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Antitetanus Toxoid Antibody Titer of Chronic Hemodialysis Patients in Iran

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ABSTRACT

Background: Patients with end stage renal disease have higher incidence of infection diseases that is thought to be related to impaired immune system. **Objective:** To determine the antitetanus IgG antibody level in Iranian hemodialysis patients with end stage renal disease and to find its association with sex, age, blood hemoglobin, serum albumin, duration of dialysis, time of dialysis per week, dialysis adequacy, erythropoietin, or iron supplementation, body mass index (BMI) and underlying renal disorder. **Methods:** We conducted a cross sectional study on a total of 108 Iranian hemodialysis patients with end stage renal disorder, and 36 healthy individuals in the control group matched with the patient group. The patients and controls did not receive any antitetanus vaccine or immunoglobulins a year prior to the investigation. The serum antitetanus IgG antibody levels were measured by an ELISA method. **Results:** We found 74.3% of patients to have unprotected antitetanus IgG antibody level compared with 52.8% of the control group. Except hemodialysis duration, none of the contributing factors seemed to affect immunity. **Conclusion:** We conclude that in our study, there is a significant difference in the antitetanus IgG antibody level between hemodialysis patients and the control group and also in the chronic hemodialysis patients.

Keywords: Antitetanus IgG, Hemodialysis, Chronic Renal Failure

INTRODUCTION

Infections are the leading cause of death in end-stage renal disease (ESRD) patients, second only to cardiovascular disease. They also contribute to a significant morbidity in patients with earlier stages of chronic kidney disease (CKD) (1). Patients with chronic renal failure have a higher incidence of infectious diseases (2), so they represent a special population because of their immunosupressed status and unique exposures (3). They are more likely to be hospitalized for bacteraemia and/or septicaemia than patients without CKD (4).

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This is thought to be related to an impaired T cell activation by antigen presenting cells (5), immunodeficiency status manifested by abnormal phagocytosis, T and B-lymphocyte abnormalities, and impaired responses to T cell dependent pathogens such as hepatitis B virus (6-10). Tetanus toxoid is an antigen known to induce strong T cell specific immune responses in humans after vaccination (11).

In many countries, non-neonatal tetanus is still a significant public health problem, particularly among children, adolescents and young adults (12). Although the vaccination against tetanus has led to a significant decrease of the disease after infection with Clostridium tetani (13), recent epidemiologic studies indicate that the number of insufficiently protected individuals has increased especially in the elderly (14, 15).

In 2004, WHO and UNICEF reported the incidence of diphtheria, tetanus and pertussis in Iran to be 6, 11 and 98 cases, respectively while in 2005, the respective incidences were 15, 8 and 125 (16,17).

Vahdani et al determined that in Iranian patients with tetanus, the age was between 45 to 60 years, in which 71.4% of patients were farmers or dairy workers. (18).

Vaccines represent the most effective means of preventing infectious diseases. However, many licensed vaccines currently induce only suboptimal immunity, requiring multiple boosts to generate a robust protective response (e.g. hepatitis B, diphtheria, pertussis and tetanus) (19-21).

In Iran, immunization against diphtheria, tetanus and pertussis has been applied since 1950 using a local vaccine manufactured by Razi Institute (Razi-DTwP), Tehran, Iran, and the efficacy of the vaccine was confirmed by previous studies (22,23) but there is no routine vaccination for hemodialysis patients and we do not have any data regarding antitetanus toxoid antibody level in these patients in Iran.

MATERIALS AND METHODES

Subjects. We conducted a cross sectional study on a total of 108 patients (60 men, and 45 women), with a mean age of 53.8 ± 13.1, who were on hemodialysis due to end-stage renal disease in the Hemodialysis Center of Shiraz University of Medical Sciences in 2006.Thirty six healthy individuals (16 men and 20 women) without any underlying renal disease with a mean age of 53.9±14.2 were selected among the family members of the patients and used as a control group.

The control group was matched based on age (p= 0.812) and sex (p= 0.187) as far as possible. Because of the unknown past history of vaccination in both groups, we decided to select the control group from the patients' relatives to increase the reliability of the results.The patients and their relatives receiving antitetanus toxoid vaccine or immunoglubins a year prior to the study were excluded.

Data Collection. Data including sex, age, blood hemoglobin, serum albumin, duration of dialysis, time of dialysis per week, dialysis adequacy, erythropoietin, iron supplementation, body mass index (BMI) and underlying renal disorder were obtained from all of the hemodialysis patients and their medical records.

Serologic Evaluations. Antibody measurements were performed on serum samples taken from patients before starting hemodialysis. Sera were separated and stored at -20 ^{o}C until analysis. Antibody levels were measured by commercial ELISA kits (IBL-Hamburg GmbH, Hamburg, Germany). Optical density was measured at 450 nm using ELISA reader (Anthos Labtec Instruments, Austria). Based on the EPI Program of

WHO, the assay cut-offs for protective level of tetanus antibody was set at 0.1 international units per ml (IU/ml) (14). Concentrations above the assay cut-offs were considered to be seroprotective.

Ethics. The study was approved by the ethics committee of Shiraz University of Medical Sciences.

Statistical Analysis. Statistical analyses were performed using SPSS ver.14 software (SPSS Inc., Chicago, Illinois) Statistical differences of various clinical and laboratory parameters between groups were evaluated by Chi-Square or Mann-Whitney U tests. To compare the means of two groups, the two independent sample t-tests were used. P-values of less than 0.05 were considered significant.

