

# Magnesium Sulphate For Tetanus, review of two cases

Tirta Darmawan Susanto<sup>1</sup>

<sup>1</sup>Faculty of Medicine, University of Pelita Harapan, Siloam Hospitals Lippo Village

## Abstract

**Citation** : Susanto TD. Magnesium Sulphate For Tetanus  
**Keywords** : Magnesium sulphate, tetanus, riview of two cases  
 Medicinus. 2018 October; 7(4):113–117.  
**\*Correspondance** : Tirta Darmawan Susanto  
 Faculty of Medicine University of Pelita Harapan, Tangerang, Siloam Hospitals Lippo Village.  
**E-mail** : tirta.susanto@uph.edu  
**Online First** : March 2020

**Introduction:** Tetanus is critically ill disease with long term hospitalization period. It need to be carefully monitored, usually in intensive care unit and involves critical care physicians. Benzodiazepine is preferred by World Health Organization (WHO) for muscle spasm control in tetanus, but it will be less costly if magnesium sulphate can be used alone to control spasm and autonomic dysfunction in tetanus. We report a series of 2 tetanus cases that were treated using magnesium sulphate to provide a brief clinical description about the use of magnesium sulphate in tetanus. We also give a brief review on epidemiology, pathophysiology, clinical findings, diagnosis, and treatment of tetanus to provide implications for intensive care physicians. Methods : Case series report

**Results :** Two patients with tetanus was given magnesium sulphate infusion to control muscle spasm and autonomic dysfunction with good results as expected. Both of them were survive and discharged home in healthy condition.

## Conclusions :

Magnesium sulphate can also be used to control muscle spasm and autonomic dysfunction although WHO recommend benzodiazepines for controlling muscle spasm. Intensive care physicians should have enough knowledge about tetanus and how it should be managed adequately to ensure survival from tetanus.

## Introduction

Tetanus is an infectious disease caused by exotoxin from *Clostridium tetani*. It causes generalized muscle spasm and autonomic dysfunction.<sup>1, 2, 3</sup> Onset of tetanus is acute and often fatal. Incubation period of tetanus varies between several days to several months.<sup>3</sup> The most common treatment for muscle spasm caused by tetanus are sedation, neuromuscular blockade, and controlled ventilation.<sup>2</sup> Benzodiazepines often used to control muscle spasm. Magnesium sulphate also has therapeutic properties to control spasms and autonomic dysfunction in tetanus.<sup>1</sup>

There are about 1 million cases of tetanus every year are hospitalized worldwide, and tetanus causes about 400 thousand death every year.<sup>1</sup> It is uncommon in developed country, mostly because of the good immunization system and coverage.<sup>4</sup> In Indonesia, tetanus reported as an outbreak after tsunami in Aceh province and earthquake in Yogyakarta province.<sup>5,6</sup>

Approximately 1 month after tsunami in Aceh on December, 26<sup>th</sup>, 2004, 106 tetanus cases reported and most cases were in adults. Case fatality ratio was reported 18,9 %, and higher among older patients and among those with quite short incubation periods.<sup>5</sup> After earthquakes in Yogyakarta on May, 27<sup>th</sup>, 2006, 26 tetanus patients were reported.<sup>6</sup> In Siloam General Hospital, Lippo Karawaci, Tangerang, Indonesia, 30 cases of tetanus were recorded from 2012 – 2016.

Since majority of tetanus cases needed to be admitted to intensive care unit because of its effect to respiratory system and autonomic dysfunction,<sup>2</sup> it will spent so much money to take care of tetanus patients, especially in an outbreaks. In this case series report we review magnesium sulphate as an alternative drug to control muscle spasm and autonomic dysfunction with cheaper cost. We also give brief review about epidemiology, pathophysiology, clinical findings, diagnosis, and treatment of tetanus.

