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ORIGINAL ARTICLE

Do High-Risk Patients with Infected Puncture Wounds Get Appropriate Tetanus Prophylaxis?

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Background: To evaluate clinicians’ compliance to follow national guidelines for tetanus vaccination prophylaxis in high-risk foot patients.

Methods: We retrospectively evaluated 114 consecutive patients between June 2011 and March 2019 who presented with a foot infection resulting from a puncture injury through the emergency department. Eighty-three patients had diabetes mellitus and 31 patients did not have diabetes mellitus.
Electronic medical records were used to collect a broad range of study data on patient demographics, previous medical history, previous tetanus immunization history and tetanus status upon presentation to the emergency department (ED), peripheral arterial disease, sensory neuropathy, laboratory values, and clinical/surgical outcomes.

Results: 46.5% of the patients who presented to the ED with a puncture wound did not have up-to-date tetanus immunization. Of those patients, 79.2% received a tetanus-containing vaccine booster, 3.8% received intramuscular tetanus immunoglobulins (TIG), 3.8% received both tetanus-containing vaccine booster and TIG, and 20.8% received no form of tetanus prophylaxis. When comparing data between patients with and without diabetes, there were no statistical significant differences in tetanus prophylaxis.

Conclusion: Guidelines for tetanus prophylaxis amongst high-risk foot patients in this study center are not followed in all patients. Patients with DM are at high risks of exposure to tetanus, we recommend physicians to take a detailed tetanus immunization history and vaccinate them if tetanus history is unclear.

Tetanus can be a life-threatening disease caused by a toxin produced by *Clostridium tetani*, an anaerobic Gram-positive, spore-forming bacillus found predominantly in soil and animal excrement. The potent neurotoxin has profound effects on skeletal muscle function. In the United States, tetanus is an increasingly rare diagnosis with the incidence of tetanus declining dramatically due to the widespread
use of the Tetanus vaccine.² Despite this, there still remains high-risk populations for tetanus which include the elderly, individuals with diabetes, intravenous drug users, and unvaccinated individuals.³

Tetanus occurs when spores of C. tetani enter the body through breaks in the protective barrier of the skin. C. tetani spores germinate under anaerobic conditions such as those provided by deep, devitalized tissue, which likely explain the presenting mechanism of injuries. Therefore, patients who sustain wounds via mechanisms of traumatic foreign body breaches to the skin should be assessed for tetanus risk and screened for tetanus vaccine status. The Centers for Disease Control (CDC), Infectious Disease Society of America (IDSA), and World Health Organization consider patients with puncture wounds to be high-risk for tetanus.³⁵ Furthermore, studies have shown that puncture wound injuries are associated with high risk of infection, multiple surgeries, osteomyelitis, and amputation.⁶⁻¹⁰ Tetanus prevention guidelines from both the IDSA and CDC⁴¹¹ recommend the following management for patients with tetanus prone wounds: (1) patients with an unknown status or no previous vaccination should be given both tetanus-containing vaccine and intramuscular tetanus immunoglobulin (TIG); (2) if the last tetanus-containing vaccine dose was over 5 year: patients should receive only the tetanus-containing vaccine booster and no TIG is needed; (3) if the last tetanus-containing vaccination was within the last 5 years: no additional tetanus immunization is needed.

Despite clear recommendations from both the CDC and IDSA, there seem to be gaps in the delivery of care in ensuring patients who require tetanus prophylaxis receive appropriate therapy. Abbate and colleagues (2008) evaluated 502 patients who presented to Emergency Departments (ED) across Italy with tetanus-prone wounds. Of the 502 patients, 210 patients were undertreated for tetanus with only 1.5% of treating physicians correctly adhering to tetanus prophylaxis and
immunization practices based on Italian recommendations.\textsuperscript{12} Talan and colleagues (2000) evaluated information from 1,988 patients with tetanus-prone wounds from five university-based EDs and found that 60.9\% of patients required tetanus-containing vaccination; however, only 42.4\% of patients received it.\textsuperscript{13,14} Most of the described studies include mixed populations of low and high risk individuals with tetanus-prone wounds in varying anatomical locations. However, there are limited studies that evaluate high-risk patients with a focus on tetanus-prone wounds occurring on the foot.\textsuperscript{15} In the current study, we compared the recommended practices outlined by the CDC and IDSA guidelines on tetanus prophylaxis in high-risk patients attending a level I trauma emergency department with an infected puncture wound to the foot.

