

POST TRAUMATIC TETANUS AND ROLE OF MAGNESIUM SULPHATE

Rana Imran Sikendar, Bader us Samad, Safdar Ali, Mohammad Iqbal Memon

Department of Anaesthesia and Intensive Care Unit, Pakistan Institute of Medical Sciences, Islamabad, Pakistan

Background: Tetanus is a life threatening disease. Reported mortality for tetanus is 15–39%. Conventional treatment includes heavy sedation and artificial ventilation. Complications resulting from long term heavy sedation and artificial ventilation contribute to 60% of the total mortality caused by tetanus. In this study magnesium sulphate was used to reduce the need for sedation and artificial ventilation. Objectives of this prospective study were to determine the role of magnesium sulphate in post traumatic tetanus. **Methods:** The study was carried out in surgical Intensive Care at Pakistan Institute of Medical Sciences (PIMS), Islamabad from Jan 2004 to Dec 2007. Forty-four patients presented during this period and 33 patients were included in the study. All patients had tracheostomy done within 48 hours. Every patient was started Magnesium Sulphate therapy for control of spasms after sending baseline investigations. Patients were given ventilatory support when needed. All data was entered in well structured proforma. SPSS-10 was used to analyse data. **Results:** Thirty-three patients were included in the study and all patients were given magnesium sulphate. Out of these, 45.5% cases were grade 4 tetanus, 73.6% and 63.3% cases did not require artificial ventilation and additional sedation respectively, 51.1% patients remained free of complications of tetanus. Overall mortality was 30.3%. **Conclusions:** Use of Magnesium Sulphate is safe and reduces the need for sedation and artificial ventilation in high grade tetanus thus contributing to survival benefit in adult post-traumatic tetanus cases.

Keywords: Post traumatic tetanus, artificial ventilation, Magnesium Sulphate

INTRODUCTION

Post traumatic tetanus is a life threatening disease of third world requiring modern technology for treatment. Its severity was graded by Phillips *et al*¹ but system given by Ablett² is most commonly used (Table-1). Mortality reported for tetanus ranges from 15–39%.³⁻⁵

Conventional treatment for control of spasms is diazepam. Autonomic dysfunction is treated with alpha and beta blockers, ganglion blockers and sodium nitroprusside. If respiratory muscles are involved, artificial ventilation is instituted using muscle relaxants. Complications resulting from heavy sedation and artificial ventilation contribute to 60% of the total mortalities. Therefore there was continuous search to control spasms without the need for heavy sedation and artificial ventilation.⁶⁻⁸

Magnesium is essential for the activity of enzyme system and plays an important role with regard to neurochemical transmission and muscular excitability.⁹⁻¹³ Magnesium has the special advantage of controlling spasms by neuromuscular blockade without the need for artificial ventilation and stability of cardiovascular system.¹⁴ During recent days magnesium sulphate has been used successfully as a drug of choice to control spasms of severe tetanus without sedation and ventilatory support.¹⁵⁻²⁰

Very few studies have been carried out in Pakistan to determine the effect of magnesium sulphate in post traumatic tetanus patients. The purpose of this study was to determine the role of magnesium sulphate for control of muscle spasms in

severe tetanus (Ablett grade 3, 4) and minimising the need for sedation and artificial ventilation.

PATIENTS AND METHODS

This prospective study was carried out in the Department of Anaesthesia, Surgical Intensive Care Unit, Pakistan Institute of Medical Sciences (PIMS), Islamabad. All post traumatic tetanus patients admitted from 1 January 2004 to 31 December 2007 were assessed for the suitability of initiating magnesium sulphate infusion. A total of 44 patients presented during this time and 33 cases were included in the study having post traumatic severe tetanus (Ablett grade-3, 4). Two patients below 14 years of age, 04 with compromised renal function, and 05 with heart block; were excluded from the study.

All patients with post traumatic severe tetanus (Ablett grade 3 & 4) presenting to PIMS Islamabad were admitted to surgical intensive care unit. After initial assessment and resuscitation, patients were observed for any change of posture and apparent convulsions. Arterial blood gases were immediately measured. Patients were given antitoxin, tetanus toxoid, intravenous metronidazole, and surgical debridement was done where needed. Tracheostomy was done within 48 hours in all patients. General management included chest and limb physiotherapy, tracheal suction, skin and mouth care.

