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Brief report

Baseline immunity to diphtheria and immunologic response after booster vaccination with reduced diphtheria and tetanus toxoid vaccine in Thai health care workers

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A prospective study to evaluate immune status against diphtheria and immunologic response after tetanus-diphtheria (Td) booster vaccination was conducted in 250 Thai health care workers (HCWs). A protective antibody was found in 89.2% of the HCWs (95% confidence interval [CI], 83.3%-91.5%) before receipt of the Td booster vaccination, compared with 97.2% (95% CI, 95.1%-99.3%) after receipt of the first dose of booster ($P < .001$). The mean antibody level against diphtheria increased from 0.39 IU/mL (95% CI, 0.35-0.44 IU/mL) before the Td booster vaccination to 1.20 IU/mL (95% CI, 1.12-1.29 IU/mL) after the vaccination ($P < .001$). Td booster vaccination should be considered for Thai HCWs to maintain immunity against diphtheria, which still circulates in Thailand.

Health care workers (HCWs) are at risk of acquiring communicable diseases from their patients. Diphtheria is one of the fatal communicable diseases circulating in many countries, including Thailand.[1] Numerous studies have reported declining immune protection against diphtheria with increasing age.[2-5] Data on immune status against diphtheria among HCWs in countries with a high prevalence of diphtheria are lacking. In the present study, we assessed immunity to diphtheria among Thai HCWs and examined factors associated with immune protection against diphtheria. We also evaluated the immunologic response to and safety of the tetanus-diphtheria toxoid (Td) booster vaccination.

METHODS

Study design

This prospective study was conducted between March and September 2013 at Bamrasnaradura Infectious Diseases Institute in Nonthaburi, Thailand. Participants were HCWs aged 18-60 years who were willing to participate and provided written informed consent. HCWs who were allergic to Td or tetanus toxoid (TT) or who had received Td within 3 years before enrollment were excluded. Demographic data were collected using a questionnaire. Blood samples were collected before and after Td booster vaccination. The level of antibody against diphtheria toxoid was measured by indirect enzyme-linked immunosorbent assay using a commercial kit (Euroimmun Medinische Labordiagnostika, Lubeck, Germany). A diphtheria antibody level ≥0.1 IU/mL was considered sufficient to provide seroprotection. A 0.5-mL dose of Td vaccine (Serum Institute of India, Pune, India) containing 5 Lf units of diphtheria toxoid and 5 Lf units of TT with 1.25 mg of aluminium phosphate was injected intramuscularly after baseline blood collection and again 6 weeks later to those who demonstrated no seroprotection. Participants who had received the Td booster within 3-5 years before enrollment were assigned to wait for their immunity results, and were not vaccinated if immunity was established. Participants were observed directly for immediate adverse events, and were contacted by telephone at 14 days after vaccination to check for any later adverse events.

This study was approved by the Ethics Committee for Research in Human Subjects of the Department of Disease Control, Thailand Ministry of Public Health.

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Table 1
Baseline characteristics of study participants

