

Protective Status of End-Stage Renal Disease Children Against Tetanus and Diphtheria Vaccination

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ABSTRACT

Background: Vaccination against fatal viral and bacterial diseases is still the best protective way to lower morbidity and mortality rate in end-stage renal disease (ESRD) patients. It has been reported that there is high incidence of low protective levels of IgG after vaccination in ESRD adult patients. The aim of this study was to evaluate the protective status of vaccination against diphtheria and tetanus in ESRD children after completing routine vaccination.

Methods: This cross-sectional study was carried on 83 participants less than 18 years including 27 patients on hemodialysis or peritoneal dialysis and 56 normal populations from February 2008 until December 2008 at St. Alzahra hospital, Isfahan, Iran. To determine anti-tetanus and anti-diphtheria antibodies level, Tetanus IgG ELISA kit (IBL International, Germany, RE56901) and Diphtheria IgG ELISA kit (IBL International, Germany, RE56191) were used. The participants must not received immunoglobulin, blood products or immunosuppressive medication in the current 6 months.

Results: The mean age of case and control group were 12.5 ± 2.7 years and 11.7 ± 3.3 years, respectively, $P > 0.05$. According to IgG levels, 93% of hemodialysis patients and approximately 87% of peritoneal dialysis children needed booster doses of diphtheria vaccination. The results for IgG titer against tetanus revealed that in 91% of hemodialysis patients and 83% of peritoneal dialysis children booster doses of tetanus were recommended.

Conclusions: Booster doses of vaccines may be required in ESRD children. Measuring serum IgG levels against vaccines to define protective levels are recommended.

Keywords: Children, diphtheria, end-stage renal disease, prevention, tetanus, vaccination

INTRODUCTION

Infectious diseases are major concern among end-stage renal diseases (ESRD) patients, accounted for 30-36% of mortality.^[1] Vaccination against fatal viral and bacterial diseases is still the best protective way to lower morbidity and mortality rate in this group of patients. Worldwide increase in the number of unprotected

individuals to tetanus and diphtheria reinforce more attention to give booster doses of tetanus and diphtheria vaccines in immunocompromised population.^[2-6] Furthermore, multiple booster doses are required for many licensed vaccines to induce optimal protection.^[7,8] Prevention against diphtheria and tetanus are recommended for ESRD children especially before performing kidney transplantation. Whether ESRD children who had completed the routine vaccination protocol had enough protective serum IgG levels against diphtheria and tetanus, was the aim of our study.

METHODS

This cross-sectional study was carried on 83 participants less than 18 years including 27 patients on hemodialysis or peritoneal dialysis and 56 normal populations from February 2008 until December 2008 at St. Alzahra hospital, Isfahan, Iran. Fourteen out of 27 patients were on hemodialysis (HD) and the remaining was on peritoneal dialysis (PD). The participants in control group were recruited from normal children referred to private clinics for routine examination. Informed written consent was obtained from participants' parents. The survey was performed in accordance with the ethical standards of the Helsinki Declaration and approved by the Ethics Committee of the Research Department of Isfahan University of Medical Sciences.

Inclusion criteria

- End-stage renal disease patients either on hemodialysis (HD) or peritoneal dialysis (PD) at least for 6 months.
- Patients who had been received full doses of routine vaccination.
- No past history of liver diseases.
- No latest infusion of intravenous immunoglobulin or blood products during the recent 3 months.
- No massive or nephrotic range proteinuria (not more than 30-50 mg/kg/day urine protein excretion).
- No proven history of congenital immunodeficiency diseases.
- No history of receiving immunosuppressive medications (such as prednisolon, mycophenolate mofetil, cyclophosphamide, azathioprine and calcineurin inhibitors in the current 6 months).

- Control group has been selected among volunteers at the same age and gender that had been received complete doses of routine vaccination.