Case series :

#### Case 1

A 40 years old man with 60kg of body weight was brought to Siloam General Hospital Lippo Karawaci, Tangerang, Indonesia, with chief complain muscles spasm in entire body and had 1 episode of seizure at home. His left foot stepped on the rusty nail and was injured since 1 week ago. In admission the patient was conscious with Glasgow Coma Scale (GCS) was Eye (E) 4, Movement (M) 6, Verbal (V) 5, his mouth had 1 finger trismus (lockjaw), truncal rigidity (opisthotonus) was found. This patient was diagnosed as tetanus. In Emergency department, cross incision of the wound in his left foot was done and anti tetanus serum was given. This patient was admitted to intensive care unit and was given MgSO<sub>4</sub> intravenous 2gram/hour to control spasm and autonomic dysfunction in this patient. Vital signs in admission were normal and no fever. Nasogastric tube and urine catheter were used. The empirical intravenous antibiotics given were Meropenem 1 gram 3 times daily and Levofloxacin 750mg 1 time daily. Calcium carbonate tablet 500mg was given 3 times daily through nasogastric tube to reduce the side effect of magnesium sulphate.

On day 4, we did debridement of the wound and also did tracheostomy and gave mechanical ventilation with Pressure Synchronized Intermittent Mechanical Ventilation mode to secure airway and ventilation to ensure adequate oxygenation because there was still generalized muscle spasm with pain, especially provoked by touch stimulus. We added morphine 1mg/hour and increase magnesium sulphate to 3 gram/hour. On day 5 we started to wean the mechanical ventilation and on day 7 the patient was able to breath adequately with tracheostomy mask only. On day 9, trismus reduced to 2 fingers, generalized muscle rigidity provoked by touch stimulus was greatly reduced, and opisthotonus disappeared. On day 14, trismus disappeared, but generalized muscle rigidity provoked by touch stimulus was still rarely happened. We decrease magnesium sulphate infusion to 1gram/hour. Antibiotics given were changed to cefoperazone sulbactam and amikacin from the result of sputum culture. On day 16, no muscle rigidity observed and the magnesium sulphate was stopped. Vital signs were stable when this patient minute. On day 13, muscle spasm was reduced significantly and Magnesium

got magnesium sulphate infusion. We took blood Magnesium routinely and the blood magnesium ranged between 6.1 – 8.6 (N : 1.6 – 2.6). The patient moved to general ward on day 18. Tracheostomy was removed on day 22 and the patient discharged home on day 23.

#### Case 2

A 35 years old male with 66 kg of body weight was brought to Siloam General Hospital Lippo Karawaci, Tangerang, Indonesia, from other local private hospital with chief complain mouth, neck and waist stiffness since 2 days before admission. The patient was unable to eat and drink because he cannot open his mouth and also cannot swallow. He complained no fever, no headache, and no seizure. In previous local private hospital, the patient had been diagnosed as tetanus and had been given tetanus gammaglobulin intramuscularly and diazepam 5mg intravenously. The patient had a wound in his right foot because of a nail since 20 days ago. In admission, the patient's Glasgow Coma Scale (GCS) was E4 M6 V5 with 1 finger trismus, opisthotonus, and muscular spasm triggered by touch. Wound cross incision was done in Siloam General Hospital emergency room. This patient was admitted to intensive care unit. Magnesium sulphate infusion was given at 1 gram/hour combined with morphine 0.5 mg/hour and midazolam 0.25mg/hour. Vital signs was stable since admission with blood pressure 120 / 80, heart rate 90-100x / minute, temperature 36 – 37 ° Celsius, respiratory rate 22x / minute and oxygen saturation 100% on oxygen 3 liters per minute. Meropenem 1 gram 3 times daily was given intravenously. Magnesium sulphate infusion was increased to 2gram/hour and then 4gram/hour on day 2 because of frequent periodic muscular spasm with pain. On day 3, there was respiratory depression. The patient was intubated and was given mechanical ventilation with Pressure Synchronized Intermittent Mechanical Ventilation mode. Magnesium Sulphate was continued at 4 gram/hour. On day 4, the patient got fever, increased heart rate, and blood pressure. Intravenous Levofloxacin 750mg once daily was added. Vital signs were stabilized on day 5. On day 7, tracheostomy and bad teeth extraction were done. The mechanical ventilation was weaned and was stopped at day 10 replaced by oxygen given through tracheostomy mask 6 liters / sulphate was given 3 gram / hour. On day 16, the patient was moved to high care unit

because no mechanical ventilation needed. On day 27, magnesium sulphate infusion was stopped. We took blood Magnesium routinely and the blood magnesium ranged between 1.5 – 11.2 (N : 1.6 – 2.6). The patient was moved to ward on day 32. Tracheostomy was removed on day 36, and the patient was discharged home on day 37.

