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 Nemaze Hospital, Shiraz, Iran. This unit admits all sick neonates from Shiraz and the surrounding 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, chlorpromazine (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. Benzylpenicillin 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. Nasogastric 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 hydronephrosis 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.

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%.
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References


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