

ORIGINAL ARTICLE

## The Influence of Pyridoxin in the Treatment of Tetanus Neonatorum

by

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### Abstract

*During a 2-year-period (1988-1990) 31 patients with tetanus neonatorum were recruited for this study. The patients were divided into 2 groups : The first group (15 patients) was treated with ATS injection, oral metronidazole and amoxycillin, and diazepam suppositoria. The second group (16 patients) was treated with the same regimen, as the first group plus pyridoxin injection 100 mg on the first day followed by 25 mg orally on the next days.*

*There was no statistical difference in the two groups concerning the gestation period, sex, severity of the disease ( $p > 0.05$ ), place of delivery (all at home) and mode of delivery delivered by traditional midwife/dukun).*

*The mortality of the first group (without pyridoxin) was 60% and the second (with pyridoxin) 37.5% ( $p < 0.05$ ).*

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**Introduction**

Tetanus neonatorum is still a health problem in developing countries. Since the mother's immunization program had been campaigned, the incidence of tetanus neonatorum decreased substantially, though is nowadays still high. Endang et al. (1985) reported the mortality rate to be 68.9%, Soetomenggolo et al. (1981) reported a figure of 50%, and Tjandra and Munir (1980) 62.9%.

By intensive care like IPPV (intermittent positive-pressure ventilation) and neuromuscular blockade the mortality could be reduced to 0% (Adams et al, 1979). Unfortunately not all hospitals in our country can make use of that kind of facility. Therefore we have to find out a

simple but inexpensive method of treatment that can be applied in all hospitals. Some studies had found a significant decrease in the mortality of tetanus neonatorum by using pyridoxine (Daud et al., 1981; Godel, 1982; Caglar, 1989). In the study of Daud et al. (1981) the mortality had decreased from 55.13% to 23.7% while in Caglar's from 62.5% to 50%. Although Godel (1982) did not used a control group, the percentage of the mortality was quite low as being 15%.

The aim of this study is to evaluate the efficacy of the addition of pyridoxine to the conventional treatment of tetanus neonatorum.

**Materials and methods**

During a 2-year-period (1st April 1988 to 31st March 1990) 31 patients with tetanus neonatorum were taken into this prospective study in the Department of Child Health, Medical School Sam Ratulangi University, Gunung Wenang General Hospital Manado. The diagnosis of tetanus neonatorum was based on the clinical signs and symptoms like the presence of lockjaw (trismus), rhisus sardonicus and the typical spasms observed by the pediatric staff members. The severity of the disease was assessed by the following scoring system (Tjandra et al., 1976).

- A g e : equal or less than 5 days ... 4
- 6 - 10 days ..... 2
- more than 10 days ..... 1
- Spasms : paroxysmal spontaneous ... 2
- induced ..... 2

- Cyanosis : ..... 2
- Rectal temperature higher than 39° C ... 1
- Trismus and rhisus sardonicus ..... 1
- The scoring was assessed on the day of admission. The severity was classified into : Grade I (mild), if the total score was 2-5
- Grade II (moderate), if the total score was 6-7
- Grade III (severe), if the total score was 8-10.

Patients with concomitant infections e.g. sepsis, bronchopneumonia, gastroenteritis, etc. were excluded from this study. All patients were nursed in a special Tetanus Neonatorum Unit. Feeding was given through a polyethylene nasogastric tube with mother's milk or milk formula until the infant was able to suck well. All the patients were randomly allocated into two groups of treatment :

- Group I : - ATS (anti tetanus serum) 1500 U, Intramuscularly
- metronidazole (Flagyl) 25 mg/kg/Bw/day/divided 3 doses - 10 days, orally.
- Oral Amoxycillin 50 mg/kg/Bw/day (3 doses) - 10 days
- Diazepam (Valium) 12 x 5 mg/rectally
- The umbilical slung was treated with Povidin (Betadine) solution

- Special attention on cleaning the respiratory tract during and after spasms.

Group II : The same as group I plus Pyridoxin 100 mg, intramuscularly on the first day, followed by 25 mg/day orally until the absence of spasms.

