Although there is little doubt that the response of young infants to bronchodilators is less good than that of older children, I think that in the acute stage a substantial number of them do benefit and it is worth a trial.

References

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Dr Milner and co-workers comment:

We were interested to hear of Dr König’s experience with nebulised salbutamol in children under one year. We accept that all our studies were carried out during the recovery phase but we have not found that any child under one year has obtained any useful, clinical benefit from nebulised salbutamol when administered in the acute phase. Since our paper was published, two children between the ages of 12 and 18 months have responded well, and we have since heard of another who apparently obtained benefit by age 11 months. We still recommend that salbutamol be given to all wheezing children over one year but think it unlikely that many children younger than this will respond to this form of treatment.

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Intrathecal ATS and high dosage diazepam in neonatal tetanus

Sir,

We should like to make a few comments about the report by Khoo et al. (Archives, 1978, 53, 737). Seven of the 19 neonates studied required total paralysis with IPPV for uncontrolled spasms, 2 died, and 5 more might have died but for total paralysis and IPPV. Therefore, it is not justified to say that improved survival was due to administration of high doses of diazepam alone.

Recently we initiated a study on the efficacy of a regimen consisting of intrathecal administration of anti-tetanus serum (ATS), and high doses of diazepam (15–30 mg/kg per day) and chlorpromazine (15–30 mg/kg per day) intravenously.

Between July and October 1978, we studied 10 neonates (Table). Diagnosis was on clinical grounds, and severity was graded using the criteria of Patel and Joag (1959).

Immediately after admission an IV line was established and diazepam administered at the rate of 1 mg/kg per minute until the infant was free of spasm and rigidity. This was followed by administration of ATS, 250 IU intrathecally, and 1500 IU IV. Penicillin and gentamicin (5 mg/kg per day) were given. Infants were nursed in the paediatric ward. The umbilical cord was cleaned with spirit, and painted with gentian violet routinely. Pharyngeal suction was done at regular intervals.

Subsequent muscle relaxation was achieved by alternate IV administration of 2·5–7·5 mg diazepam and chlorpromazine, each at 2–4 hourly intervals (total daily dose of each drug 15–30 mg/kg). Once spasms had been controlled, a nasogastric tube was inserted for feeding and giving diazepam and chlorpromazine. Sedation was gradually tapered off at a rate of 10–15% of total dose administered at intervals of 1–2 days, depending on the degree of hypotonia. None of the infants was given IPPV with total paralysis.

Eight neonates recovered completely and 2 died, one of fulminant bronchopneumonia and the other with aspirant pneumonia. The average duration in hospital for the survivors was 20 days, and the average period for IV diazepam and chlorpromazine 3·4 days. We observed that the shorter the interval between the onset of the tetanus neonatorum and the intrathecal ATS, the quicker

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**Table. The 10 neonates* studied**

