A Review of 207 Newborn with Tetanus

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Abstract

In this study, 207 patients with neonatal tetanus admitted to Erciyes University, Faculty of Medicine, Unit of Neonatology between 1.976 and 1994 were investigated retrospectively. One hundred and sixty-seven (80.6%) patients had non-hygienic home deliveries and none of the mothers of the children had been immunised with tetanus toxoid. Of the 207 patients, 161 (77.8%) were males, 46 (22.2%) were females. Failure to suck and twitching were the most frequent symptoms. The mean age of patients who died or survived was 6.9 and 8.8 days respectively (p0.05). Mean birth weight was 3092g for the fatal cases and 3317g for the survivors (p0.05). Ninety-seven (46.8%) of the 207 patients died. Mean age of death was 9.3 days and most of the patients died at the fifth day of admission to hospital. Sex, age on admission and duration of symptoms did not affect the prognosis. In addition, the efficacy of the diazepam, phenobarbital sodium and chiorpromazine used for sedation in neonatal tetanus was investigated. Of 207 patients, 43 patients were treated with diazepam, 33 patients with phenobarbital sodium, another 33 patients with phenobarbital sodium + chlorpromazine and 94 patients were treated with d iazepam +phenoba rbital sod ium± chlorprom azine called as “combined therapy”. The least mortality rate was found in the group treated with “combined therapy” and the highest mortality rate in the group treated with phenobarbital sodium+ chlorpromazine (p<0.001). The most frequent cause of death was apnea in the first week and sepsis in the later period (JPMA 48: 93, 1998).

Neonatal Tetanus (NT) is a major health problem in developing countries.It is the second most frequent cause of infant mortality among the six vaccine preventable infections in developing countries. However, lack of reliable data has largely obscured the importance of the problem in these countries[1]. The incidence of NT in developing countries ranges between 5 and 60 per 1000 live-births and in some areas, deaths from NT account for 30-72% of neonatal mortality[2]. Evety year approximately 250.0(J0 deaths occur from NT in countries where active immunisation is not universally practised[3]. Most newborns in the world are susceptible to tetanus because their mothers have not received two Of more doses of tetanus toxoid. It has been estimated that from 1986 to 1989, only 15-25% of pregnant women in developing countries received at least two recent doses of tetanus toxoid[4,5]. The prevalence of the immunisation coverage of mother who received two injections for tetanus toxoid is 3.4% in our country[6]. However, the incidence of NT is unknown because the medical records of the patients with NT were inadequate in Turkey. in the treatment of NT, anti-tetanus serum and crystalline penicillin are used. In additioti to, diazepam. Pancuroniuni bromide and meprobamate used for control of spasms[7]. In this study, the patients with NT were reviewed and evaluated to identify the possible factors affecting prognosis of NT. Inaddition, the patients were evaluated according to the efficiencies of diazepam, phenobarbital sodium (PNB) and/or chiorpromazine (CPZ) used for sedation and the relationship between the mortality rate and treatment protocols was investigated.

Patients and Methods

Two hundred and seven cases of NT were admitted to the newborn unit of Erciyes University,

Department of Pediatrics between 1976 and 1994. In this retrospective study, the relevant data were obtained from medical records and patients' charts with hospital discharge codes indicating NT. In all cases, diagnosis was based on clinical findings. Blood glucose, calcium and magnesium were detennined in all patients.

All patients were kept in quiet, darkened rooms. Movement was kept to a minimum and all unnecessary handling was avoided. Intravenous fluids were given to maintain fluid and electrolyte balance until the patients were able to tolerate a nutrition tube.

All patients received crystalline penicillin 200.000 U/kg/24 hours, divided every 6 hours intravenously for 10 days and equine anti-tetanus serum (ATS) intramuscularly on admission. Subsequent infections were treated with antibiotics such as aininoglycoside or third-generation cephalosporin. The dose of ATS was 25.000 IU until 1979 and then the dose was decreased to 10.000 IU. In addition, pyridoxine (100 mg/day) was added to the therapy after 1982.

