THE MANAGEMENT OF NEONATAL TETANUS


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INTRODUCTION

TETANUS, in particular neonatal tetanus, is a major problem in many developing countries. The global incidence of neonatal tetanus has been estimated to be in the order of one million cases annually and it accounts for more than 30% of total neonatal deaths in certain communities (Gordon, 1961; Marshall, 1968; Schofield et al., 1961; and Tompkins, 1958). In Malaysia, although the incidence of neonatal tetanus has declined progressively through a more efficient antenatal immunization programme and improvement in the delivery of trained obstetric care, the disease is still encountered occasionally. During the period between January 1969 and June 1977, 62 cases of neonatal tetanus were admitted to the University Hospital, Kuala Lumpur. With conservative drug therapy, the mortality rate for this serious illness has been reported to be as high as 90 per cent (Adams et al., 1966; Marshall, 1968; and Low, 1961). The introduction of total paralysis with intermittent positive pressure ventilation regime in the management of neonatal tetanus has reduced the mortality rate to about 20 to 40 per cent (Symthe et al., 1974; Ganendran, 1974). Both these methods of treatment have been employed at the University Hospital. This paper reports our experience in the management of this disease.

PATIENTS

The diagnosis of neonatal tetanus was made on the characteristic clinical findings: trismus, risus sardonicus, muscular rigidity, and spasms of voluntary muscles. All infants below the age of 28 days presenting with at least 3 of the above features were included in the study. Whenever doubt existed as to the diagnosis, lumbar puncture was performed to exclude purulent meningitis. In addition, blood calcium, magnesium and glucose levels were estimated to ensure that convulsions were not related to these metabolic disturbances. The severity of tetanus was graded according to the criteria of Patel and Joag (1959), one point being awarded to each of the following:

(a) incubation period \( \leq 7 \) days

(b) inability to suck

(c) presence of muscular spasms

(d) onset of spasms occurring within 48 hours of first symptom

(e) rectal temperature \( \geq 100^\circ F \) within 24 hours of admission.

Of the total group, 89% of patients belonged to grades IV and V. Table I summarises the relationship between severity of illness and mortality rate.

TREATMENT

General measures: Upon admission, most patients required urgent relief of their muscular rigidity and spasms. This was accomplished by a slow intravenous injection of diazepam (Valium) in a dose of 5–10 mg. Once relaxation was achieved, the umbilical stump was excised and all septic wounds were cleansed with hydrogen peroxide and surgical spirit. An intravenous infusion was then set up in a peripheral vein and subsequently all drugs were
Table I
The relationship between severity of neonatal tetanus and mortality rate

<table>
<thead>
<tr>
<th>Severity of illness</th>
<th>No. of patients</th>
<th>No. of patients requiring IPPV</th>
<th>Mortality rate %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade I</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Grade II</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Grade III</td>
<td>6</td>
<td>3</td>
<td>16.6</td>
</tr>
<tr>
<td>Grade IV</td>
<td>29</td>
<td>15</td>
<td>13.9</td>
</tr>
<tr>
<td>Grade V</td>
<td>26</td>
<td>22</td>
<td>23.1</td>
</tr>
<tr>
<td>Total</td>
<td>62</td>
<td>40</td>
<td>16.1</td>
</tr>
</tbody>
</table>

either administered intravenously or through a nasogastric tube; intramuscular injections were avoided. The infant was nursed in an Isolette incubator (Fig. 1). This provided a constant environment and allowed frequent visual observations to be made with minimal disturbance to the patient. In monitoring, particular attention was paid to the pulse rate, respiratory rate, colour and frequency and severity of muscular spasms. A clear airway was ensured by periodic change of posture and by naso and oropharyngeal suction whenever secretions accumulated. Urine collection was made on small urine bags sealed over the perineum and the daily output was measured. Gentle compression over the suprapubic region was at times necessary to aid voiding of urine; in no case was bladder catheterisation required. Eye toilet was performed daily with sterile saline solution and chloramphenicol ointment was instilled several times a day. Saline enema was prescribed when facal masses were present on abdominal palpation. As a rule, the patients were nursed in the open ward near the nurses' station, and only senior doctors and trained staff nurses were involved in their management.

![Fig. 1. Neonate with tetanus nursed in an incubator. The infant is heavily sedated through a continuous intravenous infusion of diazepam.](image)

**Antibiotics and tetanus antitoxin:** All patients received crystalline penicillin in a daily dose of 100,000 to 400,000 units divided into 2 to 4 intravenous injections for a period of 7 to 10 days. A broad spectrum antibiotic, effective against gram-negative organisms (e.g. kanamycin or gentamicin), was added if pneumonia or other septic complications occurred. There was no consistent regime for serotherapy. Generally, these infants were given 1,000 to 40,000 units of equine anti-tetanus serum without prior test dose. Eight infants, however, did not receive any tetanus anti-serum.