RESULTS

The mean serum antitetanus IgG level of hemodialysis patients was 0.235±0.48 IU/ml compared with 0.573±1.13 IU/ml in the control group (p= 0.089).

The patients were divided according to their antitetanus IgG level into 3 groups, IgG<0.1 IU/ml (level 1) which are not protective and need basic immunization through tetanus booster vaccine; 0.1< IgG <1 IU/ml (level 2) who need to be controlled in 1 to 2 years; and 1<IgG<5 IU/ml (level 3) who need to be controlled in 2 to 4 years. Therefore 80 (74.1%) patients were not protected against tetanus because their IgG less than 0.1 IU/ml (14). Table 1 illustrates the characteristics of the patients and control groups.

Table 1. Comparison of the characteristics of patients and control groups

	Hemodialysis patients	Control group	P value
Age (years)	53.84 ± 13	53.9 ±14.2	p=0.812
Gender	62 (57%) men, 46 (42.9%) women	16 (44.4%) men, 20 (55%) women	p=0.187
Antitetanus IgG (IU/ml)	.23±0.48	0.57±1.13	p= 0.089
Level of protection[1]	28 (25.9%)	17(47.2%)	p=0.058

[1]patients with IgG >0.1 IU/ml

In this study diabetic patients (n=34), did not significantly differ from the rest of the hemodialysis patients (n= 68), in antitetanus IgG levels (p=0.113).

Among the contributing factors studied, only the patients with longer duration of hemodialysis had lower antitetanus IgG level (p=0.05). Therefore, we decided to study separately the chronic hemodialysis patients (n=57), who had a duration of hemodialysis longer than 3 months. The mean antitetanus IgG level of these chronic hemodialysis patients was 0.164± 0.322 IU/ml which is statistically lower than that of the control group with an IgG of 0.57±1.13 IU/ml (p=0.041).

It is also noteworthy that patients with the highest antitetanus IgG and immunization against tetanus (level 3) have the shortest duration of dialysis (p=0.03) (Table 2).

Table 2. Comparison of the characteristics of protected patients with 0.1<IgG <1 IU/ml (level 2) with those having 1<IgG<5 IU/ml (level 3)

	Level 2 (18 patients)	Level 3 (10 patients)	P value
Age (years)	49.9±13.5	49.3±11.2	0.89
BMI	24.6±4.5	23.7±6.8	0.78
Albumin (g/dl)	4.3±0.61	4.6±0.74	0.35
Hb (g/dl)	8.9±1.9	8.6±1.9	0.69
Duration of hemodialysis (weeks)	32.8±38.5	16.4±29.6	0.03
Time on Dialysis per week (hours)	8.4 ±2.4	9.2±2.8	0.91

DISCUSSION

The immunodeficiency in patients with chronic renal failure makes them prone to more fatal outcomes of infectious diseases. A few studies were done on immunization against tetanus in patients with chronic renal failure (24-29).

In our group of hemodialysis patients 28 out of 108 (25.9%) had sufficient protection against tetanus. In the healthy control group, however, 17 out of 36 (48.2%) were protected.

Kruger et al, showed that out of 71 patients with chronic hemodialysis only 31 (44%) were protected against tetanus while the rate in healthy control group was 8 out of 9 (89%) (13). It, therefore, appeared that patients' and healthy individuals' susceptibility to tetanus is much higher in our study compared to their report.

In our study, 52.6% of men and 47.4% of women were unprotected while in Kruger's investigation, the proportion of protected patients was larger in males compared to females but without any statistical significance (13).

Moreover, the mean serum antitetanus IgG level of all hemodialysis patients was 0.235±0.48 IU/ml which is lower than the value of 0.573±1.13IU/ml in the control group (p= 0.089). Duration of hemodialysis seems to have a negative effect on antitetanus IgG level of hemodialysis patients with an almost statistical significance (p=0.051). However, the mean antitetanus IgG level of the chronic hemodialysis patients (patients with more than three months on hemodialysis) was 0.164± 0.322 IU./ml which, unlike the all hemodialysis patients combined, is statistically lower than the control group with an IgG level of 0.57±1.13 IU/ml (p=0.041).

Except for the duration of hemodialysis which has significant association with antitetanus IgG level (p= 0.05), none of the other contributing factors seems to have any significant effect on antitetanus IgG level in either chronic hemodialysis or in the all hemodialysis patients.

Our finding that lower protection against tetanus is accompanied with a lower serum albumin, may disclose that malnutrition and inflammation have a crucial role in attenuating an optimal immune response, and poor nutritional state may have negative consequences on the immune status and the susceptibility to a variety of pathogens (30).

However no statistically meaningful difference was found between the patients protected against tetanus (n=28) and those not protected (n=80).

Guerin et al. showed that after the booster injection, 96.5% of patients had antitetanus antibody titers considered to be protective (0.06 IU/ml). However, the titer of these antibodies rapidly declined and after 6 months, only 62% of the hemodialysed patients had a titer greater than 0.06 IU/ml. Among the different factors considered, only age significantly impaired or reduced the immune response (31).

To conclude, it seems that most of our hemodialysis patients especially the chronic ones need booster tetanus vaccine to increase their immunity against tetanus.

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