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Original Article

Tetanus and Diphtheria Seroprevalence in Patients Infected With Human Immunodeficiency Virus

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ABSTRACT

Background and Objectives: HIV infected patients are at risk for vaccine-preventable infections such as tetanus and diphtheria (Td). In these patients, these antibodies tend to decline faster. Due to the limited data, this study assessed the seroprevalence of tetanus and diphtheria antibodies in HIV infected patients in Tehran, Iran.

Materials and Methods: This case-control study was carried out in 180 HIV infected patients from Iranian HIV/AIDS Research Center in Tehran and 90 matched healthy controls. The serum samples were checked with ELISA for tetanus and diphtheria antibodies.

Results: A total of 180 HIV positive patients with mean age 36.9±9.2 years and 90 matched controls were enrolled in the study. Tetanus antibody was lower in HIV group when compared with control group. There was no significant difference in the mean serum levels of diphtheria antibody in HIV positive patients when compared with the controls. About 93.3% and 96.6% of HIV infected patients had protective diphtheria and tetanus antibodies respectively. Mean tetanus and diphtheria antibodies levels were not significantly different based on the circulating $CD4^+$ cells.

Conclusion: HIV positive cases, who had received primary Td vaccination before they contracted HIV infection, can be expected to be protected against diphtheria, whereas revaccination against tetanus must be considered.

Keywords: Tetanus, Diphtheria, Human Immunodeficiency Virus

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Introduction

Tetanus and diphtheria (Td) are life-threatening vaccine preventable diseases. They cause a substantial disease burden affecting populations worldwide, particularly in developing countries. Once any of these diseases is contracted, treatment options can be extremely limited. Therefore, the most effective strategy to combat these diseases is disease prevention, particularly through vaccination (1).

Immunization by the triple diphtheria toxoid, whole cell pertussis and tetanus toxoid (DwPT) vaccine has been applied in Iran for almost 50 years (2). The vaccination coverage in Iran was very close to 100% from 1997 based on Eastern Mediterranean Regional Office (EMRO) data (3). According to the current Iran National Immunization program, the DwPT vaccine is administered at the 2nd, 4th and 6th months of life, in combination with two booster doses one administered in month 18 and the other between the years 4 to 6 as DwPT vaccine. The incidence of tetanus and diphtheria in Iran has reported 0.015 and 0.045 respectively in 100,000 populations in 2007 (1).

HIV infected patients are at risk for vaccine-preventable infections. In HIV infected patients who had received primary vaccination before they contracted HIV infection, antibody levels against tetanus and diphtheria tend to be similar to those found in general population (4). However, these antibodies tend to decline faster in HIV infected subjects (5). Determination of the seroepidemiology of tetanus and diphtheria in HIV infected patients makes possible the evaluation of immunity in this population, and helps define the need for Td booster vaccination in them.

To our knowledge, to date, few studies have been carried out on the prevalence of tetanus and diphtheria antibodies infection in the Iranian HIV infected patients. The aim of the present study was to assess this seroprevalence in the cohort of HIV infected patients in Tehran, Iran.

Patients and Methods

In this case-control study, 180 HIV positive patients referred to Iranian Research Center for HIV/AIDS in Tehran, Iran and 90 healthy controls were enrolled from January 2010 to January 2011. Controls were matched with cases regarding sex and age. A questionnaire that gathered epidemiological and clinical data was completed by clinicians. Immunization history was recorded in all participants. Informed consent was obtained from all cases and the project was approved by Iranian Society for Support of Patients with Infectious Diseases Ethical Committee.

HIV-antibody was determined by ELISA (MP Biomedicals, Illkirch, France); with positive tests confirmed by Western blot assay (Diaplus, San Francisco, USA). All assay protocols, cut-offs, and result interpretations were carried out according to the manufacturers' instructions. $CD4^+$ count was determined by flowcytometry and defined as cells/mm^3.

All patients were tested for tetanus and diphtheria antibodies using ELISA. The commercial enzyme immunoassay kits were (IBL International, GmbH, Hamburg, Germany). The procedure was followed as indicated by the manufacturer. Tetanus and diphtheria antibody concentrations lower than 0.01 IU/ml were considered without protection; levels between 0.01 and 0.09 IU/ml, basic immunity; and levels greater than 0.1 IU/ml, full protection (6).