**Sedation:** In the first group of 43 patients, muscle relaxation and sedation were achieved by systemic diazepam (2–10 mg/kg/day in 4 divided doses) and intragastric phenobarbitone (5–8 mg/kg/day in 4 divided doses). If spasms occurred despite the above basal medication, bolus doses of 2–5 mg of intravenous diazepam were administered. Failure to control spasms after 2 to 4 additional doses of diazepam were regarded as indication for curarisation and maintenance of respiration by intermittent positive-pressure ventilation (IPPV). Of the 43 patients in this group, 33 subsequently required the latter form of treatment.

In the second group of 19 patients, the maintenance dose of diazepam used was increased to 20–40 mg/kg/day and that of phenobarbitone to 10–15 mg/kg/day. It was observed that convulsions were often stimulated during intravenous injection of 'push' doses of diazepam. To circumvent this problem, the total daily dose of diazepam was suspended in dextrose-saline solution and administered as a continuous intravenous infusion. During the period of parenteral therapy, care was taken to ensure that the percutaneous intravenous needle was not dislodged as skin necrosis can result from subcutaneous perfusion of the drugs. Tetanic convulsions tended to increase during the initial 2 to 5 days after hospitalisation and the dose of diazepam was gradually increased to a maximum of 40 mg/kg/day according to patients' requirement. Additionally, 2–5 mg of diazepam was given intravenously in between therapy if spasms were severe and frequent. A few patients had distressing hiccups that often provoked continuous spasms; this was effectively controlled by 2–5 mg of intravenous chlorpromazine. Once spontaneous spasms had ceased, the dose of diazepam was reduced every third day by approximately 10% of the previous dose. Should spasms recur, the last effective dose was restored. As soon as the patient could tolerate nasogastric feeding, all drugs were administered via this route. In the majority of patients this was achieved after 5 to 10 days of parenteral therapy. Of the 19 patients who received the second treat-
ment regimen, 7 ultimately required assisted ventilation. The indication for IPPV was similar to that of the first group.

**Total paralysis with IPPV:** This was reserved for those infants in whom conservative therapy failed to control spasms and apnoeic episodes became life-threatening. Forty infants received IPPV during the eight and a half year period. Eighty-five per cent of them required this form of treatment within 24 hours of admission. These infants were transferred to the intensive care unit of the same hospital where nursing care was provided by trained staff nurses on the basis of one nurse per patient per shift. All previous sedatives were discontinued and tubocurarine was employed to provide muscle relaxation. The patients were intubated with a Jackson-Rees nasotracheal tube (Rees and Owen-Thomps 1966) and IPPV was maintained using a volume-cycled respirator. Tracheostomy was performed in 3 patients. The duration of artificial ventilation ranged from 2 to 52 days (mean 18.8 days). Details of the anaesthetic care provided and the hazards of treatment encountered have been reported elsewhere (Ganendra, 1974).

**Feeding:** Fluid and electrolyte balance was maintained by intravenous fluids during the first 48 hours when there was an increased risk of aspiration consequent on uncontrolled convulsions and intestinal ileus. Thereafter, nasogastric feeding was introduced with 5% glucose solution. The stomach was aspirated before each feed; milk feeds were not started until there was no residue. If gavage feeding was not established by the third day, additional nutrition was provided intravenously by 7.5–10% dextrose solution, amino acid infusion (Sohamin G 20 ml/kg/day), vitamins and lipids (Intralipid 2–4 gm/kg/day). The acid-base status, urea, glucose and electrolyte levels were determined twice weekly during the period of intravenous therapy.

**Tetanus toxoid:** Patients who recovered from tetanus received a full course of tetanus toxoid as the disease does not confer long-term immunity.

**RESULTS**

Fifty-two patients survived the illness. The mortality rate was 16.1 per cent. One infant died from asphyxia soon after arrival at the University Hospital and another succumbed at the age of 3 months from complications of tracheostomy. Respiratory failure from tension pneumothorax or extensive bronchopneumonia was the cause of death in the remaining 8 patients; all had previously received IPPV. Among the survivors, the average time taken to re-establish complete oral feeding was 33.4 days; the mean period of hospitalisation was 43 days. Thirty-one patients had at least one follow-up evaluation after discharge. Of these, 5 showed clinical evidence of neurological or developmental impairment. Neurological damage was probably the result of brain anoxia from asphyxiating laryngeal spasms and apnoeic spells rather than from the effects of tetanus toxin.

**DISCUSSION**

Neonatal tetanus is an entirely preventable disease. Improving the level and acceptance of obstetric and post-natal care will reduce but not preclude the occurrence of neonatal tetanus. A far more effective and economical method of prevention is through active immunisation of pregnant mothers. Standfield and Gall (1970) has documented that 2 doses of absorbed toxoid in the antenatal period afford complete protection against neonatal tetanus. Until universal antenatal immunisation becomes a reality, however, the clinician will continue to be confronted with the problems in the management of this disease.

