



Tetanus: Continuing Problem in the Developing World

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Abstract. Despite diligent efforts by the World Health Organization and the governments of developing world countries, tetanus persists as a global health problem. This retrospective study was undertaken to assess the outcome for victims of tetanus presenting to the Baptist Medical Centre in Ogbomoso, Nigeria and to develop better management techniques for future patients. Sixty patients (46 males, 14 females) with nonneonatal tetanus were seen over a 5-year period (1995–1999). The mean age was 26 years, and 74% were 30 years or younger. All patients were treated with antitetanus serum, antibiotics, wound débridement (when a wound was identified), and antispasmodics. No patients underwent tracheostomy or gastrostomy. The mortality rate was 44%. Factors significant for predicting mortality were age greater than 14 years, occupation as a farmer, short incubation period, short symptom duration, high degree of severity on presentation, and high temperature during hospital care. The best hope for improvement in the treatment of tetanus in our institution is more conscientious titration of antispasmodics to control spasms without causing significant respiratory depression. The only real hope for reducing the global mortality for tetanus, however, lies in renewed immunization efforts by all health care providers in developing world countries, not just community health workers.

Tetanus, described 3000 years ago in ancient Egypt, has been a plague for mankind throughout recorded history. Passive immunization for tetanus has been available since 1893 and active immunization since 1923. As a result there have been great strides toward eliminating tetanus in industrialized countries, with only 33 cases reported in the United States in 1999. The World Health Organization (WHO) identified tetanus as one of six target diseases for the Expanded Program on Immunization (EPI) in 1974. Despite diligent efforts by the WHO and the governments of developing world (DW) countries, tetanus persists as a global health problem. This study was undertaken to assess the outcome for victims of tetanus presenting to a general medical practice hospital in the DW and to develop better management techniques for future patients.

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Materials and Methods

This is a retrospective study of 60 consecutive cases of nonneonatal tetanus presenting over a 5-year period (January 1995 to December 1999) to the Baptist Medical Centre of Ogbomoso, Nigeria (BMCO), a general medical practice hospital in the DW. The severity of the disease on admission was graded as: (1) mild, when there were no spasms; (2) moderate, when spasms occurred only on provocation; and (3) severe, when spasms occurred spontaneously. All patients were given antitetanus serum (ATS) in a dose of 20,000 IU after a test dose; active tetanus immunization with tetanus toxoid was later given to survivors. Procaine penicillin was given intramuscularly for 5 to 7 days. Wounds, when identified, were débrided, irrigated, and left open to heal by secondary intention. Children were treated with diazepam, chlorpromazine, and phenobarbitone orally or through a nasogastric tube. Patients older than 14 years were treated using a continuous intravenous diazepam infusion, with chlorpromazine added when spasms were not controlled well with diazepam. Patients were managed in a regular multibed ward setting, as an intensive care unit (ICU) is not available at BMCO. No patients were managed with a ventilator, and none underwent tracheostomy or gastrostomy.

Only two outcomes were considered in this study: survival and death. The following factors were analyzed to determine their significance in predicting outcome: age, gender, occupation, season of the year, portal of entry, length of incubation period, duration of symptoms, degree of severity at the time of admission, and vital signs on admission and during hospitalization. All potential predictors of outcome were subjected to statistical analysis. For normally distributed, continuous data, groups were compared using Student's two-independent sample *t*-tests. For not normally distributed, continuous data, Mann-Whitney U-tests were used. Categorical or dichotomous variables were analyzed using the chi-square or Fisher's exact test (when the assumptions of chi-square were not met). SPSS version 10 was used for all analyses with alpha set at 0.05.

Table 1. Predictors of mortality.

Outcome	Occupation		Age		Incubation period (days)	Symptom duration (days)	Severity on presentation	
	Farmers	Nonfarmers	≤ 14 Years	> 14 Years			Severe	Mod/Mild
Total (n = 57)	15	42	10	47	10.4	3.3	23	34
Recovered (n = 32)	5	27	9	23	12.7	4.0	6	26
Expired (n = 25)	10 (67%) ^a	15 (36%)	1 (10%)	24 (51%)	6.8	1.9	17 (74%)	8 (24%)
<i>p</i>		0.026		0.032	0.005	0.005		0.032

Mod: moderate.

^aPercents represent the mortality rate.

Table 2. Vital signs as predictors of mortality.

