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Original Contribution

Tetanus Quick Stick as an applicable and cost-effective test in assessment of immunity status

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Abstract

Introduction: Tetanus vaccine and immunoglobulin administration are challenging decisions mostly because of the fact that the current protocol for immunization against tetanus is based on 2 variables: the vaccination status of the patient and the nature of wound and its exposure. To solve this problem, Tetanus Quick Stick (TQS; Nephrotek Laboratory, Rungis, France), an immunochromatographic dipstick test, was developed to determine the tetanus immunity of the patients. The aim of this present study was to investigate the sensitivity, specificity, and the positive and negative predictive values and cost-effectiveness of TQS in the emergency department (ED) setting.

Methods: Blood samples were collected from 200 patients presenting to our ED. Information including demographic information, tetanus immunization status, wound description, and the preventive measures taken by the emergency physician were gathered by a preeducated nurse. Tetanus Quick Stick test and enzyme-linked immunosorbent assay were performed as the standard diagnostic test by an emergency physician and a laboratory technician, respectively; and results of the 2 techniques were compared.

Result: Overall, tetanus vaccine was administered to 141(70.5%) patients and immunoglobulin to 105 (52.5%) patients. The analysis revealed 88.1% sensitivity and 97.6% specificity for the TQS test. The positive and negative predictive values of TQS test were 99.3% and 66.1%, respectively. Our analysis is also showed a significant decrease in cost when TQS was applied for patients with dirty, tetanus prone wounds or injuries and unknown or incomplete vaccination history (€ 9.48 versus € 12.1).

Conclusion: This study revealed TQS test to be appropriate and cost-effective for ED use especially in evaluating patients who do not remember or cannot give their tetanus immunization history.

1. Introduction

Although preventive medicine has progressed in recent decades, tetanus infection remains a life-threatening condition and is still an important health issue worldwide. Tetanus

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is caused by *Clostridium tetani*, an anaerobic, motile, gram-positive rod found worldwide in the soil, as well as in animal and, occasionally, human feces. Although tetanus is ubiquitous, infections in certain developing regions of the world are associated with high mortality and morbidity largely because of a lack of rigorous immunization programs and available treatment options. Consequently, tetanus has become one of the target diseases of the World Health Organization (WHO) Expanded Program on Immunization.

In the clinic, patients often present with an array of injuries and wounds in which tetanus prophylaxis should be considered. Current protocols for immunization against tetanus are dependent on 2 factors: (1) the nature of the injury and (2) the vaccination status of the patient (Table 1). With respect to the former, wounds are classified as clean minor or dirty. With respect to the latter, patient recollection of past immunizations and the physician carrying out proper protocols are important considerations. For example, if the physician cannot remember the proper course of action, he or she may simply administer both vaccine and immunoglobulin to err on the side of caution. Indeed, although many patients do not remember their vaccination history, the attending physicians' memory may not be relied upon either [1]. Although this course of action could be lifesaving for some patients, it is a considerable waste of resources from the level of community medicine. Moreover, booster vaccines have adverse effects, such as moderate and severe local reactions, Arthus reactions (type III hypersensitivity reactions), or Guillain-Barré syndrome, particularly if it is administered in less-than-5-year intervals [2-5].

Based on what WHO has declared, concentrations of tetanus antibody greater than 0.1 IU/mL in the serum are deemed to be protective [6]. The criterion standard method for evaluating tetanus antibody concentrations in serum is enzyme-linked immunosorbent assay (ELISA). However, this assay is time consuming, expensive, and technician and instrument dependent and is therefore not aptly suited for many clinical settings. To this end, Tetanus Quick Stick (TQS; Nephrotek Laboratory, Rungis, France), an immunochromatographic dipstick test, was developed to determine the immunity status of the patients against tetanus [7-9] faster and that is more applicable than ELISA.

Given that prior immunizations may negate the need for expensive immunoglobulin treatments, the aim of the present study was to assess the cost-effectiveness of TQS in our emergency department (ED). In addition, we sought to assess the sensitivity, the specificity, and the positive and negative predictive values of the test.

Table 1 Guide to tetanus prophylaxis in routine wound management

Vaccination history	Clean minor wounds		All other wounds [a]	
	Tdap or Td [b]	TIG [c]	Tdap or Td [b]	TIG [c]
<3 or unknown	Yes	No	Yes	Yes
≥3 doses	No [d]	No	No [e]	No

Adopted from *VPD Surveillance Manual, Fourth Edition, 2008 Tetanus* (chap 16-5).