METHODS

This study was approved by the Institutional Review Board at the two institutions where the study was conducted. A retrospective review of individuals presenting to a university-based emergency department with a puncture wound to the foot (tetanus-prone wound) was conducted between June 2011 and March 2019. All patients included in this retrospective review required in-patient admission for management of their puncture wounds, primarily (but not exclusively) due to bacterial infections (non-tetanus related). Individuals under the age of 18 or over 90 years of age were excluded. Electronic medical records were used to collect a broad range of study data on; patient demographics, previous medical history, previous tetanus immunization history and tetanus status upon presentation to the emergency department (ED), peripheral sensory neuropathy, foot ulceration, peripheral arterial disease, and clinical/surgical outcomes including lower extremity amputation.\textsuperscript{16,17}
The diagnosis of diabetes mellitus (DM) was based on American Diabetes Association criteria.\textsuperscript{18} Peripheral sensory neuropathy was defined as abnormal vibration sensation (>25 volts) or abnormal sensation with a 10-gram Semmes-Weinstein monofilament.\textsuperscript{19,20} We defined peripheral arterial disease as an ankle to arm systolic blood pressure ratio of <0.90. Leukocytosis was defined as white blood count (WBC) >11.0 x 10^9/L.

Data was compiled using Microsoft Excel (Microsoft Corporation, Redmond, WA). Continuous data are given as mean, median, 95\% confidence intervals (CI) and standard deviation (±). A chi square test was used to compare dichotomous variables. A one-way Analysis of Variance (ANOVA) was used to evaluate continuous variables, and the Mann-Whitney U Test was used for non-parametric data. For all comparisons and modelling, the level of significance was set at P< .05. Data were analyzed using calculators on www.socscistatistics.com.

RESULTS

In this retrospective review, 114 eligible patients were included for analysis. There was no difference in patient demographics or co-morbidities as presented in Table 1. Tetanus immunization history was documented in 71 of 114 (62.3\%) individuals, the majority (n=61; 53.5\%) of which had a tetanus-containing vaccination within the last five years. Ten patients (8.7\%) presented with tetanus-containing vaccination history in the last five years, of which 80\% (n=8) of these individuals received a tetanus-containing vaccination booster, and two patients (20\%) did not receive any vaccination.
Forty-three (37.7%) Individuals were identified with an unknown tetanus immunization status or no previous immunization history. In this group only two (4.7%) individuals were treated appropriately; given both tetanus-containing vaccine and intramuscular tetanus immunoglobulin (TIG). Thirty-four individuals (n = 34 of 43, 76.1%) were “under-vaccinated” and treated with only the tetanus-containing vaccine. Nine (20.9%) individuals received no tetanus vaccination (Figure 1).

In this study population, 53 (46.5%) individuals required vaccination. Of these, eight (15.1%) individuals received a tetanus-containing vaccine booster, 32 (60.4%) received intramuscular tetanus Immunoglobulin (TIG), two (3.8%) received both, and 11 (20.8%) received no tetanus prophylaxis. Overall, only 38.6% (n=44) of individuals were treated appropriately, 23.7% (n=27) were “over-vaccinated”, and 37.7% (n=43) were “under-vaccinated”. (Figure 2).

Individuals with DM and associated co-morbidities comprised the majority of subjects in this cohort. This is not surprising given the increased risk of puncture wounds reported in this population owing to the loss of protective sensation amongst other variables. Despite this, there were no statistically significant differences between those with and without DM (Table 2), with the exception of tetanus-containing vaccine booster. Individuals with DM were 2.3 times more likely to receive a tetanus-containing vaccine booster even if their tetanus vaccination status were up to date (DM 46.5% vs No DM 27.8%, p=0.17, CI 0.69-7.45). Individuals with DM were also poor historians being 1.7 times more likely to not know the status of their tetanus immunization history (DM 41% vs No DM 29%, p=0.24, CI 0.7-4.13) (Table 2). There was no statistical difference in clinical outcomes in correlation to tetanus prophylaxis (healed vs amputation, p=0.21, OR 1.65, CI 0.76 – 3.61, Figure 3).
DISCUSSION

