

COMPARISON OF THE EFFICACY OF MAGNESIUM SULPHATE AND DIAZEPAM IN THE CONTROL OF TETANUS SPASM

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ABSTRACT

Objective: To compare the efficacy of magnesium sulphate and diazepam in controlling the tetanus spasm.

Methodology: This randomized clinical trial was conducted in Intensive Care Unit, Lady Reading Hospital, Peshawar from April 2009 to October 2010. Thirty six patients were included in study after fulfilling inclusion criteria. They were divided into 2 groups equally. Group I included patients that received intravenous diazepam, while Group II patients received intravenous magnesium sulphate for the control of spasm. Outcome variables included cessation of spasm, uncontrollable spasm, death, stay in Intensive Care Unit, need for artificial ventilation and complications. These were analyzed and the comparison was done in both groups to see the outcome of patients.

Results: Male to Female ratio was 5:1. Mean stay (in days) in Intensive Care Unit was 30 ± 6 for Group I, while 14.2 ± 3 for Group II. Outcome was better in Group II as compared to Group I with p -value < 0.01 , except for the cessation of spasm and death which were almost equal in both groups. Eighteen patients needed ventilatory support in Group I, while 4 patients needed ventilatory support in Group II. The length of stay was double in Group I as compared to Group II. Only one patient had developed Magnesium toxicity, which was successfully managed, while 8 patients developed complications from diazepam.

Conclusion: Magnesium sulphate was found superior in terms of reducing severity of spasm and minimizing stay of patients in Intensive Care Unit as compared to diazepam.

Key Words: Tetanus, Magnesium Sulphate, Diazepam, Ventilatory Support.

INTRODUCTION

Tetanus though preventable through vaccination, it continues to be a major scourge and a common cause of death in developing countries¹. Tetanus is a life threatening disease of third world requiring modern technology², as heavy sedation and ventilatory support (with or without muscle relaxants) are the main stay of management, and these are not always available to tetanus patients in those developing countries in which the disease is prevalent³. Reported mortality for tetanus ranges between 15-39%^{2,4,5}, and depends on the availability and quality of intensive care. Its severity was graded by Phillips et al⁶ but system given by Ablett is most commonly used⁷.

Conventional treatment for control of spasms in tetanus patients is diazepam. Autonomic

dysfunction is treated with alpha and beta blocker, ganglion blocker and sodium nitroprusside⁸. If respiratory muscles are involved, artificial ventilation is instituted using muscle relaxants. The complications resulting from long term heavy sedation and artificial ventilation contribute to 60% of the total mortality^{5,9-11}. There is, therefore, a continuing search for drugs which can control the spasms and the autonomic dysfunction of tetanus without the need for heavy sedation and artificial ventilation¹²⁻¹⁴.

The role for magnesium sulphate in the management of tetanus has been suggested by many authors¹⁵⁻¹⁷, but its usefulness in the control of spasms has not been explored. Majority of our population is poor socioeconomically and magnesium sulphate is cost effective drug, because

it reduces the stay of tetanus patients in intensive care unit due to its special advantage of controlling spasms by neuromuscular blockade without the need for artificial ventilation and stability of cardiovascular system¹⁸. The magnesium sulphate has been used effectively as a drug of choice to control spasms of tetanus without sedation and ventilatory support^{1, 3, 17, 19-21}.

The aim of this study was to investigate the efficacy and safety of intravenous magnesium sulphate in controlling of spasms of tetanus without the need for sedation and ventilatory support.

METHODOLOGY

This randomized clinical trial was conducted in Intensive Care Unit, Post Graduate Medical Institute, Lady Reading Hospital Peshawar from April, 2009 to October, 2010. Sample size was 36. Patients were divided equally (18 each) into two groups by randomization through sealed envelopes. Group I includes those Tetanus patients who were treated with conventional intravenous diazepam for the control of spasm and Group II comprises those, whose spasm was treated with intravenous magnesium sulphate.

The study included all tetanus patients above 10 years of age regardless of any gender and the presence of severe tetanus patients qualified them for inclusion to Grade III A of Ablett's classification⁷. Tetanus patients with compromised renal functions on the basis of blood urea > 108 mg/dl or urine output < 50 ml/hour were excluded from the study.

All these patients admitted in intensive care unit were observed for any change of posture and apparent convulsions after initial assessment and resuscitation. Informed written consent was taken from the first degree relatives of all patients included in the study. Patients were given anti tetanus toxin, tetanus toxoid, intravenous benzyl penicillin and metronidazole, and debridement and dressing of wound was done where needed. Tracheostomy was done within 48 hours after their admission in intensive care unit. General management included Chest and Limb physiotherapy, tracheal suction, skin and mouth care.

In Group II patients, before starting magnesium sulphate, serum magnesium, serum calcium, serum electrolytes, serum creatinin and blood urea of the patients were checked. A loading dose of 4g magnesium sulphate intravenously over 20 minutes in 100 ml Dextrose Saline followed by infusion of 2g/hour⁸. The rate of magnesium sulphate was increased by 0.25-0.5g 8 hourly till

control of spasm was attained, as long as patellar reflex was elicited. The knee jerk was used to monitor magnesium sulphate overdose. Incidental complications like hypocalcaemia, hypermagnesaemia and ventilatory failure were managed accordingly.