Conventional treatment consisted of the following:

Group 1: Diazepam was given 20-40 mgfkg/24 hr by nasogastnc tube. In the initial days of admission, it was given every 2 hours. Then the dose interval was increased to every
3-6 hours and it was stopped according to the receding severity of the spasms between 10 and 14 days.

Group 2: Phenobarbital sodium was given 5 mg/kg/24 hours 6 hourly intravenously for 10-14 days.

Group 3: Phenobarbital sodium (5 mg/kg/24 hr) and CPZ (2 mg/kg/24 hours) were given intravenously. Phenobarbital sodium was administered similarly as in group 2 and CPZ was given every 4 hours for 10- 14 days.

Group 4: Diazepam and PNB±CPZ were given the same as in groups 1 and 3.

Student's t-test was used for comparison of the means of continuous variables unmatched data and X^2 was used for multiple matched data.

Results

Of the 207 patients, 161 (77.8%) were males, 46 (22.2%) welt females and the male to female ratio was 3.5/1. The annual distribution of the patients and distribution of the cases according to sex are shown in Table I and II.

Table 1. Annual distribution of patients with neonatal tetanus.

Years	n
1976-1981	63
1982	14
1983	31
1984	15
1985	13
1986	16
1987	17
1988	9
1989	12
1990	6
1991	3
1992	4
1993	2
1994	2
Total	207

Table II. Distribution of patients according to sex and prognosis.

Males					Females					Male/Female
Survivors		Deaths		Total	Survivors		Deaths		Total	
No.	%	No.	%		No.	%	No.	%		
88	54.6	73	45.4	161	22	47.8	24	52.2	46	3.5/1

X^2: 0.695 $p>0.05$

Of the 161 boys, 73 (45.4%) and of the 46 girls, 24 (52.2%) died ($p>0.05$).

Distribution of the cases according to age, birth weight, age at onset of symptoms and the period between onset of symptoms and admission to hospital are shown in Table III.

Table III. Distribution of deaths and survivors according to age, birth weight and age at onset of symptoms.

	Deaths (n=97) Mean±SD	Survivors (n=110) Mean±SD	t	P
Age (days)	6.92±2.15	8.81±3.13	1.52	>0.05
Birth weight (g)	3092±403	3317±438	3.84	<0.01
Age at onset of symptoms (days)	5.58±0.50	6.54±2.07	3.87	<0.01
Mean period between onset of symptoms and admission to hospital (days)	1.58±1.51	2.11±2.31	1.66	>0.05

The age of the patients ranged from 3 to 19 days. The mean age of admission was 6.9 days forthe deceased and 8.8 days for the survivors (p>0.05). The mean birth weight was 3092 g for the fatal cases and33 17 gforthe survivors (p<0.05). Nine patients had a low birth weight (<2500 g), and six of them died. The mean age at onset of symptoms was 5.5 days for those who of symptoms (p>O.O5). Of 207 patients with tetanus, 43 were treated with diazepam, 33 were treated with PNB, another 33 with PNB + CPZ and 94 with diazepam + PNB ± CPZ called as "combined therapy" (Table VI).

Table IV. Instruments used in delivery and delivery place of the patients.

Instruments used in delivery and delivery place	n	%
At home		
Scissors	104	50.2
Razor	58	28
Knife	5	2.4
At hospital		
Sterile medical instrument	40	19.4
Total	207	100

The treatment protocol of the survivors and deaths is shown in Table VI.

Table V. Symptoms of the patients with NT.

Symptoms	Survivors		Deaths		Total	
	n	%	n	%	n	%
Failure to suck and twitching	74	67.2	68	70.1	142	100
Failure to suck	20	18.1	18	18.5	38	100
Fever	19	17.2	16	16.4	35	100
Jaundice	12	10.9	10	10.3	22	100
Twitching	10	9.0	7	7.2	17	100
Weeping	8	7.2	6	6.1	14	100
Abdominal fullness	3	2.7	2	2.0	5	100
Diarrhoea	2	1.8	2	2.0	4	100
Constipation	2	1.8	1	1.0	3	100
Vomiting	1	0.9	1	1.0	2	100

$p>0.05$

The least mortality rate was found in the group treated with "combined therapy" and the highest mortality rate was found in the group treated with PNB + CPZ.