The results of this study demonstrate the lack of adherence to CDC and IDSA tetanus prophylaxis guidelines for tetanus prone wounds by physicians consulting in the ED. Our results demonstrate a 38.6% physician adherence to tetanus prophylaxis recommendations, with similar findings noted by several other studies.\textsuperscript{12,13} One reason why most physicians may not be concerned with tetanus immunization in patients presenting with puncture wounds could be because tetanus is increasingly uncommon. The CDC reports that from 2001-2008, there were only 233 cases of tetanus in the United States.\textsuperscript{2} The incidence of tetanus was 1 per 10 million people per year or about 29 cases per year. However, among patients that develop tetanus infections, the overall mortality rate was 13.2% or about 4 people per year. Of the reported cases, 72% presented with acute wounds, and 96% of patients did not receive appropriate tetanus prophylaxis.\textsuperscript{7} Given that there are less than 30 cases per year in the United States, tetanus may not be at the forefront of a physician’s workup when they are evaluating high-risk/complex patients with puncture wounds and any associated skin, soft tissue, bone and systemic manifestations of illness.

The incidence of tetanus in the USA is fairly low, but most epidemiologists believe that the number of cases is underreported.\textsuperscript{21} The national tetanus surveillance is a passive system that is dependent upon the physicians self-reporting the cases to the health departments. Because of this, some epidemiologists believe that only about 40% of the cases are actually being reported, leading to underrepresentation of the disease.\textsuperscript{21}
The findings of this study have some clinical relevance and ramifications to the largest sub-set of patients evaluated in this study. Whilst we evaluated Individuals without DM, these were outnumbered by those with DM, the latter being a high-risk population. Patients with diabetes innately have a high risks of contracting tetanus. Patients with diabetes have marco- and microvascular disease that cause them to have lower perfusion to the foot, which is favorable to anaerobic condition. Due to this, they are more likely to develop gangrene, which is considered a tetanus-prone wound. Furthermore, patients with diabetes are considered to be immunocompromised with abnormalities in B lymphocytes, which is responsible for maintaining antibodies response in vaccination. In a seroprevalence of tetanus antitoxin, Kilic and colleagues found that 26% of immunized diabetics have antitoxin titers that were too low to actually offer immunity. Collectively, these all suggest that diabetic foot ulcers (DFU) are innately at higher risks for contacting tetanus. We agree with Rogers and Frykberg that DFU should be considered a tetanus-prone wound and prophylaxis as such.

Adverse events associated with tetanus prophylaxis are distinctly uncommon. Severe reactions to tetanus vaccine (such as serious allergic reaction, long-term seizure, coma, and brain damage) are exceedingly rare and occur less than 1 out of 1 million. Moderate reactions (such as high fever and seizure) are uncommon and occur in about 1 out of 16,000. Mild reactions (i.e. low-grade fever, redness, and soreness at site of injection) are common and occur about 25% of the time. Developing a severe tetanus reaction to the vaccine is 10 times higher than contracting tetanus, given the rarity of the disease. There has been no reported death from the vaccine.
The main prevention against tetanus is immunization. Overall, patients generally have poor recall of their tetanus immunity status. McVicar evaluated 200 patients in a single center ED and found that 68% tested positive for tetanus immunity.27 One hundred fifty-one patients (75.5%) did not know their status. Of those, 101 patients (66.9%) tested positive, and 50 patients (33.1%) were negative. Forty-nine patients (24.5%) states that they knew their status; however, 38.8% of them were wrong. According to McVicar, the cost of testing and treating all 200 patients appropriately would save $1194.84, or $5.97 per patient. So if we treated patients based on their recall ability, then we would treat 38.8% of patients inappropriately.

On the other hand, Rhee et al.25 did a retrospective review of literature on tetanus and concluded that it is not possible to identify which wounds are tetanus prone, and thus, they did not recommend routine prophylaxis. They recommend that tetanus vaccine should be reserved for patients who never received primary immunization. However, the CDC attributes the decline in tetanus infection to the introduction of tetanus prophylaxis in wound management and continues to urge the practice of tetanus prophylaxis as there has been a 99% reduction in the disease since 1940s.29

There are several limitations to this study. The first limitation is the retrospective nature of the study and relying on the accuracy of patient medical records. Measurement bias is possible because clinicians often use different operation definitions for disease states. Since our study was conducted in a teaching hospital, a number of junior and senior physicians are routinely involved in patient care. Selection bias may also present due to the hospital serving a low socioeconomic community with a disproportionate number of ethnic minorities; our study was conducted at a level 1 trauma center and teaching hospital, so our patient population and practice may not be generalizable outside this context.
The retrospective design of the study did not rely on a sample size and power calculation meaning it may have been underpowered to evaluate factors that might have been associated with patients not receiving tetanus prophylaxis.