Before starting magnesium sulphate therapy, sample for serum magnesium, calcium, sodium and potassium were taken. A loading dose of intravenous magnesium sulphate 4 g diluted in 20 ml of 5% dextrose water was given over 20 min, followed by

an infusion of 2 g per hour. The rate of infusion was increased by 0.25–0.5 g 8 hourly till control of spasm was achieved. Once the patient was stabilised, infusion rate was reduced to achieve minimum required dose. Evidence of hypocalcaemia was sought using clinical signs and serial measurement of serum calcium levels. Incidental complications were treated accordingly. In the event of magnesium overdose (Magnesium levels above 4 mmol/lit, muscle flaccidity, loss of patellar reflex, respiratory depression and prolonged PR interval on ECG), magnesium therapy had to be temporarily discontinued followed by forced diuresis and decrease in dose to half.

Ventilatory support was given if the tidal volume was <5 ml/kg or respiratory rate was >35/min. Additional sedation, injection diazepam 10mg in incremental doses, was given for the immediate treatment of muscle spasms. Hypocalcaemia was treated with 10 ml of 10% calcium gluconate whenever required.

Data was collected on a well formed proforma prospectively. Mean and standard deviation were calculated for age, incubation period and stay in intensive care unit. Frequency was presented for gender, artificial ventilation, additional sedation and mortality using SPSS 12.0.

RESULTS

A total of 33 cases of Ablette grade 3 and 4 post traumatic tetanus (Table-1) were included, admitted and followed during their course of surgical intensive care stay. Mean age of the patients was 30±8.1 years, ranging between 15–50 years. There were 25 male (75.8%) and 8 female patients. Patients who presented with Ablette grade-3 tetanus were 54.5%, while the rest were in grade 4. Incubation period ranged from 4–29 days with mean being 11.3±7.0 days.

Magnesium sulphate was given to all patients, 72.7% patients did not need artificial ventilation, and only 9 patients (27.3%) needed IPPV, out of which 3 were Ablette grade-3 tetanus patients presenting with aspiration pneumonitis. Sedation was used only in 12 patients (36.4%) that were on ventilators along with 2 patients of Ablette grade-4, and 63.6% patients did not require sedation for controlling spasms.

Table-2 shows complications in post-traumatic tetanus patients. No complications were seen in 51.5% cases; 9.1% were having aspiration pneumonitis due to spasms since admission; 5 patients developed wound infection (15%), 2 (6.1%) of which were tracheostomy site infection; 3 cases developed DIC, 1 (3%) due to major trauma and 2 (6.1%) following septicaemia; 6% cases developed autonomic dysfunction including hypertensive crisis (3%) and cardiac arrest (6%). Artificial ventilation led to pneumonia in 6.1% cases

and proved fatal in all. Duration of intensive care stay ranged between 3–35 days with mean being 11.3±7.3 days. Most of the complications were related to ICU stay beyond 10–12 days.

Mortality was found to be 30.3%. Incubation period above 9 days, artificial ventilation and Ablette grade-4 cases were associated more with mortality than the age of the patient.

Table-1: Ablett² classification of severity grading

Grade	Clinical features
1	Mild: mild trismus; general spasticity; no respiratory embarrassment; no spasms; no dysphagia.
2	Moderate: moderate trismus; well-marked rigidity; short spasms; moderate respiratory embarrassment with increased respiratory rate greater than 30; mild dysphagia
3	Severe: severe trismus; generalized spasticity; reflex prolonged spasms; increased respiratory rate greater than 40; apnoeic spells; severe dysphagia; tachycardia greater than 120.
4	Very severe: grade 3 and violent autonomic disturbances involving the cardiovascular system. Severe hypertension and tachycardia alternating with relative hypotension and bradycardia, either of which may be persistent.