Outcome	Admission vital signs			Maximum vital signs		
	Temperature (°C)	Pulse (beats/min)	Ventilatory rate (breaths/minute)	Temperature (°C)	Pulse (beats/min)	Ventilatory rate (breaths/min)
Total (n = 57)	37.8	107	30	39.1	120	39
Recovered (n = 32)	37.6	104	30	38.5	118	38
Expired (n = 25)	37.7	112	30	39.8	124	40
<i>p</i>	NS	NS	NS	< 0.001	NS	NS

Results

There were 60 patients (46 males, 14 females) presenting with nonneonatal tetanus to BMCO during the 5-year study period, representing 0.3% of 20,803 nonneonatal hospital admissions. The mean age was 26 years (range 5–80 years). Forty-four (74%) patients were 30 years of age or younger. The major occupational groups included 18 students, 17 farmers, and 9 market traders. There was a relatively even distribution of cases throughout the dry and rainy seasons of the year and a surprisingly even distribution for farmers during the active and inactive farming months. The portal of entry was unknown in 11 (18%), the lower extremity in 32 (53%), the upper extremity in 10 (17%), the trunk in 4 (7%), and the ear, scalp, or uterus in 1 patient each.

The mean incubation period, which was defined as the time between trauma and the onset of symptoms, was 10.4 days (range 3–90 days) in the 49 patients with known traumatic events. The mean duration of symptoms, which was defined as the time from onset of symptoms until presentation to a health care facility, was 3.3 days (range 1–14 days). On presentation to the hospital, the severity of tetanus was assessed as mild in 12 (20%) patients, moderate in 25 (42%), and severe in 23 (38%). The mean values for vital signs on admission were temperature 37.8°C, pulse 107 beats/min, and ventilatory rate 30 breaths/min. The mean values for maximum vital signs during the hospitalization were temperature 39.1°C, pulse 120 beats/min, and ventilatory rate 39 breaths/min.

Three patients, two with moderate and one with mild disease, were granted discharge from the hospital against medical advice. Outcome determination was available for the remaining 57: 25 (44%) patients died, and 32 (56%) recovered. The mean hospital stay for survivors was 15 days (range 5–32 days). The mean time from hospital presentation until death for the nonsurvivors was 4 days (range 1–28 days). Tables 1 and 2 summarize the potential predictive factors of mortality and their statistical significance. Factors statistically significant in predicting mortality included occupation as a farmer (*p* = 0.026), age > 14 years (*p* = 0.032), short incubation period (*p* = 0.005), short duration of symptoms

(*p* = 0.005), a high degree of severity on admission (*p* = 0.032), and a high maximum temperature during the hospital course (*p* < 0.001). Insignificant predictors of mortality included gender, portal of entry, vital signs on admission, and highest vital signs (other than temperature) during hospitalization.

Discussion

Tetanus is caused by *Clostridium tetani*, which usually enters the body through external penetrating injuries (including nonsterile intramuscular injections and burns), internal skin disruption processes (open fracture, guinea worm eruption [1]), and postpartum or postabortion infections of the uterus. In approximately one-fourth of cases the portal of entry is never identified. When the *C. tetani* organisms multiply in an anaerobic setting they release tetanus toxin, which attaches to peripheral nerves and then moves in centripetal fashion from the peripheral to the central nervous system affecting muscles, neuromuscular junctions, peripheral nerves, the spinal cord, and the brain stem [2]. The clinical spectrum of tetanus ranges from localized rigidity and pain without mortality to severe generalized rigidity and muscle spasms resulting in death.

The profile of patients in this series is not significantly different from that reported by Adeuja and Osuntokun [1] from Nigeria almost 30 years ago. Most of our patients and theirs were farmers or students, a reflection of our population at large. Victims are usually young, with 74% being 30 years of age or younger in this series. In DW locations family members depend for their existence on the current and future economic production of each family member of this age group, and the loss of a single member can bring devastating consequences. The distribution of tetanus entry points, with most (53%) in the lower extremity, was not significantly different from entry points reported by other observers in DW countries [1, 3, 4]. Because the severity of tetanus on presentation to the hospital is a significant predictor of mortality, it should be emphasized that in this series the affection was mild in only 20% and severe in 38%. Because of a lack of agreement on

the best way to determine the severity of tetanus at presentation, meaningful comparisons cannot be made with other reported series.