Data was analyzed using SPSS version 10. Outcome variable was cessation of spasm, uncontrollable spasm, death, need for artificial ventilation and presence of signs of magnesium toxicity or of excessive sedation of diazepam. Chi square was applied to compare the outcome of patients in both groups and "p" value < 0.01 was considered significant. Mean \pm Standard deviation were calculated for age and total stay of patients in Intensive Care Unit. Student "t" test was applied to compare the mean total stay of patients in both Groups and "p" value < 0.01 was considered significant.

RESULTS

In this study, Male to Female ratio was 5:1. Out of 38 patients included in both Groups, 28 (73.65%) were male and 10 (26.35%) were female. In Group I, 12 (66.6%) were male and 6 (33.3%) were female, while in Group II, 14 (77.7%) were male and 4 (22.2%) were female. Mean Age in years was calculated as 31.2 ± 11.2 for Group I, while 28.6 ± 13.2 standard deviation was determined for Group II. Mean stay (in days) in intensive care unit was analyzed as 30 ± 6 for Group I, while 14.2 ± 3 standard deviation for Group II (Table 1).

Outcome criteria was cessation of spasm, uncontrollable spasm, death, presence of signs of magnesium toxicity or of excessive sedation of diazepam and need for artificial ventilation. The outcome was better in Group II as compared to Group I with "p" value < 0.01, except for the cessation of spasm and death which was almost equal in both groups with "p" value > 0.01 (Table 1). Nine patients were successfully recovered in Group I, but their stay in intensive care unit was double as compared to Group II, in which 8 patients were recovered. Twelve (66.66%) patients out of 18 needed ventilatory support in Group I, while only 4 (22.22%) needed ventilatory support in Group II (Table 1).

The highest risk factor in female resistant to therapy was tetanus due to septic abortions. Magnesium toxicity was noted in only one patient out of 18 in Group II, which was successfully reversed with intravenous calcium gluconate and forced diuresis, while in Group I, 8 patients went into respiratory failure due to excessive sedation of diazepam, needing ventilatory support (Table 1). Furthermore, control of spasms in tetanus patients

Table 1: Comparison of Outcome of Patients in Two Groups (n=36)

	Group I (n=18) I/V diazepam	Group II (n=18) I/Vmagnesium sulphate	p -Value
Mean Age in Years	31.6±11.2	28.6±13.2	0.102
Mean Stay in ICU (days)	30.6±6	14.2±3	0.001
Cessation of spasm	9	8	0.201
Uncontrollable spasm	6	4	0.015
Death	9	10	0.201
Need for artificial ventilation	12	4	0.001
Toxicity	8 patients developed respiratory failure	1 patient developed signs of magnesium toxicity	0.001

were very rapidly achieved with intravenous magnesium sulphate as compared to intravenous diazepam.

DISCUSSION

The effectiveness of magnesium sulphate was clearly recognized in the management of tetanus in other parts of the world without causing sedation. The results of this randomized clinical trial are in line with study done by Attygalle et al³. The results are also comparable to the study done by Osalusi et al¹, which clearly shows that magnesium sulphate is a suitable alternative to diazepam for the control of spasm of moderate tetanus.

The results of this study is also similar to the local study done by Khan et al²¹. This prospective observational study was done on 32 patients, of which 11 were found refractory to the treatment and required ventilatory support and intensive care unit coverage, and ultimately expired. In one other local study done by Sikendar et al⁸ clearly indicates the magnesium sulphate infusion can be safely used as a drug of choice to control muscle spasms and reduce the need for artificial ventilation in post traumatic tetanus patients. It minimizes the nursing monitoring and proved to be cost effective therapy, but true mortality cannot be estimated in this study.

The development of hypocalcaemia seen in our patients in response to hypermagnesaemia has been well documented^{22, 23}. Its return to normal value within 2-3 days of stopping magnesium therapy indicates that hypocalcaemia

was only temporary.

In all our patients included in Group II, cardiovascular stability was maintained during magnesium therapy without need for sedatives. This is contrary to the findings in the case report by Lipman¹⁷, who questioned the ability of magnesium sulphate to control autonomic dysfunction in the absence of sedation.

In comparison magnesium sulphate effectively controlled the spasms of severe tetanus with no failure, no need for ventilatory support except when indicated for lung pathology²⁴. The ease of nursing care in conscious cooperative patients was in marked contrast to the author's personal experience of 42 patients previously managed with sedation and paralysis.

Intravenous magnesium sulphate infusion helps to control the rigidity and mild spasms in tetanus. In more severe forms of tetanus with generalized and severe spasms, an adjuvant sedative drug is required in addition to magnesium. Attygalle et al¹⁹ had stated that the dose of magnesium required in the very severe form of tetanus may have unacceptable cardiovascular side-effects. By following a strict protocol to avoid such side-effects, while at the same time trying to get the maximum effect of magnesium in the therapeutic range for control of spasms, we have probably shown the most practical and feasible utility of magnesium infusion in tetanus.

Earlier authors have reported the utility of magnesium as the single agent to control spasms

of tetanus^{21,25}. However, our series has not supported this conclusion. This may be due to the severe form of disease encountered in our series characterized by severe generalized spasms and autonomic instability. However, in mild forms of the disease the benefit was obvious since the rigidity and mild spasms were controlled solely by magnesium infusion, thereby avoiding sedation.

CONCLUSION

Magnesium sulphate was found superior in terms of reducing severity of spasm and minimizing the stay of patients in intensive care unit as well as complications occurring from spasm, but it does not affect the mortality with this dreadful disease. Furthermore these results should be cautiously interpreted due to small sample size.

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