Characteristic	All (n = 250)	Immune (n = 223)	Nonimmune (n = 27)	*P* value
Sex, n (%)				.153
Male	59 (23.6)	50 (22.4)	9 (33.3)	
Female	191 (76.4)	173 (77.6)	18 (66.7)	
Age, y, mean (SD)	35.4 (11.7)	35.2 (11.9)	37.9 (9.9)	.363
Year of birth, n (%)				.482
Before 1977	110 (44.0)	97 (43.5)	13 (48.1)	
1977-1981*	30 (12.8)	27 (12.1)	5 (18.5)	
1982-1991*	82 (32.0)	72 (32.3)	8 (29.6)	
After 1991*	28 (11.2)	27 (12.1)	1 (3.7)	
Body mass index, mean (SD)	23.4 (5.6)	23.7 (5.5)	24.4 (6.2)	.525
Staff position, n (%)†				.579
Clinical	155 (62.0)	137 (61.4)	18 (66.7)	
Nonclinical ancillary	87 (34.8)	78 (35.0)	9 (33.3)	
Laboratory	8 (3.2)	8 (3.6)	0	
Home town, n (%)				.368
Bangkok	37 (14.8)	32 (14.3)	5 (18.5)	
Province	213 (85.2)	191 (85.7)	22 (81.5)	
Primary school, n (%)				.616
Bangkok	29 (11.6)	26 (11.7)	3 (11.1)	
Province	221 (88.4)	197 (88.3)	24 (88.9)	
History of childhood vaccination, n (%)				.030
Complete	100 (40.0)	86 (38.6)	14 (51.9)	
Incomplete	5 (2.0)	3 (1.3)	2 (7.4)	
Unknown	145 (58.0)	134 (60.1)	11 (40.7)	
History of diphtheria infection, n (%)				.795
Yes	2 (0.8)	2 (0.9)	0	
No	248 (99.2)	221 (99.1)	27 (100)	
History of close contact with patients with diphtheria, n (%)				.605
Yes	8 (3.2)	7 (3.1)	1 (3.7)	
No	242 (96.8)	216 (96.9)	26 (96.3)	
Adult booster with TT or Td vaccine, n (%)				.539
Yes	183 (73.2)	163 (73.1)	20 (74.1)	
No or unknown	67 (26.8)	60 (26.9)	7 (25.9)	
Type of vaccine, n/N (%)‡				.096
TT	119/183 (65.0)	104/164 (64.2)	15/19 (78.9)	
Td	55/183 (30.1)	53/164 (32.7)	2/19 (10.5)	
Not sure	9/183 (4.9)	7/164 (3.1)	2/19 (10.5)	
Time from last booster to enrollment, n/N (%)‡				.372
3-5 y	36/183 (19.7)	32/164 (19.5)	4/19 (21.1)	
6-10 y	37/183 (20.2)	34/164 (20.7)	3/19 (15.8)	
>10 y	25/183 (13.7)	20/164 (12.2)	5/19 (26.3)	
Unknown	85/183 (46.4)	78/164 (47.6)	7/19 (36.8)	

*1977: year of implementation of the first routine infant immunization program with 2 doses of diphtheria and tenanus toxoids, and whole-cell pertussis (DTP) vaccine for all Thai infants. In 1982, the recommendation was changed to 3 doses of DTP vaccine, and in 1992 it was modified to 5 doses of DTP at age 2, 4, 6, and 18 months and 4-6 years.
†Clinical staff: those who had regular contact with patients; nonclinical ancillary staff: those who may have had social contact with patients.
‡One hundred and eighty-three HCWs had a history of adult booster with the TT or Td vaccine before enrollment.

Data analysis

The Pearson correlation coefficient (r) was used to evaluate the correlation between age and diphtheria antibody levels. Mean antibody levels and rates of seroprotection to diphtheria before and after the first Td booster vaccination were compared using the paired t test and χ^2 test, respectively. Variables with a $P < .10$ in univariate analysis were included in multiple logistic regression models to identify factors associated with immune protection to diphtheria at baseline. All statistical analyses were performed with SPSS version 15.0 (SPSS, Chicago, IL).

RESULTS

Baseline characteristics of the 250 HCWs participating in this study are shown in Table 1. The correlation (r) between age and baseline diphtheria antibody level was 0.14 ($P = .024$) (Fig 1). Seroprotection was detected in 89.2% of the HCWs before receipt of the Td booster immunization, compared with 97.2% after receipt of the first Td booster dose ($P < .001$). The mean antibody level against diphtheria was 0.39 IU/mL (95% confidence interval [CI], 0.35-0.44 IU/mL) before immunization and 1.20 IU/mL (95% CI, 1.12-1.29 IU/mL) after the first booster dose ($P < .001$). Among immune HCWs, 9.9% had an antibody level >1 IU/mL at enrollment, which increased to 65.2% after receipt of the Td booster ($P = .015$).

For exploring the factors associated with immune protection to diphtheria at baseline, among the variables listed in Table 1, only a history of incomplete childhood vaccination (odds ratio [OR], 0.12; 95% CI, 0.02-0.82) and a history of receipt of the adult Td booster vaccination (OR, 10.6; 95% CI, 1.22-92.27) had a P value < .10 in univariate analysis. In multivariate analysis, only a history of receipt of the adult Td booster vaccination was a significant associated factor (OR, 5.39; 95% CI, 1.08-26.80; $P = .040$). Pain at the injection site was the most frequently reported local adverse effect of the Td vaccine, and myalgia was the most common systemic adverse effect. No serious adverse events were observed.

DISCUSSION

Our results demonstrate that Thai HCWs may be at risk of acquiring diphtheria infection. Compared with other studies of