Tetanus usually occurs in areas of the world that are least able physically and economically to treat the disease. It costs at least \$2000 per day to manage a patient in an ICU in the United States or the United Kingdom. This amount for 1 day of ICU care is more than the annual per capita income for many DW countries where tetanus commonly occurs. BMCO is a general medical practice hospital in a DW country. There are some hospitals in Nigeria and other parts of the DW that have better facilities than ours, but there are many more hospitals where the standard of care is lower than that at BMCO. With other DW hospitals around the world we share a common set of problems: a lack of supplies and functioning equipment, an unreliable supply of electrical power, and a lack of clean water. Intensive care takes on a different meaning in such a context, where it may mean nothing more than a conscientious nurse who stays awake all night taking care of a tetanus patient by kerosene lantern light in an overcrowded ward with 30 other patients.

Successful treatment of tetanus depends on prompt diagnosis, neutralization of circulating toxin, elimination of the *C. tetani* infection, control of spasms and convulsions, and maintenance of the airway. The 3.3-day delay in seeking health care, which impedes prompt diagnosis, is typical of delays reported in other series and reflects a combination of lack of perception of the seriousness of the disease on the part of the victim or family, lack of transportation from remote areas, and lack of money needed to pay for health care. As soon as tetanus is diagnosed, the circulating toxin should be neutralized by administration of antitoxin. Human tetanus immune globulin (HTIG) is the safest antitoxin, but it is not as readily available in DW countries as is ATS. Because ATS is made from horse serum, a test dose is needed before administering the full dose. ATS was used exclusively in this series, and there were no significant reactions noted to it. The optimal dose of ATS is controversial, but the recommended dose has decreased significantly over the past 25 years [4, 5]. Elimination of *C. tetani* organisms involves administration of antibiotics and operative débridement. Penicillin, the traditional drug of choice, was used for all patients in this series, although metronidazole is currently the recommended antibiotic for clostridial infections [2]. If a portal of entry was identified in our patients, local débridement was performed. Débridement is relatively easy when the portal is in the extremities. When tetanus results from a septic abortion, however, removing the source of infection involves a hysterectomy, and many families in our locale prefer death over sterilization.

Control of spasms and maintenance of the airway are the most formidable obstacles to the proper management of tetanus patients in most DW institutions. Diazepam and chlorpromazine are the least expensive and most readily available antispasmodic agents in our institution and in many areas of the DW. These drugs must be given in adequate quantities to prevent spasms from inhibiting ventilation but in small enough quantities that the sedative drugs themselves do not suppress the ventilatory drive. In ideal circumstances patients can be paralyzed for long periods of time and mechanically ventilated; ideal circumstances, however, rarely exist in the DW. Although there is a functional ventilator at BMCO, we have not been able to use it successfully for prolonged periods of time because of an erratic supply of electricity. As a

result, none of the patients in this series were managed with positive-pressure ventilation, and none underwent tracheostomy.

Considering the limitations discussed above, a mortality rate of 44% is not surprising and is consistent with the mortality rates of 22% to 45% reported by other DW hospitals [1, 3–5]. Some of the statistically significant predictors of mortality in this series (short incubation period, short duration of symptoms, severity of illness on admission) are consistent with predictors in other published reports. Age was also a significant ($p = 0.032$) predictor of mortality in this series. The mortality rate for children (14 years or younger) was 10%, whereas that for victims older than 14 years was 51%. Our rate for pediatric mortality is lower than the 39% rate reported from Mumbai, India [5] and the 19% rate reported from Haiti [4]. However our adult mortality rate of 51% is higher than most adult rates reported from DW countries. Mortality among the elderly (> 60 years old) is usually reported as higher than that for younger patients [6], but because there were only three patients older than 60 years in this series, a meaningful comparison could not be made.

One of the purposes of this report is to develop better management techniques for future tetanus patients at BMCO. There does not appear to be a need for better availability of pharmaceuticals in the management of tetanus as adequate antitoxin, antibiotics, and antispasmodics were readily available and relatively inexpensive. The greatest hope for improving treatment lies in more intense care when titrating the antispasmodic drugs to achieve control of spasms without significantly depressing the ventilatory drive. This requires great cooperation between all members of the health care team, with the care of the tetanus patient viewed as a team effort, not just as a nursing care problem. Secretions are certainly a major problem when managing the tetanus patient, and we can only speculate that early tracheostomy might have prevented some deaths in this series, although tracheostomy in a DW setting carries its own morbidity and mortality separate from tetanus. Using parenteral betamethasone and small intrathecal doses of ATS (instead of larger parenteral doses), Sanders reported a decrease in mortality to 5% for tetanus patients presenting to a rural hospital in North India [7]. Some success with steroid administration has also been reported from other institutions. There have not, however, been randomized series to test the efficacy of either parenteral steroids or intrathecal ATS, and the challenge exists for centers that see large numbers of tetanus patients to begin such randomized trials. Tetanus patients are quite hypermetabolic, and little attention was paid to providing adequate nutrition to patients in our series. Although nutrition would probably not have helped patients dying early in their hospital course (84% of deaths occurred within 4 days of admission), nutrition through a gastrostomy tube may have led to a reduction in mortality in the remaining 16%.