The patients were considered cured when the following criteria were fulfilled :  
 a. absence of spasms for 48 hours after stopping the sedation.  
 b. able to take normal oral feeding.

**Results**

The characteristics of the two groups were similar. There were no statistical differences in the 2 groups regarding to gestational age, body weight, sex, severity

of the disease, mother's TT (tetanus toxoid) vaccination, and mode of delivery (all delivered at home by traditional midwife also called *dukun*) (Table 1).

Table 1 : Characteristics of the two groups

	Group I	Group II
Gestational age	38.3 ± 2.2 weeks	37.3 ± 2.5 weeks
Body weight (gram)	2920 ± 570	2950 ± 450
Severity scoring		
mild	2	2
moderate	5	6
severe	8	8
Sex : Male	9	10
Female	6	9
Mother's TT vaccination :		
Never	12	13
Vaccination 1 x	2	3
2 x	1	-

p > 0.05

In table 2 it is shown that the total mortality of group I was 60% and group II 37.5%.

Table 2 : *Mortality in the 2 groups*

Scoring	Group I			Group II		
	Number	Died	%	Number	Died	%
Mild	2	-	0	2	-	0
Moderate	5	3	60	6	2	33.3
Severe	8	6	75	8	4	50
Total	15	9	60	16	6	37.5

### Discussion

Neonatal tetanus in developing countries is a major cause of neonatal mortality (Bytchenko, 1966). In many reports of conventional treatment for tetanus neonatorum in developing countries it was stated that the overall mortality was still high, varying from 60 to 90% (Salimpour, 1977; Endang et al., 1985; Tjandra and Munir, 1980). In Tunisia, before the treatment with pyridoxine, the mortality of the infants with tetanus neonatorum was almost 100%, but became 15% in the group of infants treated with pyridoxine in addition to conventional treatment (Godel, 1982). Pyridoxine is a coenzym of glutamate decarboxylase necessary for the production of gamma amino butyric acid (GABA) from glutamic acid. It is known that tetanus toxin suppresses the release of the inhibitory neurotransmitters like GABA and glycine. GABA is believed to be a pre-synaptic inhibitor in the spinal cord (Davidoff, 1972). Thus theoretically,

any measure that increases production of GABA and glycine at the nerve ending shall increase inhibitory responses and then reduces spasms. Therefore pyridoxine has been used in the treatment of tetanus neonatorum. The route of administration can be orally (Caglar, 1989), intramuscularly (Godel, 1982), or intravenously (Daud et al, 1981). As there has been no conclusion concerning the result of the treatment we assigned to administer pyridoxine intramuscularly in the first day and continued orally on the next days.

In general, antitoxin therapy does not significantly have an effect on the prognosis. The toxin has usually been fixed and is not available for neutralization; there were even doubts whether or not antitoxin is needed (Krugman and Katz, 1981; Barten, 1971). In our study, we only gave 1500 U of antitoxin (ATS), intramuscularly. Antibiotic treatment i.e. amoxycillin was given for ten days to

combat the umbilical infection; as for the anaerob infection, we gave metronidazole (Flagyl). Metronidazole, a compound widely used in man with minimal side effects, has been proven to be very effective against experimental infections of *Clostridium tetani* (Freeman et al., 1968). What is important in the management is the administration of appropriate drugs to reduce the number and severity of the spasms. Diazepam (Valium) has been proven to be a very valuable drug because it effectively controls spasms and hypertonicity without depressing the cortical centers (Krugman and Katz, 1981). Some

studies showed that diazepam administered rectally is effective in reducing convulsions and spasms (Ismael et al., 1981; Kaspan et al., 1981; Knudson, 1979). Basen on this finding we used diazepam rectally in our study. The result of this study showed that the mortality of the group treated with pyridoxine was 37.5%, significantly lower than the group without pyridoxine, which was 60% ( $p < 0.05$ ). In this study we only had 16 cases who were treated with pyridoxine. Further investigation with a greater number of cases is necessary to know the influence of pyridoxine in the treatment of tetanus neonatorum

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