Treatment of Adult Severe Generalized Tetanus with Magnesium: A Case Report

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The prevalence of tetanus has steadily decreased with widespread immunization programs. This decrease in prevalence does not mean that therapy has been improved or that the risk of death has been reduced. However, the development of modern critical care has led to changes in treatment strategies. Nevertheless, the mortality rate is still high even with the support of modern critical care systems. Avoidance of therapeutic complications, which are commonly the major causes of fatality with tetanus, is a major concern. To decrease the risk of ventilator-associated pneumonia and deep vein thrombosis, many medications have been reported to minimize the need for heavy sedation and muscle relaxation. Among these agents, magnesium sulfate is relatively inexpensive, is convenient to administer, and is better ability to control spasms. We report our successful experience with magnesium therapy for a case of an adult with severe generalized tetanus.

Key words: tetanus, magnesium sulfate

Introduction

Tetanus is a disease caused by tetanospasmin produced by Clostridium tetani, a noninvasive gram-positive anaerobic bacillus(1). Tetanospasmin is taken up by the neuronal end plates and irreversibly inhibits release of the neurotransmitter, gamma-aminobutyric acid (GABA), at the synaptic junction, leading to muscle spasms(1). Different forms of tetanus exist: generalized, cephalic, localized, and neonatal forms. The severest one is the generalized form, involving the bulbar and paraspinal muscles; its manifestations include lockjaw, risus sardonicus, difficulty swallowing, muscle rigidity and spasms, and opisthotonos. Death, if left untreated, is caused by respiratory compromise or fracture of the spine.

There was a decreased prevalence in tetanus during the 20th century in the wake of widespread immunization programs(1). There is an average of 15 suspected cases of tetanus reported annually in Taiwan(2) but only 1 case was confirmed in Yunlin, southwestern Taiwan, in 2001. Mainstay management is supportive care. Even with the introduction of heavy sedation, muscle relaxation, and intensive care support, the fatality rate is still unacceptably high due to complications of the therapy itself.

We report a case of severe generalized tetanus in a 40-year-old man who received magnesium sulfate via an intravenous infusion. Successful control of the muscle spasms and clinical improvement without sedation-associated complications were achieved.
Case Report

A 40-year-old man with chronic hepatitis C was brought to the emergency room of the hospital because of difficulty swallowing, trismus, paroxysmal spasms of the 4 limbs, and a backache for 3 days. He is a factory worker, and he sometimes receives intravenous analgesics for general soreness associated with his work. The patient had no other underlying medical diseases, no known allergies, and no trauma or admission history. Upon arrival, his blood pressure was 102/53 mmHg, temperature was 36.6 °C, respiratory rate was 18 breaths/min, and the pulse was 70 beats/min. On examination, the patient was found to be well nourished, alert, and non-cyanotic. No goiter or stridor was noted. The heart sounds were regular without a heart murmur, and breath sounds were clear in auscultation. The results of other exams were unremarkable.

Laboratory data were as follows. The electrocardiograph revealed a sinus rhythm. Chest radiography showed unremarkable findings. The white cell count was 13,700 cells/L and C-reactive protein was 73.7 mg/L. Biochemical laboratory tests included a blood urea nitrogen level of 19 mg/dL, creatinine of 1.2 mg/dL, sodium of 136.3 mEq/L, potassium of 4.02 mg/dL, and glucose of 161 mg/dL.

Initial management included supplemental oxygen at 2 L/min. Intravenous metronidazole at 500 mg every 8 hours and 500 units of subcutaneous anti-tetanus immunoglobulin were immediately administered. Thereafter, he was admitted to the intensive care unit. During the first 12 hours of hospitalization, arterial oxygen saturation decreased from 100% to 88% due to trismus and generalized muscle spasms, so the patient was intubated with the use of propofol and tracurium, and mechanical ventilation used the pressure control mode.

On the second hospital day, the patient developed excessive sweating, sinus tachycardia with pulse rates of 120~140 beats/min, and severe generalized muscle spasms and rigidity. Lorazepam at 40 mg in 20 ml of normal saline was administered, and the infusion rate was gradually increased to 6 mg/h. In addition, intravenous tracurium was administered with an infusion rate ranging between 5 and 35 mg/h. On the 15th hospital day, a tracheostomy was created due to prolonged endotracheal intubation. Paroxysmal right lower limb rigidity was still noted although 800~1000 mg tracurium and 120 mg lorazepam were administered daily from the 19th hospital day. Severe generalized muscle spasms occurred when the infusion dose of either atracurium or lorazepam was reduced.

Therefore, intravenous magnesium sulfate at a dosage of 2~3 g/h was added to the lorazepam and tracurium therapy on the 20th day. On the day following magnesium therapy, it was possible to decrease the respective infusion rates of lorazepam and tracurium to 3 and 15 mg/h. On the 22nd day, lorazepam and tracurium were successfully discontinued. Sinus tachycardia and excessive sweating improved. The plasma magnesium level was 4.0~5.5 mg/dL in regular biochemical follow-up after continuing magnesium therapy. Free movement of the four limbs was noted. The patient was able to communicate with medical staff by writing. He was successfully weaned from the ventilator on the 24th hospital day.

The patient was transferred to a general ward on the 35th day and was discharged on the 40th day. At the follow-up exam 9 month later, the patient was well, remained uneventful and there had been no recurrence.