Table-2: Complications in Post traumatic Tetanus

Complications	%
No complication	51.5
Cardiac Arrest	6.0
Hypertensive crisis	3.0
DIC	9.5
Wound infection	15.0
Pneumothorax	3.0
Ventilator associated Pneumonia	6.1
Tracheostomy infection	6.1
Total	100.0

DISCUSSION

Tetanus is a life threatening disease of poor and developing countries claiming very high mortality due to associated phenomena of autonomic dysfunction, aspiration pneumonitis and sudden cardiac arrest along with complications due to artificial ventilation and heavy sedation^{6-8,15} Conventionally the muscle spasms are controlled by benzodiazepines. Continued search of newer modalities for effective control of spasms, complications and reducing mortality has led to the use of magnesium sulphate. Research data on its usage in adult post traumatic tetanus is scarce but strongly supporting its usage.¹⁴⁻¹⁹ This study was conducted in an effort to evaluate the role of magnesium sulphate in controlling muscle spasms in high grade post traumatic tetanus patients thereby decreasing the use of sedation and artificial ventilation which greatly contributes to mortality.^{8,15}

Adult tetanus is a disease of younger age group with predominant number of males. Most of the patients presented to us sustained injuries while working in the fields or during cattle handling. Incubation period was calculated from date of injury till admission in the hospital. Higher mortality and

severity of grade was noted with incubation period of >9 days. Saltoglu *et al*¹⁹ also reports that incubation period >7 days is a bad prognostic factor associated with 75% mortality in tetanus patients.

Due to our management of tetanus patients with magnesium sulphate therapy, average stay of the patient in intensive care unit was reduced to 11 days. Effectiveness of magnesium sulphate could be demonstrated in majority of cases for controlling muscle spasms and greatly reducing need for artificial ventilation only being in 9 patients and additional sedation in 12 patients compared to previous practice of 100% use of ventilatory support with prolong stay in our intensive care. Our results are also supported by Attygale^{15,17} and Osalusi *et al*.¹⁸

In grade-4 tetanus patients magnesium sulphate therapy failed to control muscle spasms. Twelve patients (36.4%) required sedation in spite of magnesium sulphate therapy in order to control their muscles spasms. In 7 patients spasms were refractory to all kind of treatment that is magnesium sulphate and benzodiazepines. These patients were put on ventilator and kept paralysed all the time.

Complications were related to ICU stay beyond 11 days and artificial ventilation. Forty-nine percent cases in our study developed some sort of complication during their stay. Delay in reporting injury as shown by longer incubation period and associated severe trauma can be demonstrated as contributing factors. Flail chest, nosocomial pneumonia, aspiration pneumonitis, and hypoventilation due to heavy sedation all led to use of artificial ventilation hence related complications. None of the patients developed complications of magnesium sulphate therapy like renal failure, hypocalcaemia or heart block and the presence of patellar reflex proved a valid end point to ensure safe therapeutic range as reported by Attygale.^{15,17}

Overall mortality in our study was 30.3%, higher than reported by Attygale of 12%¹⁷ and lower than that reported by Osalusi (47.5%)¹⁸ and Khan *et al* (34.4%)²⁰. Mortality was associated with grade-4 patients, also noted by Saltoglu *et al*¹⁹ and use of artificial ventilation in patients having aspiration pneumonitis on admission which deteriorated further during the course of illness. Two patients developed pneumonia in intensive care unit and died. Hypertensive crisis and sudden cardiac arrest which is a prominent feature of tetanus was well controlled by magnesium use as reported by Thwaites *et al*¹⁴ and observed only in 2 grade-4 tetanus patients contributing to mortality. Major trauma with DIC proved fatal for our 3 patients.

Use of magnesium sulphate alone showed 70.6% survival proving its safety and effective contribution to survival benefit both directly by

controlling autonomic responses and indirectly by minimising use of heavy sedation and artificial ventilation.

LIMITATIONS OF STUDY

There were certain limitations of our study:

1. We do not have control group (conventional sedation group) to compare the morbidity and mortality of 2 groups.
2. Most of the patients were already having complications while arrival to hospital so true complication rate cannot be calculated.
3. Few patients had major trauma and other associated injuries, so true mortality cannot be estimated.

CONCLUSION

Magnesium sulphate infusion can be safely used as a drug of choice to control muscle spasms and reduce need for artificial ventilation in post traumatic tetanus patients. It reduces complications attributed to artificial ventilation and thus indirectly contributes to survival benefit in high grade tetanus cases.

