Intrathecal serotherapy in neonatal tetanus:  
a controlled trial

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SUMMARY  60 infants with neonatal tetanus were treated at random either by 40 000 units of equine  
tetanus antitoxin (TAT), intravenously and intramuscularly, or by 40 000 units TAT, IV and IM,  
plus 150 units of human tetanus immune globulin (TIG) intrathecally. There were 30 infants in each  
treatment group. Babies were similar in age, sex, weight, incubation period, temperature, and  
signs and symptoms on arrival at the hospital. The mortality rate, days in hospital, and days of  
sedation were not significantly different in the two groups.

Tetanus is still a major health problem in developing countries both in incidence and mortality. The  
mortality is particularly high in neonates (Nourmand et al., 1970; Salimpour, 1977).  
Although equine tetanus antitoxin (TAT) has been used to treat this disease for many years, the  
preferred dose, efficacy, and route of administration are not clear (Brown et al., 1960; Athavale and  
Pai, 1966). The present tendency is to give a single dose of TAT initially (McCracken et al., 1971). In  
children 20 000 to 100 000 units have been used (Spaeth, 1941; Brown et al., 1960). It was  
suggested that intrathecal administration of tetanus immune globulin (TIG) together with  
corticosteroids reduced the mortality in neonates (Ildirim, 1967, 1974). The purpose of this report  
is to evaluate intrathecal administration of 150 units of TIG without corticosteroids in the  
treatment of tetanus neonatorum.

Patients and methods

During the 50-month period from January 1974 to  
February 1978, 64 newborn infants with the clinical  
diagnosis of tetanus were admitted to the newborn  
unit of Nemazee Hospital, Shiraz, Iran. This unit  
adopts all sick neonates from Shiraz and the sur-  
rounding area, altogether a population of about  
600 000. The diagnosis was made clinically by  
M.R.S.

All newborn babies in this prospective study were  
alternately assigned to one of two treatment groups.  
The control group received 20 000 units of TAT IV  
and 20 000 units IM in the first few hours after  
admission. The study group received the same  
amount of TAT by the same routes, plus 150 units  
of TIG intrathecally.

Blood cultures and spinal taps were performed in  
both groups of babies.

Valium (15 mg/kg per day) was given initially  
intravenously and then by nasogastric tube. If the  
valium failed to control the convulsions, chlorpro-

mazine (Largactil) 2–3 mg/kg per day was added.

Initially, all babies were given benzylpenicillin  
50 000 to 100 000 units/kg per day and gentamicin  
5 to 6 mg/kg per day in two divided doses. Benzyl-
penicillin was continued for 10 days, but gentamicin  
was stopped after 5 days if the spinal fluid and blood  
cultures remained negative.

Each infant was admitted to a separate room.  
The umbilical area was thoroughly cleaned. Naso-

gastric tube feeding was initiated as soon as the  
baby's convulsions were under control.

Age, sex, weight, incubation period, rectal  
temperature, clinical symptoms, and signs of  
pneumonia were recorded for each baby at the time  
of admission. Days in hospital, days to death, days of  
sedation, and mortality for both treatment groups  
were recorded.

Results

Of 64 neonates with the clinical diagnosis of tetanus,  
60 were admitted to the trial, 30 in each treatment  
group. Four patients were excluded within the first  
3 days: 2 because of associated meningitis and 2  
because they had received some TAT before arrival  
at the hospital.
All infants had been delivered at home with the help of unqualified midwives. 14 (23 %) of 60 were from Shiraz and the rest came from villages nearby.

There were 2 preterm babies and one term small for gestational age (SGA) infant in the control group, and one term SGA infant in the study group. Table 1 shows the main signs and symptoms in these babies on admission. Table 2 compares various characteristics in the two groups.

The two groups were comparable for sex, age, weight, incubation period, temperature on admission, days in hospital, days of sedation, days to death, and number dying. There was no significant difference in survival rate between the two groups.

There were 2 babies, one in each group, who recovered from tetanus but died from other causes. One died 60 days after admission from gastroenteritis, urinary tract infection, and hydrenephrosis and the other baby died 30 days after admission from hepatitis and septicemia. The days to death for these 2 patients are excluded from the analysis.

### Table 1  Signs and symptoms in both groups of babies on admission

<table>
<thead>
<tr>
<th>Signs and symptoms</th>
<th>Study group</th>
<th>Control group</th>
<th>Total (n = 60)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refusal to feed</td>
<td>29 (97)</td>
<td>29 (97)</td>
<td>58 (97)</td>
</tr>
<tr>
<td>Convulsion (tetric spasm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>followed by clonic movement</td>
<td>28 (93)</td>
<td>28 (93)</td>
<td>56 (93)</td>
</tr>
<tr>
<td>Trismus</td>
<td>27 (90)</td>
<td>26 (87)</td>
<td>53 (88)</td>
</tr>
<tr>
<td>Generalised rigidity on arrival</td>
<td>28 (93)</td>
<td>22 (73)</td>
<td>50 (83)</td>
</tr>
<tr>
<td>Cyanosis</td>
<td>18 (60)</td>
<td>20 (67)</td>
<td>38 (63)</td>
</tr>
<tr>
<td>Irritability</td>
<td>18 (60)</td>
<td>16 (53)</td>
<td>34 (57)</td>
</tr>
<tr>
<td>Respiratory distress</td>
<td>17 (57)</td>
<td>12 (40)</td>
<td>29 (48)</td>
</tr>
<tr>
<td>Opisthotonus on arrival</td>
<td>15 (50)</td>
<td>14 (47)</td>
<td>29 (48)</td>
</tr>
<tr>
<td>Poor reflexes</td>
<td>5 (17)</td>
<td>5 (17)</td>
<td>10 (17)</td>
</tr>
<tr>
<td>Rius sardonicus</td>
<td>2 (7)</td>
<td>2 (7)</td>
<td>4 (7)</td>
</tr>
</tbody>
</table>

Percentages are given in brackets.