For each participant, 4 milliliter fasting blood sample was obtained to measure anti-tetanus and anti-diphtheria antibody (IgG). To determine anti-tetanus and anti-diphtheria antibodies level, Tetanus IgG ELISA kit (IBL International, Germany, RE56901) and Diphtheria IgG ELISA kit (IBL International, Germany, RE56191) were used. The results were interpreted according to the instruction for use, Tables 1 and 2. In hemodialysis group, the blood samples were taken just before hemodialysis session.

Statistics

Regarding shortage of patients in each group, Kruskal-Wallis test was used. Mean, standard deviation, and median were measured for different variables. The difference between groups was evaluated by *t*-test.

RESULTS

The mean age of case and control group were 12.5 ± 2.7 years (minimum: 8 and maximum: 15.5 years) and 11.7 ± 3.3 years (minimum: 7 and maximum: 15.1 years), respectively, $P > 0.05$.

Table 1: The interpretation of the results for anti-tetanus IgG level

Category	IgG level (IU/mL)	Interpretation
1	<0.1	Basic immunization recommended
2	0.1-1	To be controlled after 1-2 years
3	1-5	To be controlled after 2-4 years
4	>5	To be controlled after 4-8 years

IgG=Immunoglobulin

Table 2: The interpretation of the results for anti-diphtheria IgG level

Category	IgG level (IU/mL)	Interpretation
1	<0.1	Basic immunization recommended
2	0.1-1	Booster vaccination recommended
3	1-1.5	To be boosted in 5 years
4	1.5-2	To be boosted in 7 years
5	>2	To be boosted in 10 years

IgG=Immunoglobulin

There was no significant difference between genders in two groups. The overall male to female ratio was 1.02/1. The mean time of dialysis for HD and PD groups were 14.1 ± 5.6 months and 12.5 ± 4.3 months, respectively, $P > 0.05$. According to IgG levels [Tables 1 and 2], 93% of hemodialysis patients and approximately 87% of peritoneal dialysis children needed booster doses of diphtheria vaccination (category 2). The results for IgG titer against tetanus revealed that 91% of hemodialysis patients and 83% of peritoneal dialysis participants placed on the category 1 and a booster dose of vaccination was recommended. Kruskal-Wallis test showed significant differences among anti-tetanus and diphtheria antibody titers between groups. The mean of anti-tetanus and anti-diphtheria antibodies in case and control groups are demonstrated in Table 3. Although the mean values of antibodies against tetanus and diphtheria in peritoneal dialysis patients were higher than hemodialysis patients, the differences were not significant. Mann-Whitney test did not reveal any significant difference between mean of anti-tetanus and diphtheria antibodies in case group according to gender, Table 4.

Table 3: This table shows antibody titers against tetanus and diphtheria in case and control groups

Participants	Number	Anti-diphtheria	Anti-tetanus
		IgG titer IU/mL	IgG titer IU/mL
Peritoneal dialysis group	13	0.29±0.25	0.56±0.11
Hemodialysis group	14	0.21±0.04	0.29±0.07
Control group	56	0.77±0.61	1.75±1.2
<i>P</i> value between case and control group		<0.001	<0.001

IgG=Immunoglobulin

Table 4: The mean values of antibodies in case group according to gender

Variable	Male	Female	Significance
Anti-tetanus antibody titer (mean±SD)	0.41±0.14	0.4±0.15	$P=0.49$
Anti-diphtheria antibody titer (mean±SD)	0.34±0.28	0.15±0.05	$P=0.19$

DISCUSSION

In this study, we evaluated anti-tetanus and anti-diphtheria antibodies in children and adolescents less than 18 years. We showed that in ESRD children, irrespective of receiving full doses of vaccination, booster doses were required.