CONCLUSION

In summary, the CDC and IDSA provide a framework for tetanus prophylaxis, but these were not consistently followed at our institution. Our results probably reflect treatment at other hospitals. Infected puncture wounds to the foot in individuals with and without DM are a common presentation to the hospital ED, yet clinicians generally do not provide prophylaxis against tetanus even in very high-risk cases, and in most cases national guidelines are not followed.

REFERENCES


Table 1: Demographic, clinical, and laboratory features

<table>
<thead>
<tr>
<th></th>
<th>Tetanus Up-to-Date</th>
<th>Tetanus Not Up-to-Date</th>
<th>Tetanus Status Unknown</th>
<th>p-value</th>
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<tbody>
<tr>
<td>N (Total = 114)</td>
<td>61 (53.5)</td>
<td>10 (8.8)</td>
<td>43 (37.7)</td>
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<tr>
<td>Age (Years)</td>
<td>49, 51 (10.9)</td>
<td>48, 46 (13.6)</td>
<td>52, 55 (11.2)</td>
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<tr>
<td>Male</td>
<td>44 (72.1)</td>
<td>8 (80)</td>
<td>35 (81.4)</td>
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<tr>
<td>Diabetes Mellitus</td>
<td>40 (65.6)</td>
<td>6 (60)</td>
<td>33 (76.7)</td>
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<td>Peripheral Arterial Disease</td>
<td>12 (19.7)</td>
<td>2 (20)</td>
<td>10 (23.3)</td>
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<td>Sensory Neuropathy</td>
<td>45 (73.8)</td>
<td>5 (50)</td>
<td>34 (79.1)</td>
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<td>Labs</td>
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<td>White Blood Count</td>
<td>11.3, 9.77 (4.8)</td>
<td>10.6, 11.2 (3.6)</td>
<td>11.8, 11.3 (4.4)</td>
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<tr>
<td>WBC &gt;11,000</td>
<td>23 (37.7)</td>
<td>5 (50)</td>
<td>23 (53.5)</td>
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<td>Erythrocyte Sedimentation Rate</td>
<td>64.6, 55 (39.7)</td>
<td>48.9, 50 (31.3)</td>
<td>53.5, 52 (32.4)</td>
<td>.75</td>
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<td>ESR &gt;30</td>
<td>42 (68.9)</td>
<td>6 (60)</td>
<td>27 (62.8)</td>
<td>.75</td>
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<td>C-Reactive Protein</td>
<td>8.8, 6.2 (8.4)</td>
<td>7.3, 3.5 (7.8)</td>
<td>9.7, 5.1 (9.8)</td>
<td>.66</td>
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<td>CRP &gt;7.9</td>
<td>21 (3.4)</td>
<td>3 (30)</td>
<td>18 (41.9)</td>
<td>.66</td>
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<td>Glomerular filtration rate &lt; 60</td>
<td>49 (80.3)</td>
<td>7 (70)</td>
<td>41 (95.3)</td>
<td>&lt; .04</td>
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<td>Albumin</td>
<td>3.6, 3.6 (0.6)</td>
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<td>3.4, 3.4 (0.6)</td>
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<td>Pre-Albumin</td>
<td>16.1, 14.2 (7.3)</td>
<td>15.7, 9.2 (7.6)</td>
<td>11.2, 9.6 (4.9)</td>
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<td>Osteomyelitis</td>
<td>17 (27.9)</td>
<td>2 (20)</td>
<td>14 (32.6)</td>
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<td>Number of surgeries</td>
<td>2.3, 2 (1.3)</td>
<td>2, 2 (1.1)</td>
<td>2.4, 2 (1.3)</td>
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<td>Hospital Length of Stay</td>
<td>14, 10 (11.6)</td>
<td>11, 11.5 (6.7)</td>
<td>14.4, 12 (10.4)</td>
<td></td>
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OR = Odds Ratio; 95% CI = 95% Confidence Interval; TIG = Tetanus Immunoglobulin
TMA = Transmetatarsal Amputation; BKA = Below-Knee Amputation; WBC = White Blood Count;
ESR = Erythrocyte Sedimentation Rate; CRP = C-Reactive Protein
Descriptive variables are represented as N (%)
Continuous variables are represented as median, mean (standard deviation)
Figure 1: Vaccination received by patient in each group (TIG = Tetanus Immunoglobulin). Descriptive variables are represented as N (%)
Figure 2: Overall tetanus status of all patients. Description variables are represented as N (%)
Figure 3: Clinical outcome of patients based on their vaccination status. Descriptive variables are represented as N (%)