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Note

Assessment of the antibody response in 110 healthy individuals who have been subject to Vi capsular polysaccharide vaccine

Ufuk Dizer[a,*], Levent Görenek[a], Özgür Güner[a], Tamer Pehlivan[b], Volkan Özgüven[a], Alaaddin Pahsa[a]

[a] *GATA Infectious Diseases and Clinical Microbiology Department, Ankara 6010, Turkey*
[b] *Medical Director Aventis Pasteur, Istanbul, Turkey*

Abstract

Thyphoid fever is a disease predominant in underdeveloped and developing countries. Thyphoid fever is more prevalent, in fact endemic, in countries where fecal contamination of water and food sources are very common. The majority of the reported cases are in the adult age group. There are three different vaccines which can be used to prevent thyphoid fever. In this study, we have used the parenteral Vi vaccine which was developed using the polisaccharide Vi antigen that covers the bacteria's surface, thus, concealing the O antigen protecting the bacteria against Anti-O antibodies and regarded as virulence factor. A total of 110 individuals whose sera were negative for seroconversion prior to vaccination were included in this study in which we have assessed Anti-Vi antibodies by tube agglutination. Serum and stool samples of 110 individuals were assessed 1 month after the vaccination. A total of 105 (95.5%) of the vaccinated people were considered to have positive (1/40 and higher) response and this result was regarded as prophylactic seroconversion. None of the people in the study group had *Salmonella typhi, S. paratyphi A,B,C* isolated from their stool cultures.

Keywords: Vi vaccine; Thyphoid fever

1. Introduction

Thyphoid fever remains to be a health hazard in a lot of countries around the world. Although the incidence is negligible in many of the developed countries in our country it still is an important issue. Food and water hygiene is under well control in urban life but those who travel to epidemic areas, those living in the rural parts of the country and military personnel are subject to the illness frequently. Each year there are approximately 16 million new cases of whom 600,000 deaths occur all around the world [1]. *Salmonella typhi* strains contain two O antigens which are 9 and 12 and a flagellar H antigen which is "d". In most of the *S. typhi* strains there is a capsular antigen "Vi" which is responsible for the virulence. *S. typhi* strains with the Vi antigen are more virulent. This antigen, decreases the bactericidal effect of the serum and inhibits the death of the bacteria within the makrofage. Vi antigen disturbs the bactericidal functions by inhibiting C3 from attaching to the surface of the bacteria, thus, inhibiting phagocytosis. Vi antigen also increases the resistance of the bacteria to the cytolitic effect of hydrogen peroxide within the macrophage, aiding the bacteria to within the cell. Detecting antibodies (Anti-Vi) against capsular polysaccharide Vi antigen is an invaluable serologic finding in pointing out the carriers [1,2]. The first vaccine developed against thyphoid fever is the whole bacteria, inactivated by phenol and applied parenterally (TAB vaccine). The other vaccine; is an oral vaccine obtained from live *S. typhi* which is mutant and whose metabolism is altered in order not to replicate (Ty21a). The third type of vaccine is a parenteral Vi vaccine, prepared by using the polisaccharide Vi antigen which is considered as the virulence factor, which covers the surface of the bacteria, thus, covering the O antigen and protecting the bacteria from Anti-O antibodies [3,4].

2. Materials and methods

A total of 110 individuals, whose sera were negative for Anti-Vi antibodies prior to vaccination with Vi capsular polisaccharide vaccine (Typhim Vi; Aventis Pasteur) were included in this study. The mean age of the study group was 23.8 ± 4.5 (mean age $\pm$ S.D.) and all of the subjects were male (100%). A total of 110 healthy individuals, who did not have an infectious disease within the last month, who had no history of thyphoid fever and who had not received any

* Corresponding author. Tel.: +90-312-3044301/533-4323461 (mobile); fax: +90-312-3044301.
E-mail address: ufukdizer@hotmail.com (U. Dizer).

