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Research Article

Seroprevalence of Antibodies to Tetanus Toxoid and Diphtheria Toxoid in Perinatally Human Immunodeficiency Virus (HIV) - Infected Children and Adolescents

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ABSTRACT

Introduction: Although data presented in this study is a few years old, the author believes it is important to review in this era of the COVID-19 pandemic in order to underscore the importance of timely immunization of all children, particularly those who are HIV-infected. Even in the era of Highly Active Antiretroviral Therapy (HAART), HIV-infected individuals are at a higher risk of complications from vaccine-preventable diseases than the uninfected.

Methods: Anti-diphtheria and anti-tetanus antibodies (correlate of protection: antibody level>0.1 IU/ml) were assessed by ELISA in 29 HIV-infected and 20 uninfected children.

Results: HIV- infected children were significantly more likely to have lower levels of antibody to diphtheria toxic when compared to their uninfected counterparts, in both the four dose (p=0.004) and the five dose (p=0.007) recipients. HIV-infected children were significantly (p=0.02) more likely to have non-protective immunity (antibody level<0.1 IU/ml) for diphtheria and tetanus toxoids than their uninfected counterparts, in the five dose recipients only. This difference in immunity between the groups, in the four-dose recipients was observed for diphtheria toxoid (p=0.05) only.

Conclusion: Our study has determined that immunity to tetanus and diphtheria toxoids in HIV-infected children and adolescents is suboptimal when compared to their uninfected counterparts. We therefore, strongly recommend developing strategies within the scope of all pediatric practices, to keep up with timely vaccinations of all children and adolescents, particularly the high risk groups, in this era of COVID-19 pandemic.

Keywords: COVID-19; Immunization; Antiretroviral therapy; HIV; Vaccinations

INTRODUCTION

Although data presented in this study is a few years old, the author believes it is important to review in this era of the COVID-19 pandemic in order to underscore the importance of timely immunization of all children, particularly those who are HIV-infected. HIV-infected children are a select immune compromised population within our community who are at risk for a resurgence of forgotten infectious diseases of the past. Even in the era of Highly Active Antiretroviral Therapy (HAART), HIV-infected individuals are at a higher risk of complications from vaccine-preventable diseases than the uninfected [1-4]. Studies have suggested that these children not only have suboptimal coverage rates for routine childhood vaccinations [5-7], but also have suboptimal immunity to vaccine-preventable infections when compared to their uninfected counterparts [8,9]. Thus, in this era of the COVID-19 pandemic when children remain at risk for non-compliance to well-child visits and routine childhood vaccinations, HIV-infected children remain at a higher risk for susceptibility to preventable infections and are prone to severe complications. It is also crucial to identify those HIV-infected children and adolescents who have disease progression (clinical and immunological), and ensure them adequate protective immunity through the specific

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immunization schedules in terms of timing, number of doses, and booster doses as indicated [9,10].

METHODS

Study population

The study was conducted between August 1995 and April 1997 following approval of the protocol by the Ethics Committee of Interfaith Medical Center in Brooklyn, New York. The study was performed as part of the routine standard of care for these patients.

A convenience sample of twenty-four HIV-infected children was selected from the pediatric infectious disease clinic. All of these children had contracted the disease through vertical transmission from their mothers. Of the available evaluable HIV-infected children, fifteen children had received four doses of the diphtheria-tetanus toxoid vaccine and fourteen children had received five doses. Five of the four-dose recipients enrolled a second time into the study as five-dose recipients. All HIV-infected children were either on mono therapy or on combination antiretroviral therapy. Within the HIV-infected group, evidence of moderate to severe clinical disease (Centers for Disease Control and Prevention [CDC] class B and C) prevailed in sixty-five percent of the children and moderate to severe immunological disease (CD4 count<15% for age) prevailed in fifty-two percent [11]. None of the children received intravenous immunoglobulin at any time during the study. HIV-related information regarding HIV testing results, antiretroviral therapy, T-cell counts, and viral loads was obtained from the patients' medical records. Twenty children (nine in the four-dose group and eleven in the five-dose group) whose mothers were HIV-sero negative were recruited from the general pediatric clinic as the control group; they were matched approximately by the number of doses of the vaccine.

Determination of antibody levels

Baseline anti-tetanus and anti-diphtheria antibodies were assessed following routine fourth and fifth doses of the diphtheria and tetanus toxoid vaccinations. All children received three doses of adsorbed DPT (diphtheria-tetanus toxoids – pertussis [Connaught Labs, Inc., Swift water, PA]) or tetrameter (diphtheria-tetanus toxoids-pertussis-Hemophilusinfluenzae type b [Lederle-Wyeth, Inc]) as their primary series followed by the fourth and fifth routine booster doses. Only one child from the HIV-infected group (98 months) received the Td vaccine as his fifth dose. The anti-tetanus and anti-diphtheria Ig Antibody was assayed using an enzyme-linked immunosorbent assay (ELISA) (Specialty Labs, Santa Monica, CA). The level of anti-tetanus and anti-diphtheria antibody of>0.1 IU/ml was considered a correlate of protection [12-15]. Fourteen HIV-infected children (six from the four-dose and eight from the five-dose group) had follow-up antibody levels evaluated after a mean of ten months (range 2-17 months) from baseline.