## Discussion

### Epidemiology

Tetanus is still a major problem, especially in developing country. In developed country it is uncommon because of the good immunization coverage for tetanus.<sup>4</sup> Tetanus have caused approximately 1 million cases need to be hospitalized, and cause 400,000 deaths every year.<sup>1</sup> Another record inform that from 2002 there are 213,000 – 293,000 deaths caused by tetanus worldwide each year.<sup>7</sup>

In Indonesia, immunization programme for tetanus have been done since 1974 for pregnant women, infants and children. Surveillance data on tetanus in Indonesia showed that the incidence for tetanus of 0.2 per100,000 population annually. In Hasan Sadikin Hopital, Bandung, from 1991 – 1995, there were 85 cases of tetanus in adults.<sup>8</sup> One month after tsunami in Aceh on December, 26<sup>th</sup>, 2004, there was an outbreak of tetanus. There were 106 tetanus cases reported and most cases were in adults. Case fatality ratio was reported 18,9 %, and higher among older patients and among those with quite short incubation periods.<sup>5</sup> Other 26 cases of tetanus were reported in Yogyakarta after earthquakes on May, 27<sup>th</sup>, 2006.<sup>6</sup> In Siloam General Hospital, Lippo Karawaci, Tangerang, Indonesia, we have 30 cases of tetanus from 2012 – 2016.

### Pathophysiology.

*Clostridium tetani* form spores that are able to live in soil and stools.<sup>7, 9</sup> *Clostridium tetani* spores enter the tissue through contaminated wound. In anaerobic condition they become bacilli.<sup>7</sup> tetanus bacilli produce two toxins : tetanospasmin and tetanolysin.<sup>9</sup> Tetanus is not transmitted from person to person.<sup>10</sup>

Tetanolysin damage the tissues surrounding the infection site.

Tetanospasmin cause the clinical syndrome of tetanus.<sup>9</sup> Tetanospasmin has 2 chain, heavy chain and light chain. Light chain acts at presynaptic site to prevent neurotransmitter release. Tetanospasmin binds to gangliosides on the membranes of local nerve terminals. Some toxin may enter the bloodstream and diffuses to nerve terminals in all of body parts. The tetanospasmin will be internalized and transported intra-axonally and retrogradely. Transport occurs in motor and autonomic nerves. Toxin can diffuse out and enter nearby neurons, spread to brainstem and midbrain. Tetanospasmin light chain will prevent neurotransmitter release, predominantly in inhibitory neurons, inhibiting release of glycine and gamma-aminobutyric acid (GABA). Interneuron inhibiting alpha motor neurons are first affected causes motor neurons lose inhibitory control. Effect on prejunctional of neuromuscular junction causes weakness between spasm.<sup>9</sup> Treatment with immune globulin is needed to binds free toxin, but it does not treat toxin that has entered within neurons.<sup>7</sup>

Uncontrolled efferent discharge with no inhibitory activities from motor neurons in spinal cord and brainstem cause muscular rigidity and spasm and mimic convulsion. Agonist and antagonist muscle groups contract simultaneously without inhibition reflex. Muscle spasm are very painfull. Autonomic discharge also have no inhibitory activity causes uncontrolled autonomic activities and sympathetic over activity.<sup>9</sup>

This neuronal binding is irreversible. It causes recovery need prolonged time duration. Recovery will be completed if the new nerve terminals grow.<sup>9</sup> It need approximately 4 – 6 weeks to be recovered from tetanus.<sup>7</sup>

### Clinical findings.

Clinical findings can be presented as a triad of rigidity, muscle spasm, and autonomic dysfunction. Early symptoms are neck stiffness, sore throat, and trismus because of masseter spasm. Spasm of facial muscles causes typical facial expression called “risus sardonicus”.