The treatment of tetanus should be directed to several goals: elimination of organisms producing the toxin; neutralisation of any circulating toxin; provision of skillful care to prevent death from tonic seizures while the fixed toxin is being metabolised in the body. The first two aims can be accomplished by antibiotics, surgical excision of the wound, and by administration of antitoxin. Penicillin effectively kills the vegetative forms of Cl. tetani. In order to be effective, the antibiotic must reach the multiplying bacilli, so that if there is a large area of necrotic tissue into which penicillin cannot reach, treatment may fail unless surgical debridement is adequate. The therapeutic effect of antitoxin depends on the neutralization of toxin that is passing from the wound to be taken up by the neural tissue. Antitoxin cannot reverse the effects of the toxin once it has penetrated into the central nervous system (Webster and Lawrence, 1963). The value of antitoxin is thus limited and clinical trials have suggested that administration of 10,000 units of equine tetanus antitoxin is sufficient for treatment (Vakil et al., 1968). Human antitetanus immunoglobulin is preferable to the equine preparation (Editorial, Lancet, 1974) because of its relative freedom from allergic side-effects and from risk of immune elimination. The value of human antiserum injected intrathecally into the cerebrospinal fluid is currently being investigated (Ilidirim, 1972).

Until an agent becomes available which can displace tetanus toxin from the neural tissue or can effectively antagonise its actions, treatment must remain symptomatic. In a disease which needs
almost continuous observations and therapeutic modification until recovery, it is hardly surprising that the most important contributory factor towards success in treatment is the quality of the nursing care (Smythe et al., 1974). This can only be provided for on a 24-hour basis in major hospitals, so that treatment of tetanus is best confined to these medical centres. In addition, all current therapeutic regimes of proven value carry with them serious hazards in the hands of the inexperienced.

Curarization with IPPV was the mainstay of treatment for tetanus, at the University Hospital until 1973 (Ganendran, 1974). The mortality rate was 23% among 34 patients treated. Although the mortality rate was low, one or more serious therapeutic complications, viz., pneumothorax, pulmonary atelectasis, bronchopneumonia, blocked endotracheal tube, apnoea and cardiac arrest from mechanical failure of the respirator occurred in almost every patient. In addition, strained facilities and the prohibitive cost of treatment from prolonged mechanical ventilation, prompted us to seek an alternative form of therapy.

Diazepam was first used successfully in tetanus by Weinberg (1964). Hendrickse and Sherman (1966) subsequently reported the use of this muscle relaxant in 53 patients with neonatal tetanus. In their experience, although diazepam (up to 4.4 mg/kg/day), was useful as an adjunct for relieving muscle spasms, the mortality rate of 53%, when employing other drugs for sedation, was not improved upon. Our experience with low dosage of diazepam (<10 mg/kg/day) in neonatal tetanus has been similarly disappointing; 76.7% required curarization with IPPV after initial trial of diazepam. The introduction of large doses of diazepam (20-40 mg/kg/day) in treatment, reduced the rate of therapeutic failure to 36.8 per cent. However, in our experience, increasing the dose beyond 30 mg/kg/day did not significantly reduce the failure rate. Diazepam is not soluble in water and forms a fine precipitate when diluted in infusion fluid. This does not however cause a reduction in its therapeutic potential nor does it result in any adverse reaction (Smith and Masotti, 1971). The major side effects of this form of treatment was the induction of severe drowsiness and coma. In these patients there was a constant risk of inhalation and asphyxia from pooling of secretions, so that the most meticulous nursing care must be provided. Respiratory arrest is another potential hazard (McMorris and McWilliam, 1969). However, in our patients, the continuous infusion of diazepam did not seriously depress respiration nor did it adversely affect the hepatic, haematological or renal function. Upon withdrawal of the drug, consciousness was gradually regained and in patients who did not suffer prolonged episodes of cerebral anoxia, the subsequent neurological and developmental growth had progressed normally. The judicious use of high dosage continuous intravenous infusion of diazepam will thus reduce but will not eliminate the need for total paralysis with IPPV in the treatment of neonatal tetanus. Clearly, the search for more effective muscle relaxants and sedatives must continue.

**SUMMARY**

This paper reports our experience in the management of 62 cases of neonatal tetanus at the University Hospital, Kuala Lumpur. In the first group of 43 patients, relaxation of rigidity and muscle spasms was achieved by the intermittent administration of phenobarbitone (5-8 mg/kg/day) and diazepam (2-10 mg/kg/day). In a latter group of 19 patients, diazepam was administered as a continuous infusion in a daily dose of 20-40 mg/kg body weight. When conservative drug therapy failed to control the spasms, total paralysis and intermittent positive-pressure ventilation was instituted (IPPV). It was observed that the use of continuous diazepam infusion reduced significantly the proportion of patients that subsequently required IPPV. Problems related to these forms of therapy are discussed. The overall mortality rate was 16.1%. Among the survivors, 16.3% had significant neurological sequelae at follow-up evaluation.

**REFERENCES**


