
ORIGINAL ARTICLE

Failure of High Dosage Valium in the Treatment of Neonatal Tetanus

by

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Abstract

The fact that the mortality rate of neonatal tetanus is still high, and that the use of high dosage of valium has been reported to be of no side effect, encouraged the authors to use a high dosage of valium in the treatment of neonatal tetanus, particularly in severe cases.

This study was performed on 35 cases using 20 — 30 mg./kg. bw/day of valium from July 1, 1976 through October 1977.

The outcome of this study indicates that the treatment of neonatal tetanus using high dosage valium remained poor, where 22 out of 35 cases died (62.9%) with the following specifications :

- all of 6 mild cases survived,*
- 2 out of 6 of moderate cases died,*
- 20 out of 23 severe cases died.*

The authors believe that the simplest and the more effective way to overcome this disease is to give either tetanus prophylaxis to expectant mothers or 1500 U ATS prophylaxis to every newborn delivered by a traditional midwife (dukun bersalin).

Introduction

In variable dosages and combinations, Diazepam (Valium) has been widely used in the treatment of Neonatal Tetanus. High dosage of Valium has been tried for children and adult tetanus with favourable results.

The facts that Valium has a wide margin of safety (Randall et al., 1961); elasticity of dosages (Herrero, 1967); and no side effect was observed in the neonate (Hendrickse and Sherman, 1966), even in high dosage (Thomas et al., 1972), encouraged the authors to use a high dosage Valium as a single muscle relaxant in the treatment of Neonatal Tetanus.

This study is to evaluate whether high dosage of Valium has a beneficial effect on Neonatal Tetanus.

Materials and Methods

A prospective study was conducted at the Child Health Department, Medical School, Sam Ratulangi University/Gunung Wenang Hospital, Manado, from July 1, 1976 until October 1, 1977. Thirty-five patient comprising 24 male and 9 female infants were included in this study. They were grouped into 3 categories according to the authors' classification of severity (Tjandra and Munir, 1976). Six patients belonged to Grade I, another 6 to Grade II and 23 to Grade III.

They were given the same treatment and management:

- ATS 10.000 U, single dose, i.m., on admission.
- Oral Amoxicillin (Amoxil) 50 mg thrice daily.
- Intravenous fluid drip with Saline/Dextrose solution (1:6) 6 drops/minute using Mediset microdrip.
- Diazepam (Valium) in an average total daily dose of 25 mg/kg b.w., divided into:
 - a. 5 mg, intramuscularly on admission.
 - b. 20 mg incorporated into the intravenous fluid required for 24 hours.
 - c. the remainder was reserved for spasm attacks; 2½ mg each, intravenously when necessary.

The dosage of Valium and the duration of intravenous fluid were then adjusted according to the frequency and severity of spasm attacks. Feeding and nursing care were instituted as has been described elsewhere (Tjandra and Munir, 1976).

Results

All patients belonged to Grade I recovered. Two out of 6 patients of Grade II expired. And 20 out 23 of Grade III succumbed. This gave a mortality of 0%, 33.3% and 86.9% respectively.

The overall mortality rate was 62.9% (Table 1)

TABLE 1: *Mortality according to the classification of severity*

| Severity | No of cases | Died | Recovered | Mortality |
|-----------|-------------|------|-----------|-----------|
| Grade I | 6 | 0 | 6 | 0 % |
| Grade II | 6 | 2 | 4 | 33.3% |
| Grade III | 23 | 20 | 3 | 86.9% |
| T o t a l | 35 | 22 | 13 | 62.9% |

Discussion

In comparison with the authors' previous results (Tjandra and Munir, 1976), a better survival rate was attained for Grade II, although a definite conclusion could not be drawn owing to the small number of the present series (6 patients).

As in a previous study (Tjandra and Munir, 1976), almost similar results were achieved for Grade I. The results for Grade III, however, remained disappointing, though they were better in this study. The overall mortality of the 2 series were almost similar (Table 2).

TABLE 2: *Comparison of mortality between 2 series of studies*

| Severity | 1 9 7 6 | | | 1 9 7 8 | | |
|-----------|-------------|------|-----------|-------------|------|-------|
| | No of cases | Died | Mortality | No of cases | Died | Mort. |
| Grade I | 18 | 1 | 5.6% | 6 | 0 | 0 % |
| Grade II | 43 | 25 | 58.1% | 6 | 2 | 33.3% |
| Grade III | 47 | 43 | 91.5% | 23 | 20 | 86.9% |
| T o t a l | 109 | 69 | 63.9% | 35 | 22 | 62.9% |

All patients did not show any evidence of toxic effect of Valium given. The effect of Valium lasted for 1 - 8 hours according to the severity of the disease (Herrero, 1976). A continuous drip of Valium was given to keep the serum level high enough to suppress the initiation of spasm. The result, however, was poor. Nearly all Grade III patients did not show obvious diminishing spasm attacks. This conformed to the finding of Femi-Pearse (1966) who stated while dosages of Valium were being adjusted to the severity of cases, it should be born in mind that failures could occur.

