Original article

Patients with severe accidental tetanus admitted to an intensive care unit in Northeastern Brazil: clinical–epidemiological profile and risk factors for mortality

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ABSTRACT

Introduction: Tetanus, an acute infectious disease, is highly prevalent worldwide, especially in developing countries. Due to respiratory failure and hemodynamic instability associated with dysautonomia, severe cases require intensive care, but little has been published regarding the management in the Intensive Care Unit.

Objective: To draw a 10-year clinical–epidemiological profile of Intensive Care Unit patients with severe tetanus, observe their evolution in the Intensive Care Unit and identify risk factors for mortality.

Methods: In this retrospective study, we used a standardized questionnaire to collect information from the records of patients with severe tetanus admitted to the intensive care unit of a referral hospital for infectious and contagious diseases in Northeastern Brazil.

Results: The initial sample included 144 patients, of whom 29 were excluded due to incomplete information, leaving a cohort of 115 subjects. The average age was 49.6 ± 15.3 years, most patients had no (or incomplete) vaccination against tetanus, and most were male. The main intensive care-related complications were pneumonia (84.8%) and dysautonomia (69.7%). Mortality (44.5%) was higher than expected from the mean APACHE II score (11.8), with shock/multiple organ failure as the main cause of death (72.9%). The independent factors most predictive of mortality were APACHE II score, dysautonomia, continuous neuromuscular blockade and age.

Conclusion: A high mortality rate was observed in our cohort of Intensive Care Unit patients with severe tetanus and a number of risk factors for mortality were identified. Our results provide important insights for the development of intervention protocols capable of reducing complications and mortality in this patient population.

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Introduction

Tetanus is a non-contagious acute infectious disease caused by exotoxins (tetanolysin and tetanospasmin) produced by *Clostridium tetani*. Despite being well documented since antiquity, tetanus remains an important cause of mortality worldwide. It is infrequently observed in developed countries but still represents a public health issue in developing nations.[1–4]

In severe cases the release of tetanolysin and tetanospasmin can lead to respiratory failure and hemodynamic instability associated with dysautonomia. The high doses of sedatives required to control muscle spams justify the frequent use of mechanical ventilation in the intensive care unit (ICU) setting. However, proper management can significantly reduce the risk of mortality.[5–9]

The literature provides few guidelines for the monitoring of ICU patients with severe tetanus. Management is currently based primarily on expertise. However, we believe the mortality rates observed in this patient population would be significantly reduced by the adoption of a carefully designed intervention protocol. The development of such a protocol requires further investigations into the clinical–epidemiological profile of ICU patients with severe tetanus in order to identify avoidable risk factors for mortality and subsidizing preventive measures.[10]

Materials

The study was based on information collected from non-electronic medical records and mechanical ventilation monitoring charts of patients with severe accidental tetanus admitted to the intensive care unit of a referral hospital for infectious and contagious diseases (Hospital São José de Doenças Infecciosas – HSJ) in Fortaleza, a state capital in Northeastern Brazil.

Patients under 18 years of age and patients with incomplete or illegible medical records and mechanical ventilation monitoring charts were excluded from the analysis.

The study protocol was approved by the HSJ Research Ethics Committee and filed under entry number CAAE #0053.0.042.000-08.

Methods

In this retrospective and descriptive study, we analyzed a cohort of patients with severe tetanus admitted to the intensive care unit of HSJ between May 2003 and December 2013.

Using a questionnaire designed specifically for the study, three trained investigators collected patient information directly from non-electronic medical records at the hospital, covering the period from admission to discharge, transfer or death. Abstracted information included clinical–demographic data, intensive care data, and parameters potentially associated with mortality to be submitted to logistic regression. The patients were grouped according to outcome (death/survival).

Vaccination against tetanus was considered to be complete in patients who had received three doses of vaccine plus booster shots, as recommended by the National Immunization Service (PNI) of the Brazilian Ministry of Health (MoH).[11] In patients with incomplete vaccination schedule, the time between the last vaccine shot and ICU admission could not be determined.

With regard to complications, dysautonomia included symptoms such as labile hypertension, tachycardia, heart rate irregularities, peripheral vasoconstriction, sweating, pyrexia, hypotension, and bradycardia, with no other obvious cause.[12] Shock was defined as hypotension requiring vasoactive medication for more than 6 h, except if dopamin was <5 μg/mL. Acute renal failure was defined as a 1.5–2-fold increase, or a ≥0.3 mg/dL increase, in serum creatinine levels in relation to baseline, or a <0.5 mL/kg/h decrease in urinary output during 6 h.[13] Evidence of blood loss and need for transfusion were interpreted as bleeding. Pneumonia, atelectasis, pneumothorax, and obstructed tracheostomy were counted as complications if mentioned in the medical record.

In order to better evaluate severity, the respiratory data used in our analysis corresponded to the maximum values observed during mechanical ventilation.

Categorical variables were expressed as absolute and relative (percentage) frequencies while numerical variables were expressed as mean values ± standard deviation. Continuous variables and their respective standard errors were tested with regard to distribution (skewness/kurtosis ratio) with the Kolmogorov–Smirnov test and the Shapiro–Wilk test.

Student's t test was used to compare means of two independent samples of variables with normal distribution. Pearson's chi-square test was used to verify compare dichotomous variables with non-normal distribution. Variables that did not satisfy Cochran's rule were analyzed with Fisher's exact test.

Variables of ICU patients with severe tetanus associated with mortality in univariate analysis were analyzed using a stepwise logistic regression model, calculating adjusted odds ratios and a 95% confidence intervals. The level of statistical significance (rejection of the null hypothesis) was set at 5% ($p < 0.05$) in all tests.

In the logistic regression, "death of any cause" was the dependent variable while "APACHE II score", "dysautonomia", "continuous neuromuscular blockade" and "age" were used as independent variables.

The statistical analysis was performed with the software SPSS v. 19.0 (Statistical Package for the Social Sciences) for Windows.

Results

The collected data of 144 patients are presented in Table 1. Twenty-nine subjects were excluded due to incomplete or illegible medical records, leaving a final cohort of 115 patients (Tables 2 and 3).

All ICU patients followed the same protocol during the first 24 h after admission: surgical debridement of infected tissue, antibiotic therapy (metronidazole), and administration of immunoglobulin or anti-tetanus serum, as specified in the MoH guidelines in effect during the study period.[10]

In general, patients were discharged from the ICU shortly after weaning from mechanical ventilation.