Management of severe tetanus using magnesium sulfate – The experience in a tertiary health institution in Southern Nigeria

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ABSTRACT

Tetanus is a vaccine-preventable disease caused by the neurotoxin of *Clostridium tetani*: A motile, Gram-positive, spore-forming obligate anaerobe commonly found in the soil, dust, and alimentary canals of various animals. It remains a public health challenge in the developing countries as the morbidity and mortality rates remain high unlike in the developed world where the incidence is markedly low and no longer contributory to significant mortality. We report two male adolescents admitted in the pediatric department of a tertiary medical center of Nigeria for severe tetanus following an open injury to the limbs. Due to poor response to initial management with the combination of chlorpromazine, phenobarbitone, and diazepam, the latter was replaced with continuous infusion of magnesium sulfate after a loading dose was administered. Both the patients recovered without any prevailing complications and were discharged after 26 and 50 days of hospitalization, respectively, after receiving tetanus toxoid and were subsequently followed up. Successful severe tetanus management without the use of sophisticated medical gadgets and expensive treatment in a resource-poor economy is achievable as demonstrated by our study with the use of magnesium sulfate infusion.

Key words: *Magnesium sulfate, Nigeria, Spasms, Tetanus*

Tetanus is a disease caused by the deadly toxin tetanospasmin from *Clostridium tetani*. It is largely preventable but still remains a major public health problem in the developing world and is associated with high morbidity and mortality rates [1]. Annual global mortality was estimated at 213,000. A total of 198 deaths occurred in children below the age of 5 years [2]. Basher documented a mortality rate of 20% [3]. Anah *et al*. reported that post-neonatal tetanus accounted for 3.7% of childhood death, with a case fatality rate of 18% among hospitalized children in Nigeria [4]. Oyelami *et al*. [5] and Fatunde and Familusi [6] reported a case fatality rate of 39% and 37.5% among children. The most common cause of mortality in individuals with severe tetanus in the absence of mechanical ventilation is spasm-related respiratory failure, whereas in ventilated patients, it is tetanus-associated autonomic dysfunction [7].

Autonomic nervous system (NS) instability as a complication of tetanus is well documented. Features of autonomic insufficiency include tachycardia/bradycardia, oropharyngeal hypersecretion, excess sweating, and urinary retention. Hyperpyrexia, persistent hypertension, cardiac arrhythmias, and "autonomic storms" (marked cardiovascular instability leading to sudden cardiac death) are serious autonomic manifestations [8-10]. These have been attributed to high catecholamine levels due to the over activity of the sympathetic NS and direct effect of the tetanus toxin on the myocardium, whereas parasympathetic dysfunction is probably due to direct damage to the vagal nucleus by the tetanus toxin [10,11].

The supportive care in the intensive care unit (ICU) is one of the key principles in the treatment for tetanus but has its own drawbacks [10]. Deaths from this disease commonly occur within the 1st week of admission. Magnesium affects both the pre-synaptic and post-synaptic terminals of the sympathetic and parasympathetic neurons, competitively blocking calcium entry into the presynaptic terminals, thus impairing neuromuscular transmission by reducing acetylcholine release and it decreases the postsynaptic sensitivity of the motor endplate to acetylcholine [12].

Magnesium sulfate is safe to be used and also reduces the need for sedation and artificial ventilation in severe tetanus patients, thus contributing to survival benefits. Magnesium sulfate has been solely used previously for the control of autonomic dysfunction, muscle spasms, and rigidity associated with severe tetanus [13-15]. However, a few authors found it ineffective in the treatment of the severe form of the disease [16,17], while few others reported that patients treated with the combination of diazepam and magnesium sulfate had better outcome than those managed with diazepam only [11,17].

CASE REPORT

We report two cases of male adolescents admitted in the department of pediatrics of the tertiary hospital of Nigeria for severe tetanus following an open injury to the limbs. Due to poor response to initial management with the combination of chlorpromazine, phenobarbitone, and diazepam, the latter was replaced with continuous infusion of magnesium sulfate after a loading dose was administered. Both the patients recovered without any prevailing complications, received tetanus toxoid and were discharged after 26 and 50 days of hospitalization, respectively, and were subsequently followed up. Written informed consent was obtained from the patient's legal guardian(s) for publication of this case report and any accompanying images.

Case 1

A 14-year-old boy brought to the children emergency room with the complaint of inability to open the mouth followed 3 days later by unprovoked generalized jerking of the body. There was no history of headache, loss of consciousness, antecedent irrational talk, behavior or head trauma, or ingestion of any substance. The patient was non-epileptic but had sustained an injury on his right forearm after being spanked with a bunch of broomsticks by the elder brother, 8 days before manifestation of these symptoms. The patient first took some herbal medications, but on deterioration of his condition, he was brought to our hospital. There was no history of previous immunization.

Examination on admission revealed a conscious patient, with unprovoked, intermittent, and painful spasms lasting for 1–2 min. There was trismus and abdominal rigidity. The pupils were of normal size reacting equally to light. Lumbar puncture could not be done due to recurrent unprovoked spasms. A clinical diagnosis of severe generalized tetanus was made using Udwadia's prognostic classification [18].

On investigations, complete hemogram was normal. Electrolytes, urea, creatinine, and calcium levels were within normal limits. Liver function test was normal. He was started on intravenous crystalline penicillin, metronidazole, phenobarbitone, chlorpromazine, and diazepam for breakthrough spasms. The patient also received 20,000 IU of anti-tetanus serum (ATS) to neutralize unbound tetanus toxin. Tetanus immunoglobulin was not given because it was unavailable. The wound on the forearm was debrided and dressed daily using honey. Feeding through nasogastric tube was avoided to minimize risk of aspiration. Euglycemic state was therefore maintained through intravenous infusion of 5% dextrose saline with vitamin B complex injection.