According to unpublished reports cited by Herrero (1967), a daily dose of 30 - 40 mg/kg b.w. has been used with success in Neonatal Tetanus. This is contradictory to our experience. Our study, on the other hand, supports Herrero's statement (1976) that Valium is still far from the ideal treatment that probably never consist of a single drug. This was substantiated by Sanders and Joseph (1977) who claimed a successful result using a combination of Valium, Chlorpromazine and Phenobarbital.

Unfortunately, no data were given to ratify their success.

Thomas et al. 1972, in using a high dosage of Valium as a single drug in 80 Neonatal Tetanus patients, who were classified according to Mollaret et al. (1965), had an overall mortality of 76% as follows.

Grade I: all 6 patients recovered (mortality 0%).

Grade II: 20 out of 33 patients expired (mortality 60.6%).

Grade III: only 2 out of 41 patients survived (mortality 95.1%).

The results were not better than ours, though comparison could not be made due to the different method of classification used.

It is evident that the severe cases are the main problem. IPPV may be the only and exact therapy for them. This was confirmed by Ganendran (1974) and many other investigators who obtained satisfactory results. A comparison of IPPV, single or mixed drug therapy can be seen in Table 3.

TABLE 3: Mortality of Neonatal Tetanus treated with IPPV, single or mixed drug

| A u t h o r s | Total Paralyzes + IPPV | Mixed drug therapy | Single-drug therapy | No of cases | Mort. |
|---------------------------|---------------------------|-----------------------|------------------------|----------------|-------|
| Adam et al. (1966) | — | + | — | 217 | 82.5% |
| Barten (1969) | — | + | — | 134 | 39.6% |
| Ganendran (1974) | + | — | — | 27 | 22.3% |
| Geh (1951) | — | + | — | 174 | 91 % |
| Smythe (1963) | + | — | — | 25 | 20 % |
| Tompkins (1958) | — | + | — | 134 | 89.9% |
| Thomas et al. (1972) | — | — | + | 80 | 76 % |
| Tjandra & Munir (1976) | — | + | — | 108 | 63.9% |
| Tjandra & Munir (1978) | — | — | + | 35 | 62.9% |
| Wright (1960) | — | + | — | 217 | 82.5% |
| Wright et al. (1961) | + | — | — | 25 | 44 % |

Adapted from Ganendran Intensive therapy in Neonatal Tetanus, 1974 (Slightly modified).

For developing countries, a lot of trials have to be conducted before a simple, conservative yet effective treatment

of neonatal tetanus can be achieved. In the mean time, tetanus prophylaxis for expectant mothers or prophylactic ATS for newborns helped by traditional mid-wives should be seriously considered. And the routine practice in the shortest possible time cannot be overemphasized.

REFERENCES

1. FEMI-PEARSE, D. : Experience with diazepam in tetanus. *Br. med. J.* 2 : 862 (1966).
2. GANENDRAN, A. : Intensive therapy in neonatal tetanus; *Anaesthesia* 29 : 356 (1974).
3. HENDRICKSE, R.G. and SHERMAN, P.M. : Tetanus in childhood; a report of a therapeutic trial of diazepam. *Br. med. J.* 2 : 860 (1966).
4. HERRERO, J. : Valium as a muscle relaxant; in *Eckmann's Principles on Tetanus*, pp. 535 - 545 (Huber, Berne 1967).
5. RANDALL, L.O. : Pharmacological and clinical studies on valium; a new psychotherapeutic agent of the benzodiazepainc class. *Curr. ther. Res.* 3:405 (1961) (Cited by Herrero, 1967).
6. SANDERS, R.K.M. and JOSEPH, R. : Tetanus; successful treatment in rural situation. *Trop. Doct.* 7 : 99 (1977).
7. THOMAS, J.; AUBRY, P.; ROSSO, A.M.; HERAUT, L.; NELLY, A.M. and LHOSTE, F. : Tetanos neonatal traitement par l'administration orale de diazepam et l'alimentation precoce par sonde nasogastrique. *Bull. Soc. Path. Ex.* 3 : 373 (1972).
8. TJANDRA, H. and MUNIR, M. : Neonatal tetanus; an analysis of 108 cases using a scoring system. *Proc. Second Asian Cong. Pediatr.* Jakarta, 3-6 August 1976 p. 462.