Episodic muscles spasm cause convulsion – like appearance that can be spontaneous

or triggered by touch, visual, auditory, or emotional stimuli.<sup>7,9</sup> Continual spasm may lead to respiratory failure, strong spasm may cause fractures and tendon avulsions, pharyngeal and laryngeal spasms associated with aspiration and life threatening airway obstruction,<sup>9</sup> and truncal spasm made classical feature called opisthotonus.<sup>7,9</sup> Muscle rigidity can cause rhabdomyolysis and resulted in renal failure.<sup>7</sup>

Sympathetic nervous system is badly affected. Increased sympathetic activity causes persistent tachycardia and hypertension, vasoconstriction and pyrexia. Basal catecholamine levels of plasma are raised. Severe hypertension and tachycardia, alternate with hypotension, bradycardia, or recurrent cardiac arrest are called "autonomic storms". Profuse salivation, increased bronchial secretion, gastric stasis, ileus, diarrhoea and high output renal failure may be related to autonomic disturbances.<sup>9</sup>

Diagnosis.

Diagnosis of tetanus is clinical, based on history taking and typical physical findings of rigidity, spasms and trismus. Tetanus is lack of specific confirmatory laboratory tests. Differential diagnosis for tetanus are temporomandibular joint disease, alveolar abscess, cerebral malaria, encephalitis, subarachnoid haemorrhage, epilepsy, hypocalcaemia, drug induced movement disorder, stiff man syndrome, drug withdrawal, rabies, and strychnine poisoning.<sup>7</sup>

Philips, Dakar, and Udwadia are several grading systems for tetanus severity. The most widely used severity grading for tetanus is the system reported by Ablett. Ablett divide the grades of tetanus severity into 4 grades. The grades are : grade I (mild), grade II (moderate), grade III (severe), grade IV (very severe).<sup>9</sup>

#### Treatment

General measures, immunotherapy, antibiotic treatment, muscle spasm control, autonomic dysfunction control, airway/respiratory control, and adequate fluids and nutrition are treatment of tetanus recommended by WHO. General measures includes separated, shaded, and protected from stimulation ward/location designated for tetanus patients and debridement or clean up of the wounds.<sup>10</sup>

Immunotherapy includes administration of human Tetanus ImmunoGlobulin (TIG) 500 units intramuscularly or intravenously (depending on the preparation) and Tetanus Toxoid (TT) vaccine 0,5cc intramuscularly at separate site.

Tetanus disease does not induce immunity, so that patients without a history of primary TT vaccination should receive a second dose 1 – 2 months after first dose and also third dose 6 – 12 months later.<sup>10</sup>

Antibiotics recommended is metronidazole intravenously or orally 500mg every six hours and Penicillin G 100,000 – 200,000 IU /kg/day divided into 2 – 4 doses. Others antibiotics can be given are tetracyclines, macrolides, clindamycin, cephalosporins, and chloramphenicol.<sup>10</sup>

Benzodiazepines are preferred for controlling muscle spasm. Intravenous diazepam in increments of 5mg or lorazepam in increments of 2mg can be titrated until spasm control achieved in adults. In children, the doses are 0,1 – 0,2 mg/kg every 2 – 6 hours and can be titrated upward as needed. They can be given up to 600mg per day.<sup>10</sup>

Magnesium sulphate is an anticonvulsant and a vasodilator. Magnesium sulphate blocks pre-synaptic catecholamine release from nerves and adrenal medulla. It also reduces receptor responsiveness to released catecholamine. It antagonises calcium in the myocardium and neuromuscular junction and inhibits parathyroid hormone release. Hypotension and bradyarrhythmia may occur. Regular monitoring of serum magnesium and calcium levels were required.<sup>9</sup> Magnesium sulphate can be used alone or in combination with benzodiazepines to control muscle spasm and autonomic dysfunction. Loading dose can be given 5 gram or 75mg/kg intravenously and followed by maintenance dose 2 – 3 grams per hour until muscle spasm can be controlled adequately. Patellar reflex should be monitored and areflexia occur at the upper end of therapeutic range (4mmol/L). Other agents that can be used for controlling muscle spasm are baclofen, dantrolene, barbiturate (especially short acting), and chlorpromazine.<sup>10</sup>