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Table 1
Anti-Vi tube agglutination and stool culture results after immunization

Male	Mean age	Negative anti-Vi	Positive anti-Vi agglutinatşon			Stool culture negative
			1/80	1/160	1/320	
$n = 110$	23.8 ± 4.5	4.5% (5/110)	20.9% (23/110)	68.2% (75/110)	6.4% (7/110)	100% (110/110)

vaccine against thyphoid fever were vaccinated with an intramuscular single dose Vi capsular polysaccharide vaccine. Before and 1 month after the immunization serum samples of the study group were assessed for Anti-Vi antibodies by using the Anti-Vi tube agglutination test (The Binding Site, Birmingham, UK). Positive results with a dilution ratio of 1/40 and higher were regarded as protective antibody levels. Any positive result below the ratio of 1/40 were considered as a previous contact with *S. typhi* or an insufficient response to the vaccine. To be able to determine whether anyone in the study group was a carrier for *Salmonella*, stool samples were taken and checked for pathogen bacteria in *Salmonella–Shigella* (SS) agar medium.

3. Results

In this study, 105 (95.5%) individuals yielded a positive (1/40 or higher) response which was considered as protective seroconversion. In five individuals (4.5%) whose sera did not show any agglutination in the test tubes were concluded to have an insufficient amount of antibody titers. *S. typhi*, *S. paratyphi A,B,C* were not isolated in the stool cultures of any of the studied individuals. In one of the subjects (0.9%) pain at the injection site and enduration was observed within the 24 h after vaccination. Fever was not detected in any of the subjects Table 1.

4. Discussion

There are three different types of vaccines developed against thyphoid fever. The first of these parenteral whole bacteria vaccine inactivated by phenol parenteral (TAB vaccine). Although the immunization rate with this vaccine is as high as 50–70% it has numerous side effects. A total of 25–40% of the people immunized by TAB vaccine develop systemic reactions, 20% of whom show absenteeism [10]. The other vaccine; is an oral vaccine obtained from live, mutant *S. typhi* whose metabolism is altered and can not replicate (Ty21a). It can not be applied to any immune-compromised patients such as those with HIV infection and it should not be used in patients undergoing antibiotic or mephlocin treatments [4,5]. It results in a reliable level of immunity (85–100%) if taken every other day 1 h before meals with cold water q.i.d. This immunity is shown to last for 7 years in 2/3 of the subjects within the endemic regions [6]. The third type of vaccine is a parenteral Vi vaccine, prepared by using the polisaccharide Vi antigen which is considered as the virulence factor, which covers the surface of the bacteria, thus, covering the O antigen and protecting the bacteria from Anti-O antibodies [3,4]. Since this vaccine does not contain any bacterial cell wall (thus, the contents of a cell wall) which might serve as an endotoxin, it does not cause any systemic adverse effects. Not containing any live bacteria, it can be used in patients with all kinds of immune deficiencies including patients with HIV infection. After a single intramuscular injection, a seroconvertion of 80–95% can be attained starting at day 7 and lasting from 3 to 10 years [4,6]. When the protectivity of the three vaccines 3 years after the immunization were compared, it was 73% after two doses of TAB vaccine, 51% after three doses of Ty21a vaccine and 55% after a single dose of Vi polysaccharide vaccine [7]. A total of 10 years after the vaccination 58% of the subjects still had the protective immunity and the sustained immunity was found to be 55% in the epidemic regions [6]. The effectivity of Vi polysaccharide vaccine in children reaches 70%. Untoward effects are very rare and in fact less than that of pneumococcus and meningococcus vaccines. The most encountered adverse effects in children and adults are pain at the injection site and rarely erythema and swelling. These reactions are mild to moderate in most of the subjects and always reversile [9]. Concomittant application of Vi polysaccharide vaccine with meningococcus, tetanus-polioyomyelitis or rabies vaccines does not seem to affect its protectivity [8]. It is recommended for those immunized with the Vi vaccine to repeat the immunization every 2 years and those receiving four doses of oral vaccine should have it repeated every 5 years [5]. Studies are carried out to develop a single dose of oral vaccine and conjugated Vi vaccine which will be more reliable for the immunization of infants [6]. World Health Organization recommends the administration of thyphoid vaccine only to those travelling to endemic regions. No other risk situation is identified. However, people living in the endemic areas, travelers, those working in the field of microbiology and children are considered to be within potential risk groups. In our study, a positive response (1/40 and higher) was detected in 105 (95.5%) subjects and was regarded as a protective seroconversion. Another study is planned to determine the antibody levels of these 105 seropositive people 3 years after the immunization.

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