconazole serum concentrations three hours after the infusion and before the next dose on day 7 of treatment were 10·30 and 6·98 μg/ml. Amphotericin B concentrations were 0·21 μg/ml on day 14 of treatment and 0·12 μg/ml 30 days after discontinuation. A first order, one compartment model was utilized in the following pharmacokinetic parameters for fluconazole:

\[ t_{1/2} = 37·4\text{ hours},\quad V_{a/V} = 1.2\text{ L/kg,}\quad CL = 0.02\text{ L/kg/hour.} \]

*(Where \( t_{1/2} \) is terminal elimination half life, \( V_{a/V} \) is the apparent volume of distribution, and \( CL \) is clearance.*) This indicates a larger \( V_{a/V} \) and a longer \( t_{1/2} \) as compared with adults.

The activities of four antifungal drugs against the isolate of *C. albicans* from this patient are indicated in the table. These results do not necessarily reflect therapeutic efficacy. Because the isolate of amphotericin B during and after fluconazole, one could speculate that fluconazole and amphotericin B acted synergistically. Other factors may have also helped to eradicate *C. albicans*. Further studies of fluconazole's efficacy in immunocompromised adults with invasive fungal disease are needed before studies in neonates are considered.

**Minimum inhibitory concentration and minimal lethal concentration of four antifungal drugs**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Minimum inhibitory concentration (μg/ml)</th>
<th>Minimal lethal concentration (μg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphotericin B</td>
<td>0·01</td>
<td>0·29</td>
</tr>
<tr>
<td>Fluconazole</td>
<td>&gt;1·25</td>
<td>&gt;5</td>
</tr>
<tr>
<td>Itraconazole</td>
<td>0·02</td>
<td>&gt;0·63</td>
</tr>
<tr>
<td>Schering 39304</td>
<td>5</td>
<td>2·5</td>
</tr>
</tbody>
</table>

Chronic vitamin D overdosage: a reminder

Sir,—After the reported increased incidence of rickets in Asian children in the late 1970s there has been increased awareness of the need for vitamin D supplementation. This is now being recommended by the Department of Health and usually in conjunction with other vitamins in multimitamin preparations.

Parents are able to obtain their supply through their local child health clinics under the Welfare Food Scheme. There are also many alternative preparations available without a prescription via other sources, however, including chemists and health shops. Therefore, self medication without professional supervision is a potential danger. Chronic poisoning as a result of inappropriate administration of vitamins is rarely reported now (though this was the case reported in the English language literature in the past 10 years) but we were recently presented with a case of gross hypercalcaemia due to vitamin D overdosage.

A 6 month old Indian boy was admitted with a six day history of vomiting, constipation, and increasing apathy. Examination revealed a drowsy, listless child with signs of 5-10% dehydration. Plasma electrolyte concentrations on admission showed a urea of 7·4 mmol/l, sodium 148 mmol/l, potassium 2·9 mmol/l, and a grossly raised calcium concentration of 8·66 mmol/l.

Subsequent investigations showed an increased increased baseline calcium concentration (25·92hydroxycholecalciferol) at 2226 mmol/l (normal 10·120 mmol/l) and undetectable parathyroid hormone. On close questioning, his parents admitted to administering a compound preparation of vitamins A, C, and D since the age of 4 months, and as he had refused to take these from the dropper, they poured the vitamin into his mouth directly from the bottle instead! They had obtained their vitamin supply from a chemist privately and had received no professional supervision of administration.

The baby was given intravenous fluids for five days and also commenced on a low calcium, low vitamin D diet. He was discharged home on day 12. His calcium returned to normal by day 19 but his vitamin D concentration remained raised for over six months. Follow up at one year showed moderate global developmental delay.

This case illustrates the dangers of unsupervised vitamin supplementation. To prevent further incidents, tighter control over availability of vitamins and improved public awareness of the potential dangers of vitamin overdosage would be helpful. Health professionals should also aim to improve supervision.

**The paediatric departmental library**

Sir,—Dr Clayden is, I fear, somewhat over optimistic when he suggests that we are 'on the brink of a breakthrough in data retrieval' by which we will 'access original articles and learned reviews at the touch of a few buttons... so the medical library will pass into the mists of memory'. Clearly this sort of thing is on the horizon. I already spend nearly as much time advising doctors on suitable
Chronic vitamin D overdose: a reminder.

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