There was statistically significant difference between the groups ($p<0.001$) and the combinedtherapy (diazepam+PNB+CPZ) was more effective than the others in the treatment of NT.

There was no statistical difference between the groups for the time of death (Table VII).

Table VI. Distribution of deaths and survivors in various treatment groups.

Drugs	Deaths		Survivors		Total	
	No	%	No	%	No	%
Diazepam	20	46.5	23	53.5	43	100
PNB	24	68.5	11	31.5	35	100
PNB + CPZ	31	88.5	4	11.5	35	100
Combined	22	23.4	72	76.6	94	100
Total	97	46.8	110	53.2	207	100

X^2: 51.85 $p<0.001$

PNB: Phenobarbital sodium, CPZ: Chlorpromazine.

The causes of death in the first week and in the later period are shown in Table VIII.

Table VII. Distribution of deaths time in various treatment groups.

Drugs	Death time: In the first week n	In the following period n	Total n	Total %
Diazepam	12	8	20	100
Phenobarbital	18	6	24	100
PNB + CPZ	16	15	31	100
Combined	8	14	22	100
Total	54	43	97	100

X^2: 7.32 P>0.05

PNB; Phenobarbital sodium, CPZ: Chlorpromazine.

The most frequent cause was apnea in the first week and sepsis in the later period without considering the treatment given.

The overall mortality rate was 46.8%. The mean age at death was 9.3 days and most of the patients died on the fifth day of admission to hospital. On the other hand, of 40 patients who delivered in a hospital , 20 died and of 167 patients who delivered at home, 77 expired (p>0.05).

Discussion

In most parts of the world, particularly in developing Countries, NT cases appear to be more cormnon in males than in females[8]. In Turkey, the ratio was reportedbetween 1.3 and 2.9 in the various series[6,9,11]. In accordance with these, the ratio was 3.5 in our series. Einterz et al[12] reported that cord care and sex were related with prognosis and death was more common in males than in females. However, Guises and Aydin[10] reported gender did not affect the prognosis in NT. In our study, although the umbilical cord had been separated by unsterile instruments in most of the patients, there was not any statistical difference between the groups who used sterile and unstcrile instruments. In addition, sex of the neonate did not affect the prognosis.

Our study indicated that the annual distribution of hospitalised NT patients had declined in recent years similarto results of other studies performed in Turkey[9,11]. The incidence of NT in Turkey is on the decline due to widespread tetanus toxoid use in pregnant women, an increasing number of hospital births and improvement in postpartum hygiene[12]. Age at onset, severity of illness, preterm birth, seconth7 infections and mode of treatment, all affect survival in NT[13,14]. In a study, authors reported an incubation period of 6 days or less was the strongest predictor of mortality[12]. In accordance with this, in our series, the age at onset of symptoms was 5.5 days for fatal cases and 6.4 days for survivors.

The mean period between onset of symptoms and admission to hospital is ranged between several hours and 15 days in various series[8]. In a study performed in Pakistan, this periodfound 3.2 days[15]. It is reportedbetween 1.2 days and 2.2 days in our country[6,9,11]. In our study, the mean period was 1.6 days (1.5 days for the deceased and 2.1 days for the survivors) (p>0.05). One hundred and sixty-seven (80.6%) of the 207 patients we studied, had unhygienic home deliveries and most of the patients were delivered by inexperienced persons. In addition, none of the mothers of the children had been immunisedwith tetanus toxoid. Similar studies from Turkey indicate that most of the infants were delivered under such circumstances and delivered from mothers who lacked adequate tetanus

immunisation[6,9,11].