<table>
<thead>
<tr>
<th>Case</th>
<th>Gestational weight (kg)</th>
<th>Age at onset (days)</th>
<th>Instrument for cord cutting</th>
<th>Grade</th>
<th>Spasm controlled (hours)</th>
<th>Duration of sedation (days)</th>
<th>Hospital (days)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2-8</td>
<td>6</td>
<td>Blade</td>
<td>V</td>
<td>48</td>
<td>20</td>
<td>30</td>
<td>Recovered</td>
</tr>
<tr>
<td>2</td>
<td>2-6</td>
<td>6</td>
<td>Blade</td>
<td>V</td>
<td>48</td>
<td>7</td>
<td>13</td>
<td>Recovered</td>
</tr>
<tr>
<td>3</td>
<td>2-7</td>
<td>5</td>
<td>Razor</td>
<td>V</td>
<td>9 days</td>
<td>25</td>
<td>25</td>
<td>Recovered</td>
</tr>
<tr>
<td>4</td>
<td>3-0</td>
<td>9</td>
<td>Scissors</td>
<td>IV</td>
<td>24</td>
<td>12</td>
<td>12</td>
<td>Recovered</td>
</tr>
<tr>
<td>5</td>
<td>2-0</td>
<td>36 weeks</td>
<td>Scissors</td>
<td>V</td>
<td>Not controlled</td>
<td>—</td>
<td>—</td>
<td>Died 50 hours after being admitted</td>
</tr>
<tr>
<td>6</td>
<td>2-4</td>
<td>7</td>
<td>—</td>
<td>V</td>
<td>36</td>
<td>9</td>
<td>10</td>
<td>Recovered</td>
</tr>
<tr>
<td>7</td>
<td>2-1</td>
<td>6</td>
<td>Kitchen knife</td>
<td>V</td>
<td>Not controlled</td>
<td>—</td>
<td>—</td>
<td>Died</td>
</tr>
<tr>
<td>8</td>
<td>2-8</td>
<td>7</td>
<td>—</td>
<td>V</td>
<td>72</td>
<td>19</td>
<td>20</td>
<td>Recovered</td>
</tr>
<tr>
<td>9</td>
<td>3-0</td>
<td>7</td>
<td>—</td>
<td>V</td>
<td>48</td>
<td>10</td>
<td>11</td>
<td>Recovered</td>
</tr>
<tr>
<td>10</td>
<td>2-7</td>
<td>6</td>
<td>Blade</td>
<td>V</td>
<td>120</td>
<td>30</td>
<td>40</td>
<td>Recovered</td>
</tr>
</tbody>
</table>

*All were term except for Cases 5 and 6.
was the control of spasm and the shorter the duration in hospital. Besides thrombophlebitis at the site of venepunctures (probably secondary to benzoic acid present in injectable diazepam) a common complication was apnoea, which responded to partial withdrawal of diazepam. At 3–4 months all 6 neonates who returned for follow-up were developmentally normal.

We feel a combination of high doses of diazepam and chlorpromazine with intrathecal ATS (given early after onset of tetanus) is effective in reducing mortality.

Reference


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Dr Khoo and co-workers comment:

We did not claim that the low mortality rate in our patients with neonatal tetanus was due to high dose diazepam alone. Other equally important therapeutic measures that contributed to the improved survival rate in our patients included good nursing care, tetanus antitoxins, antibiotics, nutritional support, and the judicious use of sedatives. In our study, the use of continuous high dose IV diazepam (20–40 mg/kg per day) certainly decreased the mortality rate and also the need for artificial ventilation from 77 to 37% (Khoo et al., 1978).

The treatment regimen advocated by Singh and Singhi is very similar to ours except for the use of intrathecal ATS and the very high dose of chlorpromazine. The role of intrathecal ATS in the management of neonatal tetanus is still controversial (Laurence, 1975). The reason for injecting ATS into the CSF is to neutralise the tetanus toxin that has penetrated the CNS but has not yet begun to act. Besides, ATS given via the IV route penetrates the blood/CNS barrier poorly, and the levels of antitoxin in the CSF are approximately 400 times less than in the blood (Patel et al., 1963; Ildirim et al., 1969).

In 1917, Sherrington obtained good results from the use of intrathecal ATS in monkeys with tetanus. It was subsequently tried in man but eventually abandoned because of adverse reactions to the CNS and doubts about its efficacy (Dietrich, 1940; Pratt, 1945). However, recent reports of the use of intrathecal ATS in tetanus are encouraging (Ildirim, 1970; Sanders et al., 1977; Salimpour, 1978). Ildirim (1970) treated 28 cases of neonatal tetanus with intrathecal ATS and prednisolone mixture and had a low mortality rate of 10.7%. In another clinical trial on 322 cases of adult-type tetanus, 200 units intrathecal ATS (horse) was found to be an effective adjuvant in reducing the mortality rate from 14.5 to 4.5% (Sanders et al., 1977). No complication was encountered apart from occasional difficulty in giving ATS intrathecally, while remarkable relaxation was observed in the patients.

With the availability of human antitetanus serum, which is relatively free of allergic side effects and less irritating to the CNS, the prospects for intrathecal ATS (human) is promising, but needs further tests before it can be recommended.

References


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