A renal scan continued to show a non-functional right kidney.

Discussion

Renal artery thrombosis with renin induced hypertension is a recognised complication of umbilical artery catheterisation. Although renin concentrations were not measured, confirmed renal artery thrombosis with failure to respond to other anti-hypertensives and prompt response to captopril make renin mediated hypertension most likely.

Hypertension in neonates has been described as blood pressure greater than 90/60 mm Hg in term infants and 80/45 mm Hg in premature infants. Cardiorespiratory symptoms and congestive heart failure are the most common symptoms of neonatal hypertension. The degree of hypertension necessary to produce congestive heart failure may vary with individual neonates. The maximum pressure of 123/81 recorded in our patient was moderate. A very limited myocardial contractile reserve in response to increased afterload has been shown in newborn lambs. Inotropes have limited effects on contractility in newborn rabbits and lambs. Limited myocardial reserve may explain why congestive heart failure is often the dominating picture in neonatal hypertension.

Hypersensitivity to captopril, manifesting in some adults as hypotensive crisis, has not been reported in neonates.

We have shown by echocardiography that adequate treatment of hypertension rapidly reverses severe myocardial dysfunction caused by neonatal hypertension. We suggest that echocardiography may be helpful to document the cardiac effects of neonatal hypertension and to determine the need for and response to treatment.

References


Correspondence to Dr M A Beaudy, Division of Neonatology, 3A3 Walter McKechnie Health Sciences Center, University of Alberta, Edmonton, Alberta T6G 2B7, Canada.

Received 5 January 1987

Anticonvulsant drugs, growth, and development

B M Macardle, M E L MCGowan, S A GREENE, AND C S MILLER

Departments of Paediatrics and Radiology, Guy’s Hospital, and Departments of Neurology and Child Health, King’s College Hospital, London

SUMMARY Height and stage of puberty of 67 children with epilepsy were measured before beginning treatment with anticonvulsant drugs and annually to a maximum five years’ treatment. Blood concentrations of the drugs used (phenytoin, sodium valproate, carbamazepine, ethosuximide, and phenobarbitone) were monitored throughout. No significant deviation in growth patterns was detected.

Anticonvulsant drugs administered during pregnancy have been postulated to retard fetal growth and head circumference. In vitro studies have shown that phenytoin and sodium valproate reduce the thickness and cellularity of epiphyseal and articular cartilage in rats. Round described a group of children with chronic epilepsy who failed to reach predicted adult height and attributed this to an early growth spurt and lower than normal growth velocity. Robinson found premature epiphyseal fusion in a group of short children with epilepsy treated medically.

In a study of adults with epilepsy McGowan identified three groups who seemed to be short: (1) males with partial seizures beginning before 18 years of age, (2) females who had taken phenytoin before...
the onset of puberty, and (3) males who were on phenytoin before 10 years.^{6} Interpretation of these studies is difficult, however, as many of the patients had chronic epilepsy treated with anticonvulsant polytherapy, without access to monitoring of drug concentrations, and many of these children were educated in a residential setting. We have therefore prospectively investigated growth in a group of children with newly diagnosed epilepsy from the beginning of treatment.

**Patients and methods**

The 67 children included in our study were already participating in a large comparative monotherapy study of children with newly diagnosed epilepsy who had had regular measurements of anticonvulsant concentrations. Of the 67, 34 were boys (mean age 7.9 years, range 3-1-15.2 years) and 33 girls (mean age 10.9 years, range 4.0-15.0 years) and 58 were white and nine Afro-Caribbean. The average duration of follow up was 3.1 years (range 0.9-5.4 years). Thirty three children had primary generalised epilepsy and 34 had partial seizures. Children were treated in accordance with the study protocol. Treatment began with a single drug in a fairly low dose calculated according to body weight, with subsequent increases until control of seizures was obtained or the anticonvulsant concentration reached the upper limit of the defined therapeutic range (Table 1). Children who failed to achieve control of seizures on treatment with a single drug were placed on polytherapy.

A standardised measure of height by two observers (BM and MM) and pubertal staging was recorded before treatment was begun (initial) and then at annual intervals; the most recent measurements have been taken as the end point for analysis (final).

Height data are presented in terms of standard deviation score (SDS), using known population measurements. This gives an indication of the stature of the subject relative to a normal population of that age. A value of 0 being average and + and – values representing degrees of tallness and shortness, respectively.

Skeletal maturity in 31 children (13 girls and 18 boys) was determined by one of us (CM) from radiographs of the left hand and wrist before treatment was begun and in 20 children at 12 months, 16 at 24 months, 11 at 36 months, seven at 48 months, and three at 60 months.

Statistical analysis of the height SDS at initial and final measurement was by comparison of mean values and 95% confidence intervals. Results are expressed as mean (SD).

**Results**

**Height SDS.** The height SDS for boys and girls at the initial and final examinations are shown in Table 2. There was no significant difference in these measurements compared with those of the normal population. The mean difference between initial and final height SDS for boys was 0.04 (95% confidence limits –0.12 to 0.19, t=0.47, df=33, p=0.64) and for girls was –0.07 (95% confidence limits –0.29 to 0.15, t=0.643, df=32, p=0.52).

