

Evaluation of Anti-Tetanus Immunity in Haemodialysis Patients

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Abstract: Problem statement: The incidence of infectious diseases is increased in patients with chronic renal failure. Chronic renal failure severely influences the immune functions of the host. **Approach:** To evaluate the antitetanus immunity level in southern Iranian patients with end stage renal disease undergoing hemodialysis and to find its association with sex, age, blood hemoglobin and serum albumin, duration of dialysis. This cross sectional study was carried out on a total of 52 patients, who were on hemodialysis and 52 age and sex matched healthy individuals with without any underlying renal disease as a control group. Individuals in the both groups receiving antitetanus toxoid vaccine or immunoglobulins a year prior to the study were excluded. The serum antitetanus IgG antibody levels were measured by an ELISA method. **Results:** Tetanus protected individuals in the patients and the control groups were 34.6 and 63.30% respectively. Of the evaluating factors just hemodialysis duration found to affect on tetanus immunity. **Conclusion:** Tetanus protected individuals in the patients group were significantly less than tetanus protected individuals in the control group ($p = 0.011$). Hemodialysis duration has significant effect on antitetanus immunity level.

Key words: Antitetanus immunity, hemodialysis, chronic renal failure

INTRODUCTION

Infectious diseases 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].

The incidence of infectious diseases is increased in patients with chronic renal failure^[2]. This is thought to be due to an immunosuppressed status in this population^[3-7]. This is thought to be related to an impaired T cell activation by antigen presenting cells^[8], impaired immune Responses and Antigen-Specific Memory CD4+ T Cells^[5], impaired monocyte and monocyte-derived dendritic cell function^[4], defects in NK cell function^[6], immunodeficiency status manifested decrease in the number of CD3+, CD4+ and CD72+ cells and phagocytosis intensification^[7], T and B-lymphocyte abnormalities and impaired responses to T cell dependent pathogens such as hepatitis B virus^[9-13]. Tetanus toxoid is an antigen known to induce strong T cell specific immune responses in humans after vaccination^[14].

In many countries, non-neonatal tetanus is still a significant public health problem, particularly among children, adolescents and young adults^[15].

Although the vaccination against tetanus has significantly decreased the disease after infection with *Clostridium tetani*^[16], recent epidemiologic studies indicate that the number of insufficiently protected individuals has increased especially in the elderly^[17,18].

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^[19,20].

The age of Iranian patients with tetanus, was reported 45-60 years, in which 71.4% of patients were farmers or dairy workers^[21].

Vaccination is the most effective means of preventing infectious diseases. Immunization programs are of great importance in the prevention of infectious diseases in immunocompromised individuals. However, the immune response to various vaccinations is impaired in patients with chronic renal failure^[16], requiring multiple boosts to generate a robust protective response (e.g., hepatitis B, diphtheria, pertussis and tetanus)^[22-24].

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The tetanus, diphtheria and pertussis vaccination programme in Iran has been running 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^[25,26], but there is no routine vaccination for hemodialysis patients and so far only a few studies have focused on seroresponse to tetanus toxoid in these patients in Iran^[27].

MATERIALS AND METHODS

Subjects: This cross sectional study was carried out on a total of 52 patients (36 men and 16 women), with a mean age of 57.75±14.26 years, who were on hemodialysis due to end-stage renal disease in the Hemodialysis Center of Jahrom University of Medical Sciences in 2009. Fifty two healthy individuals (35 men and 17 women) with normal creatinine and BUN and without any underlying renal disease with a mean age of 58.98±14.32 as a control group were enrolled in this research.

There were not significant differences between age (p = 0.912) and sex (p = 0.112) in the cases and the controls.

As there were not data indicating past history of vaccination in both groups, the control group was randomly selected among the same community of patients group to increase the reliability of the results. Individuals in the both groups receiving antitetanus toxoid vaccine or immunoglobins a year prior to the study were excluded.

Data collection: Data including sex, age, hemoglobin, serum albumin, duration of dialysis, Body Mass Index (BMI) were obtained from all of the hemodialysis patients and their medical records.