Discussion

Tetanus prevalence has steadily decreased in the wake of worldwide immunization programs. Because of unhygienic practices in childbirth and inadequate immunization of pregnant women(1), tetanus is still common in developing countries. There are an esti-
mated 50,000 cases per 1 million patients worldwide each year. Tetanus is commonly preventable through immunization. The disease reflects a failure of immunization in adult patients implying that the efficacy of tetanus immunization is not life-long. The antibody may drop below protective levels for adults over 40 years of age. A booster vaccination should be given to these adults. Upon the onset of symptoms, early blockade of toxin production by administration of tetanus immunoglobulin is believed to decrease the severity of the disease manifestations, such as diminishing the generalized convulsions and other serious complications.

Antibiotics therapy is of minor importance because the major presentations are exotoxin-mediated. Metronidazole is suggested to be superior to penicillin, which may potentially enhance the effect of the tetanus toxin by inhibiting the GABA type-A receptor. A previous randomized, controlled trial found that the differences in incidences of dysautonomia, nosocomial pneumonia, and in-hospital deaths did not significantly differ between penicillin and metronidazole. Penicillin is another drug for tetanus in Southern Asia where cost is taken consideration.

However, the management of tetanus remains a challenge in current critical care medicine. The overall mortality rate ranges from 25% to 75%. Many factors are associated with increased fatality, such as age, immunization status, the incubation period, inadequate wound care, and the lack of utilization of tetanus immunoglobulin and antibiotics. There was no significant difference in 1 study in the mean age of those who died and those who survived; however, the case fatality rate rose with age. In developing African countries, fatality rates of 16.2% for those under 40 years old and 75% for those above 70 year old were reported. Patients should be admitted to the intensive care unit immediately upon diagnosis. Early intubation, mechanical ventilation, and a tracheostomy reduce the mortality from tetanus. Other current management practices include heavy sedation with benzodiazepines, muscle paralysis with relaxants, spastic pain control with analgesics, and mechanical ventilation for respiratory compromise. Aspiration and poor cough function due to muscle paralysis may be followed by nosocomial pneumonia. Prolonged immobility may result in deep vein thrombosis and pulmonary embolization. Paralytic ileus due to the overuse of analgesics may cause translocation of the bowel flora.

Traditionally, effective management for generalized muscle spasms is achieved using the benzodiazepine group, including diazepam, midazolam, and lorazepam. Monotherapy with benzodiazepine may fail to control the rigidity associated with severe generalized tetanus; thus, additional muscle relaxants should be supplemented. A continuous intrathecal injection of baclofen in generalized tetanus was suggested, but potential risks for meningitis and catheter-related infections have been reported. Other options such as dantrolene and its combination with propofol may sometimes achieve clinical success.

Sympathetic nervous system overactivity, called dysautonomia, is another crucial problem in severe generalized tetanus, and may cause excessive sweating, bowel hypoactivity, cardiac tachyarrhythmias, and rapid changes between arterial hyper- and hypotension, which may predict a poor outcome with tetanus. Sudden cardiac arrest due to inability to control the dysautonomia has been noted in these patients. A variety of modalities, such as clonidine, fentanyl, and -blockers, have been used to stabilize the cardiovascular system. -blockers have theoretical advantages for treating the excess catecholamines, but sudden cardiac death after -blockers therapy has been reported. The safety of -blockers remained unclear.

Magnesium therapy, which offers the advantage of blocking both neuromuscular transmission and sympathetic overactivity, is currently considered a new approach.
therapeutic option. In addition, its low cost and ease of administration are also advantages\(^{(18)}\). In a prospective study which observed 40 patients with tetanus who were treated with magnesium sulfate via a continuous intravenous infusion, muscle spasms were effectively controlled in 38 patients, 23 patients were free from the ventilator, 36 patients maintained consciousness and were cooperative throughout their treatment, and no deaths were attributed to autonomic dysfunction\(^{(19)}\). A similar experience was also reported in both adults and children without the need for deep sedation, artificial ventilation, or neuromuscular blockade\(^{(20-22)}\).

Caution with a continuous infusion of magnesium sulfate is suggested because it is mainly excreted by renal clearance. Regular monitoring of serum magnesium levels is required not only for patients with normal renal function, but especially those with chronic renal insufficiency and acute renal failure. Attygalle et al. suggested that the magnesium serum level be checked every 6 hours initially, and then every 24 hours if it is stable\(^{(19)}\). This is easy, and early detection of renal function deterioration at the bedside is possible by evaluating the urine output profile, and a magnesium overdose can be detected if there is a decrease in the deep tendon reflex\(^{(19-21)}\). A patient with generalized severe tetanus should be admitted to the intensive care unit for therapy.

Based on our successful experience together with results reported in the literature, magnesium sulfate is recommended as an adjuvant to either traditional or first-line therapy for tetanus.

References


嚴重成人全身型破傷風使用鎂製劑的經驗：病例報告

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破傷風的臨床病例在疫苗的廣泛使用後已越來越少見，儘管公共衛生成功地防治，但治療得到破傷風的病人卻依然是個難題。因為現代加護醫學的進步，雖然可減少破傷風的死亡率，但現在的觀點來看，本病的死亡率一樣高的嚇人。分析這些病人死因之後，我們發現致死的原因多是因為治療本身所造成的併發症。如過度鎮靜劑使用和肌肉鬆弛劑使用所造成的呼吸衰竭與隨後發生之呼吸器相關之肺炎或靜脈血栓等等。本病例報告人物40歲破傷風的中年病人，使用硫酸鎂持續靜脈注射治療，成功地將全身肌肉痙攣控制下來，並成功存活的案例。因此我們認為硫酸鎂持續靜脈注射可以作為成人破傷風的新輔助療法。

關鍵詞：破傷風，鎂