Infectious diseases have been assumed as the second major cause of morbidity and mortality among ESRD patients.^[9,10] It accounts for approximately 25 deaths per 1000 patient-years at risk (data from the U.S. Renal Data Systems [USRDS], 1998-2000). The rate of hospitalization due to infectious diseases and septicemia is higher not only in ESRD patients but also in patients at different stages of chronic kidney disease (CKD).^[11,12] Diminishing functions of T-cell, B-cell and macrophages are responsible for immunocompromised status in CKD patients.^[13] It has been shown that proliferation and activation of T-cell are suppressed. In addition, antibody-dependent cell-mediated cytotoxicity and the number of B-cells are diminished. Impaired production of antigen-specific helper T-cells leading to inappropriate B-cell antibody synthesis causes decreased IgG production in response to vaccination.^[2] The mentioned factors are responsible for poorer seroconversion rate and lower peak antibody titers in addition to faster decline of antibody levels in CKD patients.^[2-4] Therefore, the preventive response to vaccination may be less successful among CKD patients. Many studies have been recommended different doses and protocols to increase the efficacy and seroconversion rate of vaccines against various viral and bacterial infections in ESRD patients.^[1]

Girndt *et al.* showed a lower seroconversion rate in dialysis patients than in healthy population after vaccination against diphtheria and tetanus.^[14] However, booster injection of tetanus vaccination did not preserve the seroconversion rate (>0.06 HU/ml) for more than 6 months.^[15] Kruger and colleagues demonstrated that five years after tetanus (40 UI) and diphtheria (4 UI) vaccination, approximately 71% and 33% of hemodialysis patients had protective antibody titer for tetanus and diphtheria, respectively.^[16] Therefore, monitoring of antibody for tetanus and diphtheria and giving booster doses if necessary are recommended.^[1,16] It has been revealed that the response rate to vaccines correlates with the degree of renal failure but not

with the type of dialysis (hemodialysis or peritoneal dialysis).^[17] Sagheb *et al.* showed that antibody titer to diphtheria and Pertusis in only 16% and 24% of hemodialysis patients respectively were in the protective range.^[18] The authors mentioned that only hemodialysis duration had an effect on the immunity response. Kruger *et al.* reported sufficient protection against tetanus in only 38% of unprotected hemodialysis patients after one dose of anti-tetanus toxoid. They revealed a high association between the efficacy of vaccination against diphtheria and tetanus.^[19] Jahromi *et al.* demonstrated protective anti-diphtheria titer in only 34.6% of hemodialysis patients comparing with 63.3% of normal population.^[20] A study on 8 children on peritoneal dialysis who had received routine vaccination protocol showed protective anti-tetanus and anti-diphtheria antibody in 88% of subjects.^[21] The lower response rate to vaccination reported in CKD patients has been shown even after kidney transplantation. Pedrazzi and colleagues reported an accelerated decline in anti-diphtheria antibody titers in kidney transplant recipients.^[22] In addition, children who completed vaccination in the last six months to six year prior to renal transplantation had higher rates of protective antibody titers against all pathogens compared with children who had vaccination more than six year before transplantation.^[23] Enke *et al.* described protective titer of anti-diphtheria antibody in ESRD children only in 38% of patients, while 90% of them had protective titer against tetanus. After booster immunization for diphtheria vaccine, the protection rate rose to 95% at 1 month. Nonetheless, this rate declined dramatically to 76% at the end of the first year of transplantation.^[24] No difference between the type of dialysis and response to vaccine has been reported.^[17] The routine vaccination schedule for infants and children from 2 years to 7 years is 0.5 ml DTP vaccine injected intramuscular in 5 doses at 2,4,6,18 months and 6 years.^[1] The recommended schedule for vaccination against tetanus and diphtheria in ESRD patients is still the same for the general population (Evidence level C).^[25] The results from our study recommended booster doses of diphtheria and tetanus vaccines in ESRD children irrespective of previous complete vaccination. However, prescribing booster doses needs re-evaluating of IgG titers against diphtheria and tetanus. The drawback of this study is the shortage

of samples due to the lower rate of ESRD in children in comparison with the adults.

CONCLUSIONS

Booster doses of vaccines may be required in ESRD children. Measuring serum IgG levels against vaccines to define protective levels are recommended.

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