[a] Such as (but not limited to) wounds contaminated with dirt, feces, soil, and saliva; puncture wounds; avulsions; and wounds resulting from missiles, crushing, burns, and frostbite.

[b] For children younger than 7 years, DTaP is recommended; if pertussis vaccine is contraindicated, DT is given.

[c] TIG is human tetanus immunoglobulin.

[d] Yes, if it has been 10 years or longer since the last dose.

[e] Yes, if it has been 5 years or longer since the last dose.

2. Material and methods

Between January 2009 and April 2009, 200 patients were randomly selected and enrolled in the study from those patients who presented to the ED of the Imam Hussein Teaching Hospital (Tehran, Iran) with any kind of wounds or injuries. This study was approved by the medical ethics committee of Shahid Beheshti University of Medical Sciences, and an informed consent was obtained from all subjects. Exclusion criteria were age less than 18 years, pregnancy, and inability to provide data on immunization status (eg, altered mental status, psychiatric disease). Upon the patient's arrival, a 5-mL blood sample was obtained from the patient. The patient was then treated by the emergency physician (EP), and the treatment included tetanus prophylactic measures. Finally, a questionnaire that provided information on demographics, tetanus immunization status, wound description, and the preventive measures taken by EP in the ED was completed by a preeducated ED nurse. The EP and the patients were blinded to the study. Sera were isolated from blood samples and were divided into 2 tubes: one was frozen at −20°C for pooling, and the other was temporarily refrigerated (~4°C) and used for tetanus antibody assessments. The TQS test, like other immunochromatographic dipstick tests, is made up of a solid phase and diluent and can be performed on blood, serum, plasma (citrate or EDTA), or recalcified plasma. To perform the test, 20 μL of serum was dispensed into the sample well of TQS (Nephrotek Laboratory) by a micropipette; and 3 drops of diluents were then added within 10 seconds. The tests were read and interpreted after 10 minutes. Each test panel has 2 distinct wells, indicated by "C" for control and "T" for test. Appearance of a pink to purple line in the control area indicates validity of the test process, whereas a line in the test area indicates the presence of tetanus immunoglobulin G (TIG). The limits of detection were concentrations of TIG of at least 0.1 IU/mL in serum and at least 0.2 IU/mL in whole blood. The TQS tests were performed and interpreted by a trained emergency medicine resident. The ELISAs for tetanus immunoglobulin (Tetanus ELISA IgG Testkit; Genzyme Virotech GmbH, Ruesselsheim, Germany) were also performed on the same serum samples, according to manufacturer's instructions. Investigators who performed the tests were blinded to the identity of patients and the result of

Table 2 History of previous tetanus vaccination

Vaccination history	% (n)	Detail
Believe to be vaccinated	42.5% (85)	≤5 y ago (66.5%) 5-10 y ago (17.5%) >10 y ago (16.0 %)
Without previous vaccination	8% (16)	–
No clear history of vaccination	49.5% (99)	–

the other test. Subjects' TIG levels of at least 0.1 IU/mL were considered protective, according to WHO standards. Data were analyzed using STATA Version 8 (STATACorp LP, College Station, TX).

3. Results

The mean age of patients was 33.2 years (SD = 15.9, minimum = 18, maximum = 87), and 85% were male. DT vaccine was administered to 141 (70.5%) patients and TIG to 105 (52.5%). Subjects' history of vaccination is presented in Table 2. Based on the vaccination history, 33% (66) of patients were presumed to be protected. Overall, the TQS test was positive for 137 (67.5%) patients and negative for 63 (31.5%) (Table 3). Serum TIG levels, assessed by ELISA, indicated that 79% of patients had levels deemed to be protective; this value corresponded to 68.5% for the patients that tested positive using the TQS test. The geometric mean of antibody concentration (according to the ELISA test) was 1.26 IU/mL for positive (95% confidence interval, 1.02-1.33) and 0.03 IU/mL for negative sera (95% confidence interval, 0.003-0.44). Statistical analysis revealed 86.1% sensitivity and 97.6% specificity for the TQS test. The positive and negative predictive values of TQS test were 99.3% and 65.1%, respectively. When comparing vaccination history and ELISA outcomes, analysis showed sensitivity and specificity of vaccination history to be 39% and 85%, respectively. Positive and negative predictive values of vaccination history were calculated to be 90% and 27%, respectively.