**Table 2. Height standard deviation scores (SDS) for boys and girls with epilepsy treated with anticonvulsant drugs at initial and final examinations. Values are mean (SD).**

<table>
<thead>
<tr>
<th>Height SDS</th>
<th>Boys</th>
<th>Girls</th>
</tr>
</thead>
<tbody>
<tr>
<td>At initial examination</td>
<td>0.02 (1.1)</td>
<td>–0.03 (1.1)</td>
</tr>
<tr>
<td>At final examination</td>
<td>0.06 (1.2)</td>
<td>–0.10 (0.9)</td>
</tr>
<tr>
<td>△</td>
<td>0.04 (0.44)</td>
<td>–0.07 (0.6)</td>
</tr>
</tbody>
</table>

**Table 1. Treatment protocol for administration of anticonvulsant drugs to children with epilepsy.**

<table>
<thead>
<tr>
<th>Drugs given</th>
<th>No of patients</th>
<th>Drug dosage (mg/kg)</th>
<th>Drug concentration (mg/ml)</th>
<th>Mean during treatment</th>
<th>Range</th>
<th>Therapeutic range</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Initial</td>
<td>Increment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbamazepine (CMZ)</td>
<td>21</td>
<td>8</td>
<td>4</td>
<td>5</td>
<td>8</td>
<td>1.4-18.3</td>
</tr>
<tr>
<td>Phenytoin (DPH)</td>
<td>19</td>
<td>5</td>
<td>2</td>
<td>7</td>
<td>1</td>
<td>2.0-38</td>
</tr>
<tr>
<td>Sodium Valproate (SV)</td>
<td>9</td>
<td>15</td>
<td>5</td>
<td>53</td>
<td>3.6-144</td>
<td>50-100</td>
</tr>
<tr>
<td>Ethosuximide (ESM)</td>
<td>3</td>
<td>15</td>
<td>5</td>
<td>32</td>
<td>25.3-26.5</td>
<td>50-100</td>
</tr>
<tr>
<td>Phenobarbitalone (PB)</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>13-4</td>
<td>12.8-18-6</td>
<td>20-40</td>
</tr>
<tr>
<td><strong>Patients on polytherapy</strong></td>
<td>12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SV+CMZ</td>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SV+CMZ+DPH</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SV+ESM</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SV+ESM+CMZ</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CMZ+DPH+Clozaam</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Anticonvulsant drugs, growth, and development

There was a trend towards earlier skeletal maturity in the girls, but this did not influence final height. Separate examination of children with partial seizures, those taking monotherapy, children with persistent seizures, and a small number on polytherapy, again produced no evidence of deviant growth patterns.

Some of the previously reported findings were possibly related to adverse environmental factors, high seizure frequency, or subclinical drug toxicity.

We thank Dr E H Reynolds and Dr B Neville for allowing us to study their patients.

References


Correspondence to Dr B M MacArdle, Newcomen Centre, Guy's Hospital, St Thomas' Street, London SE1 9RT.

Received 12 December 1986

Age distribution of anginose mononucleosis

Z SPIRER, M HOLTZMAN, I MELAMED, AND I SHALIT

Department of Paediatrics, Rokach Hospital, and Department of Paediatric Immunology, Tel-Aviv University, Tel-Aviv, Israel

SUMMARY The age distribution of anginose infectious mononucleosis in children was analysed retrospectively for the years 1966–85. During that period the disease became significantly more common in children of a young age and less common in older children. This shift could not be attributed either to socioeconomic conditions or to the diagnostic methods used.

The clinical and epidemiological range of infectious mononucleosis (IMN) has been appreciated only in the past decade, since the introduction of specific serological tests. Infection during infancy and childhood is usually subclinical, whereas the classical clinical manifestations are common among adolescents and young adults. It has been reported that infection generally occurs at an earlier age in low socioeconomic groups, where overcrowding and poor hygiene prevail.

One of the clinical presentations of IMN is the anginose type. Although this is said to be more prevalent in older children and adolescents, we have

Sexual maturity.

Girls

Of the 33 girls, seven had their menarche before starting medication (mean age 12-0 years, range 9-9–14-1 years), 11 girls were prepubertal, and the remaining 15 had their menarche while on treatment (mean age 13-4 years, range 11-3–15-3 years). The normal mean age for menstruation is 13-0 years. The pubertal ratings as determined at the last visit did not deviate from the normal pattern.

Boys

In the group of 34 boys, four were in puberty before starting treatment. 14 were prepubertal, 16 entered puberty while on treatment (mean age for penis stage II 11-3 years, range 8-5–14-3 years; mean for population 12-0 years; and mean age for pubic hair stage II 13-1 years, range 11-3–14-2 years; mean for population 12-5 years).

Skeletal maturity

There was a trend for girls to show slightly earlier skeletal maturity than is normal, although the maturity scores were still within normal limits. The skeletal maturity in boys was normal.

Discussion

These results show that children with epilepsy on anticonvulsant drugs for a mean of three years (range 0-9–5-4 years) grow and mature normally. We found no significant difference from the normal timing of the menarche or of onset of puberty.