Autonomic dysfunction can be controlled by magnesium sulphate or morphine. Beta blockers only esmalol is recommended, because the others can cause hypotension and sudden death.<sup>10</sup>

Airway or respiratory protections are needed if there is respiratory problem. Respiratory problem can be caused by the spasm or the drugs to control muscular spasm.<sup>9, 10</sup> Mechanical ventilation needed or if there is no mechanical ventilation available the patients must be monitored carefully and the medication doses adjusted in balance between spasm and autonomic dysfunction control and avoid respiratory failure. Early tracheostomy is preferred because endotracheal tube can provoke spasm.<sup>10</sup>

Fluid and nutrition should be given adequately, because spasm in tetanus produce high metabolic demands and a catabolic state. Nutritional support will enhance survival.<sup>10</sup>

### Conclusions

According to WHO recommendation, treatment of tetanus consist of general measures, immunotherapy, antibiotic treatment, muscle spasm control, autonomic dysfunction control,

airway/respiratory control, and adequate fluids and nutrition. Many drugs are available to control muscle spasm and autonomic dysfunction. WHO prefer benzodiazepine to control muscle spasm. Magnesium sulphate can also be used to control muscle spasm and autonomic dysfunction.

In developing countries, limited health budget makes healthcare practitioner should choose the cheapest medicine to achieve maximal results. The price of magnesium sulphate is lower than other drugs and optimal control of muscular spasm and autonomic dysfunction can be achieved safely.

Most of tetanus cases will need respiratory protection and control that can be given only in intensive care unit. For that reason, most of tetanus cases will be admitted to intensive care unit. Intensive care physicians should have enough knowledge about tetanus and how it should be managed adequately to ensure survival from tetanus.

### References

1. 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(9545):1436–1443.
2. Sutton DN, Tremlett MR, Woodcock TE, Nielsen MS. Management of autonomic dysfunction in severe tetanus: the use of magnesium sulphate and clonidine. *Intensive Care Med*. 1990;16(2):75–80.
3. Ahaduzzaman M. Updates on tetanus toxin: A fundamental approach. *J Adv Vet Anim Res*. 2015;2(1):23.
4. Amare A, Melkamu Y, Mekonnen D. Tetanus in adults: Clinical presentation, treatment and predictors of mortality in a tertiary hospital in Ethiopia. *J Neurol Sci*. 2012 Jun;317(1–2):62–5.
5. Aceh Epidemiology Group. Outbreak of tetanus cases following the tsunami in Aceh province, Indonesia. *Glob Public Health*. 2006 Jun;1(2):173–7.
6. Sutiono A, Qiantori A, Suwa H, Ohta T. Characteristic tetanus infection in disaster-affected areas: case study of the Yogyakarta earthquakes in Indonesia. *BMC Res Notes*. 2009;2(1):34.
7. Gibson K, Bonaventure Uwineza J, Kiviri W, Parlow J. Tetanus in developing countries: a case series and review. *Can J Anesth*. 2009 Apr;56(4):307–15.
8. Gunawan D. Tetanus in adults in Bandung, Indonesia. *Neurol J Southeast Asia*. 1996 ; 1 : 43 - 46.
9. Cook T.M., Protheroe R.T., Handel J.M. Tetanus : a review of the literature. *British Journal of Anaesthesia*. 2001; 87(3) : 477-87.
10. Organization WH, others. Current recommendations for treatment of tetanus during humanitarian emergencies: WHO technical note. 2010 [cited 2017 Jan 21]; Available from: <http://apps.who.int/iris/handle/10665/70219>