Cost-benefit analysis revealed that application of TQS in patients with tetanus-prone wounds and no clear history of vaccination could have reduced the mean cost per patient from €12.1 per patient to €9.48 per patient, which is a 21.66% reduction (Table 4). Although TQS test in patients with clean minor wounds and no vaccination history could help avoid redundant vaccination, overall, this outcome was not cost-effective (€4 per patient with TQS vs €0.1 per patient without TQS) (Table 4).

Table 3 Results of TQS test

Type of wounds	Vaccination history	TQS results
Dirty	Unclear	30/60 (50%) positive
Clean and minor	Unclear	25/39 (64%) positive
Any type	incomplete	10/16 (62%) positive
Any type	Complete	72/85 (84%) positive

4. Discussion

Despite the emphasis on immunization and preventive measures for wounds and injuries in medical education, tetanus infection is still common in developing countries. To help physicians take appropriate measures, an immunochromatographic dipstick test (TQS) was developed to assess the tetanus immune status of patients in an easy and timely manner. Our results are consistent with previous studies demonstrating the validity of TQS assessments of immunity against tetanus [7-12]. Although TQS is reliable, its routine use in ERs and other clinical settings is contingent upon economic feasibility. That is, to make TQS a part of standard tetanus prophylaxis protocol, cost-benefit studies should be done (Table 4); to our knowledge, such a study has only been done once [12]. Considering the low negative predictive value of vaccination history in comparison to TQS in predicting immunity (negative predictive value, 27% vs 66%), cost study was rationally performed for patients who were assumed to be tetanus vulnerable based on history. DT vaccine, which is generally produced locally (Rasi Corp., Tehran, Iran), is fairly inexpensive (€ 0.1) for the health care system and is often provided without cost to the patients even in developing countries. In contrast, the TIG required to immunize patients with "dirty wounds" is imported, considerably more expensive (€12), and not covered by most medical insurance policies. Considering the low

Table 4 Cost analysis of the TQS

Determination of antitetanus immunity		Proportion of patients eligible for treatment	Proportion of saved treatments, % (95% CI)	Mean cost/patient
Patients with tetanus-prone wounds	Vaccination history	100%	–	12.1
	TQS	46%	54% (43.5-65.4)	9.48
Patients without tetanus-prone wounds [a]	Vaccination history	100%	–	0.1
	TQS	35.4%	64.6% (49.4 -77.8)	4

[a] Incomplete vaccination program or last booster 10 years ago. The prices are in euro, taxes included.

negative predictive value of vaccination history compared with TQS in predicting immunity (negative predictive value, 27% vs 66%), a cost study was performed for patients who were deemed to be unprotected from tetanus infection based on history alone. Our analysis showed a significant decrease in cost when TQS was applied for patients with dirty, tetanus-prone wounds or injuries and unknown or incomplete vaccination history (€9.48 vs €12.1). A cost reduction of 22% could represent a dramatic financial relief considering that populations in developing countries constitute more than two thirds of the global population. The reduced costs likely reflect the high proportion of patients who do not accurately recall their vaccination history or for whom the information is not available, but actually are seroprotected. Several reasons and theories could account for this, including (1) unsubstantiated belief by patients about the safety and costs of DT and TIG, which could cause patients to give inaccurate information about their vaccination history; (2) patients' ignorance about their prior vaccination in medical centers (ie, they are vaccinated but not informed about that); (3) lack of adequate record-keeping by clinics (eg, lack of vaccination cards); and (4) lack of active vaccination program for adults. In many countries, DT is part of a comprehensive immunization program, which is implemented during early adolescence and continues throughout life (eg, before obligatory military service and pregnancy in Iran). These vaccination programs could explain why 79% of adults are protected, although 51.89% of them do not remember their vaccination or claim not to be vaccinated.

5. Conclusion

This present study demonstrates that TQS is a valid assessment of tetanus immunity status and demonstrates that this is a cost-effective approach to determining requirements for type of tetanus prophylaxis measure in patients with incomplete vaccination histories whose wounds warrant such an approach.

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