Things have not changed much in the past 30 years since Adeuja and Osuntokun wrote, "Whatever routine is adopted for treating tetanus, it is expensive in money and skilled medical and nursing care, and in a developing country such as Nigeria, these are scarce. The only hope in diminishing the mortality of the disease . . . lies in prevention by active immunization" [1]. Improvements in treatment may make a minor improvement in the global mortality rate for tetanus, but a significant impact can occur only through more conscientious efforts to immunize the population. Some claim that tetanus is a totally preventable disease [8], whereas others report that tetanus can occur in individuals who

have been “properly” immunized [9, 10]. This controversy in more developed countries may seem trivial to doctors in the DW, who are regularly reminded that after 25 years of conscientious efforts by WHO and DW governments, tetanus, although decreased in incidence, remains a global health threat. The most effective immunization programs are certainly accomplished by community health outreach programs, but these programs cannot successfully accomplish effective immunization without the help of hospital-based health care personnel. Immunization of all people who come to a hospital for any reason should be the routine responsibility of all health care workers in the DW.

Résumé. Malgré des efforts attentifs par l'organisation mondiale de la Santé et les gouvernements du tiers monde, le tétanos reste un problème de santé grave. Cette étude rétrospective a été entreprise pour évaluer les résultats des victimes du tétanos se présentant au Centre Médical Baptiste d'Ogbomoso, Nigeria, et pour améliorer la prise en charge future des patients. Soixante patients (46 hommes, 14 femmes) atteints de tétanos non-néonatal, ont été vus pendant la période de 5 ans (1995–1999). L'âge moyen a été de 26 ans, 74% avaient 30 ans ou moins. Tous les patients ont été traités par le sérum anti-tétanique, des antibiotiques, le débridement de la plaie (lorsqu'il y en avait une) et des antispasmodiques. Aucun patient n'a nécessité une trachéotomie ou une gastrostomie. Le taux de mortalité a été de 44%. Les facteurs prédictifs de mortalité significatifs ont été l'âge de plus de 14 ans, le métier de fermier, une période d'incubation courte, un intervalle symptomatique court, un haut degré de sévérité au moment de l'hospitalisation et une hyperthermie pendant l'hospitalisation. Pour améliorer le traitement du tétanos dans notre institution, il faut viser une meilleure utilisation des antispasmodiques sans provoquer de dépression respiratoire conséquente. Cependant, le seul espoir de réduction de mortalité globale pour le tétanos réside dans les efforts de tous les responsables de la santé pour vacciner l'ensemble de la population dans les pays en voie de développement et non pas seulement les professionnels de la santé.

Resumen. A pesar de los diligentes esfuerzos de la Organización Mundial de la Salud y de los gobiernos de las naciones del Mundo en Desarrollo, el tétano persiste como un problema de salud global. El presente estudio retrospectivo fue realizado con el propósito de evaluar el resultado en el

tratamiento de pacientes con tétano atendido en el Centro Médico de Ogbomoso, Nigeria, y de desarrollar mejores métodos de manejo. Sesenta pacientes (46 masculinos, 14 femeninos) con tétano no neonatal fueron vistos en un periodo de 5 años (1995–1999). Su edad promedio fue 26 años, y 74% eran de 30 años o menores. Todos los pacientes fueron tratados con suero antitetánico, antibióticos, desbridación de la herida (cuando había herida identificable) y antiespasmódicos. Ninguno fue sometido a traqueostomía ni a gastrostomía. La tasa de mortalidad fue 44%. Los factores significantes de predicción de mortalidad fueron: edad mayor de 14 años, ocupación como trabajador del campo, periodo de incubación breve, corta duración de los síntomas, gravedad de alto grado en el momento de la presentación y temperatura elevada en el curso de la hospitalización. La mejor perspectiva de superación en el tratamiento en nuestra institución es una titulación más racional del control del espasmo con antiespasmódicos, sin causar depresión respiratoria significativa. Sin embargo, la única esperanza real de reducción de la mortalidad global por tétano reside en la intensificación en las campañas de inmunización por todo el personal de salud en los países del Mundo en Desarrollo, y no sólo por los sanitaristas comunitarios.

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