Immunologic and virologic studies

T- and B-cell analyses and HIV viral loads in the HIV-infected group were performed at commercial laboratories as routine standard of care.

Statistical analysis

Comparison of antibody levels for tetanus and diphtheria toxoids between HIV-infected and uninfected groups were determined by two-tailed t-test. Prevalence of immunity against tetanus and diphtheria toxoids between HIV-infected and uninfected groups were compared by two- tailed Fisher's exact test. Software Intercooled state version 8.0 was used for statistical analysis.

RESULTS

The mean vaccination ages of four-dose recipients in the HIV-infected and uninfected groups were comparable (HIV-infected: 27 months; Uninfected: 19 months). But in the five-dose recipients, HIV-infected children happened to be significantly (p=0.02) older (mean age 70 months) when compared to their uninfected counterparts (mean age 54 months). Their ages at serology were slightly older (p=0.07) for the HIV-infected children (mean age 52 months) when compared to their uninfected four-dose recipients (mean age 34 months). Ages were comparable (mean 86 months) for both HIV-infected and uninfected groups in the five-dose recipients. Interval between vaccination to serology was comparable for both groups in either the four dose (HIV-infected: 24 months; Uninfected: 14 months) or the five dose (HIV-infected: 16 months; Uninfected: 32 months) recipients. Within the HIV-infected group, the Centers for Disease Control and Prevention (CDC) disease class, immunologic class, or mean viral loads in children between the four dose and five dose recipients did not differ significantly (Table 1) [16].

Table 1: Profile of HIV-infected children.

Groups (n)	CD4/mm3 Mean (range)	Viral load copies/ml Mean (range)	CDC Clinical Category (n)
	837.47	1,23,237	A=5
4 Doses (15)	(3- 3,147)	(10- 750,000)	B-C=10
5 Doses (14)	538.14	1,21,146	A=5

	(6- 1,928)	(2880- 389,960)	B-C=9
p value	ns	ns	ns

As shown in Table 2, HIV- infected children were significantly more likely to have lower levels of antibody to diphtheria toxoid when compared to their uninfected counterparts, in both the four dose (p=0.004) and the five dose (p=0.007) recipients. Anti-tetanus antibody levels however, were comparable between HIV-infected and uninfected children in both the four-dose and the five-dose recipients.

Table 2: Anti-TT and anti-DT antibodies in HIV- infected and uninfected children.

Groups (n) Total	Anti- TT (IU/ml)		Anti-DT (IU/ml)	
	4 Doses (n)	5 Doses (n)	4 Doses (n)	5 Doses (n)
	Mean (± SD)	Mean (± SD)	Mean (± SD)	Mean (± SD)
HIV- Infected (29)	-15	-14	-15	-14
	0.91 (+1.07)	0.45 (+0.62)	0.56 (+0.85)	0.36 (+0.42)
HIV-Uninfected (20)	-9	-11	-9	-11
	0.86 (+0.75)	1.11 (+1.54)	1.70 (+0.83)	1.14 (+0.88)
p value	ns	ns	0.004	0.007

As shown in Table 3, HIV-infected children were significantly (p=0.02) more likely to have non-protective immunity (antibody level<0.1 IU/ml) for diphtheria and tetanus toxoids than their uninfected counterparts, in the five dose recipients only.

Table 3: Prevalence of protective immunity to TT and DT in HIV-infected and uninfected children.

Groups (n) Total	TT #PI (>0.1 IU/ml) (%)		DT *PI (>0.1 IU/ml) (%)	
	4 Doses (n) (n=15)	5 Doses (n) (n=14)	4 Doses (n) (n=15)	5 Doses (n) (n=14)
HIV-Infected (29)	11/15 (73)	8/14 (57)	9/15 (60)	8/14 (57)
HIV-Uninfected (20)	09/09 (100)	11/11 (100)	09/09 (100)	11/11 (100)
*p value	ns	0.02	0.05	0.02

This difference in immunity between the groups, in the four-dose recipients was observed for diphtheria toxoid (p=0.05) only. Within the HIV-infected group, decline in follow-up mean antibody level from the baseline mean antibody level (waning immunity) after a mean of ten months was determined to be forty-six percent for tetanus toxoid versus only thirteen percent for diphtheria toxoid (Table 4).

Table 4: Waning immunity: TT and DT antibody levels in HIV-infected children.