It is reported that 9.3% to 19.9% of the cases with NT were delivered at clinics in Turkey[6,9,11]. The ratio was 11% in Mexico city[16]. It was 19.5% inourstudy, but on the other hand, we have noted that home delivery or hospital delivery, did not affect the mortality. In some rural areas of Turkey, the babies are traditionally wrapped in soil for a few weeks after birth. It was observed that in general, the ratio of wrapping in soil was 12.5% in Turkey[17]. This practice is accepted as a high risk factor for NT and in our countçy was found to be prevalent in 58.5-76% children with NT[6-11]. In our series, the ratio was 56.5% but it did not affect the mortality.

It has been reported that deaths from NT were more frequent in premature and low birth weight infants and there was a statistically significant difference in mean birth weight

•between survivors and deceased[18], in our series, mean birth weight of the neonates who died was lower than survivors ($p<0.05$) and 6 of 9 patients who had low birth weight died. The case fatality rate of NT ranges between 25-90% with therapy, depending on the intensity of supportive care[19]. In a study performed in France, the mortality rate was reported to be 71 %20, In our study, the overall case fatality rate was 46.8% which is compatible with the reports from other centres in Turkey[9-11]. In a series which consisted of 228 cases with NT, the mean age at death was found to be 9.9 days[21]. In accordance with this, in our study the mean age at death was 9.3 days which compares well with the series.

Treatment is aimed at reducing bacterial load, neutralising unbound toxin and providing supportive care. The reduction of bacterial load is achieved by wound debridement and antibiotic treatment to remove any possible source of further tetanus toxin production. The neutralisation of toxin is achieved primarily throughpassive immunotherapy with tetanus antitoxins[22]. Tetanus immune globulin (human) is used intramuscularly, in a dose of 500 units in the treatment of NT. If this is not available, 10,000 units of equine or bovine tetanus antitoxin is used intramuscularly. In addition. penicillin which kills the vegetative form of the bacterium is given[7]. In the last years, it is reported that intravenous gamma globuline might be an alternative to horse or human tetanus immune globulin[23]. In our study, all patients were treated with equine tetanus antitoxin and penicillin. Subsequent infections were treated with the appropriate antibiotics. In addition. pyridoxine (100 mg/day) was added to the therapy after 1982. as this is reported to reduce niortality rate in NT[24].

Every known sedative has been used to control spasm and there is no general agreement as to which one is superior. Diazepam, pancuronium bromide and meprobamate are the common ones. Howard and de Vere[25] used intramuscular administration of mepmbamate with no diminution of mortality but with significant reduction in the number ofdass of spasm and of hospitalisation. Zaidi et al[26] reported that NT grades IV and V with factors for poor prognosis were treated with neuromuscular blocking agents pancuroniurn whereas NT grades IV and V without such factors were initially managed with diazepam, reserving neuromuscular blockage for therapeutic failures. Finally, they suggested that NT grades I-Ill might be effectively treated with diazeparn alone.

Okuonghae and Airede[27] reported that intravenous (continuous) diazepam (25.8 mg/kg/day), in combination with sodiumphenobarbitone (10.7 mg/kg/day)were effective, economical and feasible for reducing mortality in NT and the side effects were minimal.

In our study, diazepam, PNB and CPZ were used alone or combined for the control of spasm and the least mortality rate was found i he group treated with combined therapy (diazepam + PNB FCPZ). The highest mortality rate was encountered in the group treated with PNB + CPZ ($p<0.01$).

In conclusion, cutting of the umbilical cord with unsterile instruments, home delivery, wrapping in soil and lack of adequate tetanus immunisation were associated with increased incidence of NT. While the birth weight and age of onset of symptoms were poor prognostic factors, whereas sex, age on

admission and duration of symptoms had no effect on mortality rate. We suggest that PNB and CPZ mightbe used for the control of spasms in addition to diazepam, as this combination was more effective than the others. We also stress that training of traditional birth attendants for conducting safe deliveries and educating of mothers the simple hygienic principles and basic techniques and health education of population may have a significant impact on NT mortality. In the developing countries, widespread use of tetanus toxoid in pregnant women is necessary to eliminate NT.

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