Six days into admission, unprovoked severe spasms continued unabated despite adequate doses of phenobarbitone and chlorpromazine. Temperature chart showed spikes between 38 °C and 39°C. Tachycardia and tachypnea were prominent features. Blood pressure fluctuated between normal, low, and high levels. The patient was also found to have developed pressure sores on the buttocks.

In view of this poor response to the initial treatment protocol and the presence of autonomic dysfunction, magnesium sulfate was therefore added to phenobarbitone and chlorpromazine while diazepam was discontinued. A loading dose of 3 g was first given followed by continuous infusion of 100 mg/kg/h. Serial patellar reflex was done to monitor toxicity since we could not monitor the blood level of magnesium sulfate. The patient was also transferred to an improvised water bed (bags of locally made sachet water neatly and tightly arranged on the hospital bed) to avoid further development of pressure sores.

Five days after introducing this new protocol, spasms reduced markedly and vital signs stabilized. Spasms completely abated on the 15th day of commencement of magnesium sulfate with patient able to sit out of bed as well as mobilize with support. The patient stayed for 50 days on admission in the hospital to enable complete healing of pressure sores and he received a dose of tetanus on discharge and encouraged to return for catch-up immunization.

Case 2

A 14-year-old schoolboy presented with inability to open the mouth for 2 days followed by jerking of the body 5 days later. The patient sustained a bamboo stick injury on his big toe 6 days before the development of the first symptom. There was no loss of consciousness or antecedent head injury. Jerking of the body was unprovoked and was said to involve the whole body. The child did not receive any childhood immunization. He was first taken to a general hospital from where he was referred to the emergency room of the medical center.

Examination on presentation revealed a conscious child with intermittent, unprovoked, painful spasms, and trismus. There was abdominal rigidity; tachypnea and tachycardia. The blood pressure was elevated and the rectal temperature was 38.7°C. Examination of the right foot showed a necrotic ulcer on the plantar surface of the big toe. A diagnosis of severe tetanus was made using Udwadia's prognostic classification [18]. Full blood count showed normal hemogram with normal serum electrolytes, urea, creatinine, and ionized calcium. Liver function test was normal. Lumbar puncture was not done to avoid further provocation of spasms.

The patient was admitted to a quiet isolation room and nursed on improvised water bed as described in case 1. Nasogastric tube feeding was avoided too, but euglycemic state was maintained with 5% dextrose saline. The patient commenced on chlorpromazine, phenobarbitone, and diazepam for breakthrough spasms. He also received crystalline penicillin, Flagyl, and 20,000 IU of ATS to neutralize unbound tetanus toxin. Tetanus immunoglobulin was not given (was unavailable). Oxygen saturation during spasms ranged between 86% and 90% and in between spasms ranged between 96% and 98%. The patient was neither intubated nor had a tracheostomy done.

Vital signs remained unstable as temperature spikes, ranging between 38.6°C and 39°C with unprovoked intermittent spasm persisting. On the 3rd day of admission, magnesium sulfate was added to chlorpromazine and phenobarbitone while diazepam was withdrawn, receiving a loading dose of 3 g infused into 5% dextrose saline and given over 30 min. This was followed by continuous infusion of 100 mg/kg/h, monitoring magnesium sulfate toxicity by performing serial patellar reflex.

Spasms significantly reduced to 2 in number/24 h mainly on provocation (during blood pressure check), 48 h after commencement of magnesium sulfate. The blood pressure and other vital signs normalized. By 16th day on admission, patient was able to take both liquid and semisolid feeds, sit out of bed, and mobilize with support. He was discharged home on the 26th day on admission after receiving a dose of tetanus toxoid and was encouraged to return for catch-up immunization.

DISCUSSION

The prognosis for severe tetanus characterized by severe spasms and autonomic dysfunction is poor [11,19]. Our patients who were managed for severe tetanus were neither immunized nor received booster doses of tetanus toxoid. This is in accordance with the previous studies where it was observed that post-neonatal tetanus occurs mostly in children who were not immunized against tetanus or those who received incomplete immunization during the 1st year of life [20,21]. The incubation period of the disease for our patients was short. Severity of the disease has been shown to be closely related to incubation period. Cook *et al*. [8] documented that shorter incubation period is associated with severe disease while a longer incubation period results in milder disease.

The portal of entry for one of our patients was a dirty wound on the lower limb. Oyelami *et al*. [5], Animasahun *et al*. [22], and Onwuekwe *et al.* [23] documented that lower limb injuries are the commonest portal of entry. This may be due to the fact that most adolescents in the rural setting remain without protective footwears. Autonomic dysfunction such as tachycardia, tachypnea, fluctuating blood pressure, and elevated body temperature are features of severe disease and poor prognosis [24]. Frequent, unprovoked spasms which may involve the respiratory muscles can cause death in non-ventilated patients.

Magnesium sulfate has been found to mitigate the effect of autonomic dysfunction in tetanus patients [11,15,17]. The rapid control of spasms and autonomic dysfunction in our patients by magnesium sulfate shows its effectiveness in the management of severe tetanus. Shanbag *et al*. [16] similarly infused magnesium sulfate. The respiratory insufficiency associated with spasms also resolved with the use of magnesium sulfate obviating the need for intubation, tracheostomy, or respiratory support. Similar observations were made by Ceneviva *et al*. [1]. This is of utmost interest for resource-poor economies where ICU management of these patients appears to pose a great financial challenge.

CONCLUSION

Tetanus is still prevalent in rural communities especially among the unimmunized and severe forms could be managed with positive results using magnesium sulfate infusion which can be easily procured and is highly affordable.

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