Antigens (n)	Baseline Antibody IU/ml (+SD)	Follow-Up Antibody IU/ml (+SD)	p value	% Fall Antibody Baseline -Follow-Up (%)
TT (14)	1.11 (1.12)	0.65 ((0.98)	ns	46%
DT (14)	0.73 ((0.88)	0.60 ((0.78)	ns	13%

p value	ns	ns

DISCUSSION

Our study has determined that immunity to tetanus and diphtheria toxoids in HIV-infected children and adolescents is suboptimal when compared to their uninfected counterparts. This finding is concerning, particularly in this era of COVID-19 pandemic, when there is a heightened concern for non-compliance with routine immunization schedules in all children. The burden of this crisis may disproportionately affect the HIV-infected pediatric population. Data collected in this study also underscores the fact that although antibody levels to tetanus toxoid were comparable in HIV-infected and uninfected children, prevalence of protective immunity was significantly lower in the older children (five-dose group). Additionally, a substantial decline in follow-up anti-tetanus antibody level from baseline was observed for tetanus toxoid, which may suggest waning immunity for tetanus to non-protective levels may occur in older adolescents and young adults. Studies indeed have suggested that a protective level of an anti-tetanus antibody remains the major factor determining protection against occurrence of this disease [12-14]. Studies have also shown that a substantial number of patients diagnosed with tetanus were found to be infected with human immunodeficiency virus [16,17].In this context, concerns should also remain for HIV-infected pregnant women with inadequate immunity to tetanus, are at risk of developing tetanus and tetanus in their newborns before acquisition of vaccine mediated protection.

CONCLUSION

Result from this study have also determined that HIV-infected children with the five-dose recipients were significantly older than their uninfected counterparts, indeed replicate data in literature, which nonetheless raise concerns regarding non-compliance to timely vaccinations in this select group of high risk children and adolescents. We therefore, strongly recommend developing strategies within the scope of all pediatric practices, to keep up with timely vaccinations of all children and adolescents, particularly the high risk groups, in this era of COVID-19 pandemic.

REFERENCES

1. Bousfiha A, Picard C, Boisson-Dupuis S, Zhang SY, Bustamante J, Puel A, et al. Primary immune deficiencies of protective immunity to primary infections. Clinic Immun. 2010 ;135 :204-209.
2. Fiore AE, Uyeki TM, Broder K, Finelli L, Euler GL, Singleton JA, et al. Prevention and control of influenza with vaccines: recommendations of the Advisory Commi Immun Prac (ACIP). 2010.
3. Moss WJ, Clements CJ, Halsey NA. Immunization of children at risk of infection with human immunodeficiency virus. Bulletin of the World Health Organization. 2003; 81: 61-70.
4. Levin MJ.Varicella vaccination of immune compromised children. J Infect Dis. 2008; 197.
5. Menson EN, Mellado MJ, Bamford A, Castelli G, Duiculescu D, Marczyńska M, et al. Paediatric European Network for Treatment of AIDS (PENTA) Vaccines Group, PENTA Steering Committee and Children's HIV Association (CHIVA). Guidance on vaccination of HIVinfected children in E urope. HIV Medicine. 2012; 13: 333-336.
6. Rubin LG, Levin MJ, Ljungman P, Davies EG, Avery R, Tomblyn M, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. Clinical Infectious Diseases. 2014; 58: 44-100.
7. Cagigi A, Cotugno N, Giaquinto C, Nicolosi L, Bernardi S, Rossi P, et al. Immune reconstitution and vaccination outcome in HIV-1 infected children: present knowledge and future directions. Hum Vaccin Immunother. 2012; 8: 1784-1794.
8. Choudhury SA, Hodes DS, Peters VB, Antibody response to booster Doses of HBV in HIV-Infected Children. Pediatric Infectious Disease Journal. 1995; 14: 65-67.
9. Choudhury SA, Matin F. Subnormal and waning immunity to tetanus toxoid in previously vaccinated HIV-infected children and response to booster doses of the vaccine. International Journal of Infectious Diseases. 2013;17: 1249-1251.
10. Cagigi A, Cotugno N, Giaquinto C, Nicolosi L, Bernardi S, Rossi P, et al. Immune reconstitution and vaccination outcome in HIV-1 infected children: present knowledge and future directions. Hum Vaccin Immunother. 2012; 8: 1784-1794.
11. Centers for Disease Control and Prevention. 1994 revised classification system for human immunodeficiency virus infection in children less than 13 years of age. MMWR. 1994; 43: 1-10.
12. Gupta SD, Keyl PM. Effectiveness of prenatal tetanus toxoid immunization against neonatal tetanus in a rural area in India. Pediatr Infect Dis. J1998 ; 17: 316-321.
13. Gentili G, Pini C, Collotti C. The use of an immunoenzymatic assay for the estimation of tetanus antitoxin in human sera: a comparison with seroneutralization and indirect haemagglutination. J Biol Stand.1985; 13: 53-59.
14. Simonsen O, Bentzon MW, Heron I. ELISA for the routine determination of antitoxic immunity to tetanus. J Biol Stand.1986; 14: 231-239.
15. Plotkin SA. Correlates of protection induced by vaccination. Clin Vaccine Immunol. 2010; 17: 1055-1065.
16. Wateba MI, Diop SA, Nichols S, Adjoh S, Gbadamassi G, Patassi A, et al. Tetanus and HIV: A fortuitous association? Cahiers d'études et de recherches francophones/Santé. 2008; 1;18(3): 131-4.
17. Sticchi L, Bruzzone B, Caligiuri P, Rappazzo E, Lo Casto M, De Hoffer L, et al. Seroprevalence and vaccination coverage of vaccine-preventable diseases in perinatally HIV-1-infected patients. Hum Vaccin Immunother. 2015;11: 263-269.