### Table 2  Summary of various characteristics of the two groups

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Study group (n = 30)</th>
<th>Control group (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>13 (43)</td>
<td>15 (50)</td>
</tr>
<tr>
<td>Age on admission (days)</td>
<td>9.5 ± 8.5*</td>
<td>8.9 ± 7.8*</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>26 (87)</td>
<td>25 (83)</td>
</tr>
<tr>
<td>Female</td>
<td>4 (13)</td>
<td>5 (17)</td>
</tr>
<tr>
<td>Weight (g)</td>
<td>3025 ± 906*</td>
<td>2878 ± 995*</td>
</tr>
<tr>
<td>Incubation periods</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;7 days</td>
<td>22 (73)</td>
<td>21 (70)</td>
</tr>
<tr>
<td>8-14 days</td>
<td>8 (27)</td>
<td>9 (39)</td>
</tr>
<tr>
<td>Rectal temperature on admission</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;37°-5°C</td>
<td>13 (43)</td>
<td>13 (43)</td>
</tr>
<tr>
<td>37°-5-39°-0°C</td>
<td>11 (37)</td>
<td>11 (37)</td>
</tr>
<tr>
<td>&gt;39°-1°C</td>
<td>6 (20)</td>
<td>6 (20)</td>
</tr>
<tr>
<td>Days in hospital for survivors</td>
<td>26.7 ± 19.6*</td>
<td>26.8 ± 28.5*</td>
</tr>
<tr>
<td>Days sedated for survivors</td>
<td>21.8 ± 12.7*</td>
<td>25.2 ± 14.4*</td>
</tr>
<tr>
<td>Days to death</td>
<td>5.2 ± 7.3*</td>
<td>6.4 ± 10*</td>
</tr>
</tbody>
</table>

Percentages are given in brackets.

*Mean ± 2 SD.

### Table 3  Mortality rate according to incubation period

<table>
<thead>
<tr>
<th>Incubation period</th>
<th>Study group (n = 30)</th>
<th>Control group (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Up to 7 days</td>
<td>11/22 (50)</td>
<td>13/21 (62)</td>
</tr>
<tr>
<td>8-14 days</td>
<td>2/8 (25)</td>
<td>2/9 (22)</td>
</tr>
<tr>
<td>Total mortality</td>
<td>13 (43)</td>
<td>15 (50)</td>
</tr>
</tbody>
</table>

Percentages are given in brackets.

The mortality rate according to incubation period is shown in Table 3. The death rate for incubation periods less than 7 days was slightly higher in the control group, 13 (62 %) of 21, than in the study group, 11 (50 %) of 22.

There were 12 (40 %) of 30 babies in the study group and 8 (27 %) of 30 in the control group who showed some sign of pneumonia on admission.

### Discussion

The intrathecal administration of TAT for treatment of tetanus began early in the 20th century. The first trial was by von Leyden in 1901, and then there were trials by Penna in 1902 and Rogers in 1905. Because of fatal complications of intrathecal TAT administration and no obvious change in survival rates, this treatment was stopped (Dietrich, 1940; Pratt, 1945).

Ildirim (1974) used intrathecal TAT or TIG, combined with corticosteroids, with good results in tetanus neonatorum. At the Fourth International Congress on Tetanus in 1975, it was felt that serious consideration should be given to this method of treatment (Furste, 1976). The amount recommended was a single injection of 250 units of TIG mixed with 12·5 mg prednisolone, given intrathecally. 2500 units of TAT were given both IM and IV, plus 10 mg prednisolone in two divided doses orally. A mortality rate between 14-8 and 20 % was reported (Ildirim, 1974). However, the relative importance of each component of this treatment remained to be established. Therefore, we used intrathecal TIG without corticosteroids, choosing a dose of 150 units because we were giving 40 000 units of TAT by other routes. The results in the study group showed no advantage in this treatment (Table 2).

As intrathecal TIG did not alter the mortality rate for this disease, good results in other studies may be attributed to corticosteroids, to a higher dose of intrathecal TIG, or possibly, to synergism. A controlled trial of intrathecal corticosteroids without TIG is now in progress.

Any conclusion about therapy must be guarded since Chen (1974) showed that good nursing care can reduce the mortality rate to 20 %.
I should like to thank Dr Paul A. Steinman for his useful suggestions and guidance in the preparation of this report, and Dr A. Madani for collecting some of the data.

References


Spaeth, R. (1941). Therapy of tetanus; a study of 276 cases. Archives of Internal Medicine, 68, 1133–1160.


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