Serologic evaluations: Antitetanus toxoid IgG level was determined on serum samples taken from patients before starting hemodialysis. Sera were separated and stored at -70°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 (Awerness Instruments, USA). Based on the EPI Program of WHO, the assay cut-offs for protective level of tetanus antibody was set at 0.1 International Units (IU mL⁻¹) (14). Concentrations above the assay cut-offs were considered to be seroprotective.

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

Statistical analysis: Statistical analyses were performed using SPSS ver.16 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 0.099±0.073 Vs 0.560±0.719 IU mL⁻¹ in the control group (p = 0.001).

The patients and the control groups were divided into 3 groups by their antitetanus IgG level:

Group 1: IgG<0.1 IU mL⁻¹ which are not protective and need basic immunization through tetanus booster vaccine.

Group 2: About 0.1<IgG<1 IU mL⁻¹ who need to be controlled in 1-2 years and group 3: 1<IgG<5 IU mL⁻¹ who need to be controlled in 2 to 4 years. Therefore 34 (65.40%) patients were not protected against tetanus because their IgG less than 0.1 IU mL⁻¹^[17]. Table 1 illustrates the characteristics of the patients and the control groups.

Among the contributing factors studied, only the patients with longer duration of hemodialysis had lower antitetanus IgG level (p = 0.05).

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 1: Comparison of the characteristics of patients and control groups

Variables	Hemodialysis patients	Control group	p-value
Age (years)	57.75±14.26	58.98±14.32	p = 0.900
Gender	36 (69.23%)	35 (67.30%)	
	men	men	
	16 (30.77%)	17 (32.70%)	p = 0.900
	women	women	
Antitetanus IgG (IU mL ⁻¹)	0.099±0.073	0.560±0.719	p = 0.001
Level of protection	18 (34.60%)	33 (63.30%)	p = 0.011

Table 2: Comparison of the characteristics of protected patients (group 2 and 3)

Factors affecting anti tetanus IgG	Level 2 (12 patients)	Level 3 (6 patients)	p-value
Age (years)	48.7±13.6	51.2±10.3	0.84
BMI	25.7±4.3	24.2±5.9	0.69
Albumin (g dL ⁻¹)	4.2±0.64	4.8±0.79	0.41
Hb (g dL ⁻¹)	8.8±1.7	8.6±1.4	0.71
Duration of hemodialysis (weeks)	28.65±22.35	14.84±24.34	0.03

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^[28-33].

Tetanus protected individuals in the patients group were significantly less than tetanus protected individuals in the control group (34.6 Vs 63.30%) ($p = 0.011$).

Sagheb *et al.*^[16] reported 74.3% of patients were unprotected against tetanus compared with 52.8% of the control group, his results and our results approximately are the same.

Kruger *et al.*^[16] 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%), therefore, appeared that hemodialysis patients' and healthy individuals' susceptibility to tetanus is much higher in our study compared to their report.

In Kruger's investigation, the proportion of protected patients was larger in males compared to females and the same results was found in our study, 23.08% of men and 11.50% of women out of patient group were protected, while in Sageb's investigation, the proportion of protected patients was larger in females compared to males but without any statistical significance^[16].

The mean serum antitetanus IgG level of the hemodialysis patients was significantly lower than the mean serum antitetanus IgG level in the control group ($p = 0.001$). We found a significant negative effect by the duration of hemodialysis on antitetanus IgG level in our patients group ($p = 0.03$) and we did not find any significant effect by the other contributing factors on antitetanus IgG level in either chronic hemodialysis or in the all hemodialysis patients. Also there was not statistically meaningful difference between the protected against tetanus patients ($n = 18$) and those not protected ($n = 34$). Such results were showed by Sagheb *et al.*^[16].

According to Guerin *et al.*^[34] results indicating rapid decline in the titer of antitetanus IgG in vaccinated hemodialysed patients who had a protected status after 6 months, among the different factors considered, only age significantly impaired or reduced the immune response.

CONCLUSION

To conclude, it seems that most of our hemodialysis patients need booster tetanus vaccine to

increase their antitetanus immunity. We suggest frequent monitoring of antibody levels after immunization against tetanus in hemodialysis patients.

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