Statistical Analysis:

The Chi-square, Mann Whitney and t^2-tests were used with the SPSS 13 Package program for statistical analysis (Chicago, IL, USA). Data are presented as mean ± SD or, when indicated, as an absolute number and percentage. A *P* value of <0.05 was considered significant.

Results

A total of 180 HIV positive patients with mean age 36.9±9.2 (range: 9-67) years and 90 healthy controls with mean age 37.4±10.2 years were enrolled in the study. Seventy percent of patients were male and 30% were female. The mean $CD4^+$ count of patients was 275.6±181 (16-1000) cells/mm^3. The possible routes of HIV transmission were intravenous drug use (53.6%), heterosexual contact (28.7%), infected blood and blood products transfusion (2.8%), vertical transmission (1.1%), tattooing (0.6%), IDU and tattooing (0.6%), heterosexual contact and intravenous drug use (4.4%), heterosexual contact and infected blood (0.6%) and in 7.6% the route of HIV acquisition was not identified.

Tetanus antibody was lower in HIV group when compared with control group (1.73±1.66 IU/ml versus 2.25±1.16 IU/ml, *P*<0.004). Whereas there was no significant difference in the mean serum levels of antibody to diphtheria in HIV positive patients (0.59 ± 0.54 IU/ml) when compared with the controls (0.69 ± 0.71 IU/ml).

93.3% and 96.6% of patients infected with HIV had protective diphtheria and tetanus antibodies levels respectively.

In patients with $CD4^+$ cells of < 200 cells/µl, the mean tetanus and diphtheria antibodies were 1.50 ± 1.53 and 0.71±0.75 IU/ml respectively, while in those with $CD4^+$ cells of > 200 cells/µl, the mean tetanus and diphtheria antibodies were 1.9 ± 1.7 and 0.672±0.678 IU/ml respectively. The difference was not statistically significant.

Discussion

This study determined the serum level of tetanus and diphtheria antibodies in Iranian HIV positive patients. Our survey showed that the majority of our cohort of patients had protective tetanus and diphtheria antibodies, which is probably a reflection of the effectiveness of the National Program on Immunization in country. We did not find statistically lower diphtheria antibodies in HIV infected individuals, but found lower tetanus antibodies, in HIV positive cases compared with control HIV negative subjects. Mean tetanus and diphtheria antibodies levels were not significantly different based on the circulating $CD4^+$ cells.

Previous studies have already assessed tetanus and diphtheria antibodies in HIV infected individuals (6–13).

Bonneti *et al.* showed that both tetanus and diphtheria antibodies were lower in HIV group when compared with control group. They also reported that the large percentage of HIV infected women was in the intermediate immune category for both diseases which probably reflects the effect of faster antibody decay (6).

Kroon *et al.* (7) did not find statistically lower diphtheria antibodies in HIV infected individuals, but found lower tetanus antibodies in those with $CD4^+$ cells lower than 100 cells/l.

Another study in Nigeria, reported that there was no significant difference in the mean serum levels of antibody to tetanus in patients with HIV/AIDS when compared with the

controls. About 85.7% of patients had protective tetanus antibody. Mean antibody levels to tetanus in patients living with HIV/AIDS were not significantly different based on the circulating $CD4^+$ cells (8).

In a study by Kurtzhals *et al.*, no HIV infected patient had tetanus antibodies below the protective level, whereas 30.77% of patients were unprotected against diphtheria (9). No relationship between disease stages and antibody levels could be found. Either there was not any difference between patients with normal or reduced numbers of $CD4^+$ cells (9). These conflicting data may be related to various factors such as the size and age of the study groups, the demographic and epidemiologic factors and using different laboratory techniques to assess antibodies with different degrees of accuracy.

Conclusion

We did not find statistically lower diphtheria antibodies in Iranian HIV infected individuals, but found lower tetanus antibodies in them. Our results showed that HIV positive cases, who had received primary Td vaccination before they contracted HIV infection, could be expected to be protected against diphtheria, whereas revaccination against tetanus must be considered.

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