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REFERENCES

1. Phillips LA. A classification of tetanus. *Lancet* 1967;1:1216-7.
2. Ablett JLL. Analysis and main experiences in 82 patients treated in the Leeds Tetanus Unit. In: Ellis M, ed. Symposium on Tetanus in Great Britain. Boston Spa, UK: National Lending Library;1967.p.1-10.
3. Sun KO, Chan YW, Cheung RTF, So PC, Yu YL, Li PCK. Management of tetanus: A review of 18 cases. *J R Soc Med* 1994;87:135-7.
4. Reis S, Freire E, Alexandrino S. Tetanus in an ICU in Portugal. *Int J Intens Care* 1994/95;1:120-1.
5. Talati N, Salahuddin N. Factor's affecting tetanus mortality in a tertiary care hospital in Pakistan. *Infect Dis J Pak* 2001;10:13-5.
6. Saissy JM, Demaziere J, Vitris M, Seck M, Marcoux L, Gaye M, *et al*. Treatment of severe tetanus by intrathecal injections of baclofen without artificial ventilation. *Intens Care Med* 1992;18:241-4.
7. Checketts MR, White RJ. Avoidance of intermittent positive pressure ventilation in tetanus with dantrolene therapy. *Anesthesia* 1993;48:969-71.
8. Ceneviva GD, Thomas NJ, Kees-Folts D. Magnesium sulphate for control of muscle rigidity and spasms and avoidance of mechanical ventilation in pediatric tetanus. *Pediatr Crit Care Med* 2003;4:480-4.
9. Collins R, Peto R, Flather M. ISIS-4: A randomised factorial trial assessing early oral captopril, oral mononitrate, and intravenous magnesium sulphate in 58,050 patients with suspected acute myocardial infarction. *Lancet* 1995;345:669-85.
10. Kinlay S, Buckley NA. Magnesium sulfate in the treatment of ventricular arrhythmias due to digoxin toxicity. *J Toxicol Clin Toxicol* 1995;33:55-9.
11. Mudge GH. Agents affecting volume and composition of body fluids. In: Goodman Gilman A, Goodman LS, Gilman A (eds). *The Pharmacological Basis of Therapeutics*, 6th ed. New York:

- Macmillan; 1985.p. 879–83.
12. Witlin AG, Sibai BM. Magnesium sulfate therapy in pre-eclampsia and eclampsia. *Obstetr Gynaecol* 1998;92:883–9.
 13. British National Formulary, Royal Pharmaceutical Society of Great Britain. *Magnesium*. Wallingford UK: Pharmaceutical Press; 1999.p. 425.
 14. Thwaites CL, Yen LM, Loan HT, Thuy TTD, Thwaites GE, Stepniewska K, *et al.* Magnesium sulphate for treatment of severe tetanus: A Randomised controlled trial. *The Lancet* 2006;368:1436–43.
 15. Attygalle D, Rodrigo N. Magnesium sulphate for control of spasms in severe tetanus. Can we avoid sedation and artificial ventilation? *Anaesthesia* 1997;52:956–62.
 16. Lipman J, James MFM, Erskine J, Plit ML, Eidlelman J, Esser JD. Autonomic dysfunction in severe tetanus: Magnesium sulphate as an adjunct to deep sedation. *Critical Care Med* 1987;15:987–8.
 17. Attygalle D, Rodrigo N. Magnesium as first line therapy in the management of tetanus: A prospective study of 40 patients. *Anaesthesia* 2002;57:811–7.
 18. Osalusi BS, Ogun SA, Ogunniyi A, Kolapo KO. Comparison of the efficacy of magnesium sulphate and diazepam in the control of tetanus spasms. *Scientific Research and Essays* 2008;3:571–6.
 19. Saltoglu N, Tasova Y, Midikli D, Burgut R, Dündar IH. Prognostic factors affecting deaths from adult tetanus. *Clin Microbiol Infect* 2004;10:229–33.
 20. Khan MA, Iqbal J, Rashid A. Magnesium sulphate infusion; a novel approach to the treatment of tetanus. *Professional Med J* 2003;10:271–4.

Address for correspondence:

Dr. Rana Imran Sikandar, Assistant Professor, Department of Anaesthesia and Intensive Care, Pakistan Institute of Medical Sciences, Islamabad, Pakistan. **Cell:** +92-321-5220402
Email: ranaimransikander@hotmail.com