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Typhoid Vaccine in EPI; Relatively New Perhaps Overdue Strategy

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Abstract

Theoretically, it is possible to eliminate Salmonella, pathogenic bacteria that can cause a potentially fatal enteric fever. However, given the high prevalence of the disease in low-income countries that lack adequate facilities for sewage disposal and water treatment, and the fact that people can be long-term asymptomatic carriers, this goal is currently unrealistic. This levies constant need of a preventive measure to reduce morbidity and mortality in children associated with Typhoid Fever in endemic countries like Nepal. Currently, the best possible approach is to integrate the Typhoid vaccination into the Expanded Program of Immunization (EPI) until an improved sanitation and sewage disposal system is attained. We must acknowledge that this approach is not definitive until sufficient political and economic attention is received from all stakeholders.

Key words: Typhoid Fever, Typhoid Vaccination, Immunization.

Introduction

Typhoid Fever (Enteric Fever) is a systemic disease characterized by fever and abdominal pain caused by infection and dissemination of *Salmonella serovar typhi* or *Salmonella serovar paratyphi* in the blood[1]. Typhoid Fever continues to be a significant cause of morbidity and mortality, particularly among children and adolescents in South-central and Southeast Asia, where enteric fever is associated with poor sanitation and unsafe food and water[2].

Theoretically, it is possible to eliminate Salmonellae since the bacteria survives only in human hosts and are spread by contaminated food and water[1]. However, given the high prevalence of the disease in low income countries, lack of adequate sewage disposal and water treatment facilities, and the fact that people can be long term asymptomatic carriers, this goal is currently unrealistic. Thus, travelers to endemic countries are advised to monitor their food and water intake carefully and to consider vaccination[1]. Three vaccine alternatives are currently available:

1. Heat-killed, phenol-extracted, whole-cell vaccine (two injectable doses).
2. Ty21a, an attenuated S. typhi vaccine (four oral doses).
3. ViCPS, consisting of purified Vi polysaccharide from the bacterial capsule (one injectable dose).

While, the fourth vaccine, Vi-rEPA (two injectable doses), has been recently developed and undergone several clinical trials in China and Vietnam[2,11]. This vaccine consists of Vi polysaccharide bound to a nontoxic recombinant protein that is identical to *Pseudomonas aeruginosa* exotoxin A[1,2]. Coupling of the Vi polysaccharide to exotoxin A, results in impressive T cell responses[1]. It has been shown to be safe and immunogenic in Vietnamese children aged 2–5 years, providing protective efficacy of 91.5% and was very well tolerated, with no serious adverse reactions[2].

In a study done to measure the incidence of Typhoid Fever among preschoolers by Sinha et. al.[3] in low-income urban area of Delhi, they found Typhoid to be a common and significant cause of morbidity between one and five years of age and suggested that the optimum age of typhoid immunization and the choice of vaccines need to be reassessed. The continued high disease burden of Typhoid Fever and the alarming spread of antibiotic resistant strains led the World Health Organization (WHO), almost ten years ago, to recommend immunization. Verma et. al.[4] also found

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similar results in their study conducted in India and recommended immunization of preschool and school age children with Vi polysaccharide vaccine, particularly in areas where Typhoid Fever posed a significant problem and where antibiotic resistance is prevalent.

Despite having been evaluated in populations in middle- and low income endemic countries, Typhoid Fever vaccines have historically been used predominantly among travelers from non-endemic and high-income countries[5] and have been only occasionally used in settings of endemicity[6]. However, this situation is changing because of the availability of high-quality burden of disease data from countries of endemicity[7] such as Thailand, China, Vietnam, and India[8].

Furthermore, a 2008 World Health Organization (WHO) position paper on the use of typhoid vaccines provides a mandate to member states by suggesting that countries should consider the programmatic use of Ty21a and Vi vaccines for controlling endemic disease[9]. The position paper indicates that the use of vaccine should be based on an understanding of the local epidemiology of Typhoid Fever to target vaccines to groups at high risk of disease, such as preschool-or school-age children. It was also suggested that vaccines should be implemented in the context of broad disease control efforts[9]. Ultimately, the adoption of typhoid vaccine in settings of endemicity would be greatly aided by the availability of vaccines that are efficacious in infants to facilitate integration with Expanded Programs of Immunization, that can be administered as a single dose, and that are produced locally to reduce cost[10].

The constant need of a preventive measure to reduce morbidity and mortality associated with Typhoid Fever has also been a major issue in endemic countries like Nepal. Another randomized controlled trial in Vietnam to use Vi-rEPA in infants has shown significant evidence to support the inclusion of Vi-rEPA into Expanded Program of Immunization (EPI). A total of 301 full-term Vietnamese infants received Expanded Program on Immunization (EPI) vaccines alone or with Vi-rEPA or Haemophilus influenzae type b-tetanus toxoid conjugate (Hib-TT) at 2, 4, and 6 months and Vi-rEPA or Hib-TT alone at 12 months[11]. They also measured maternal, cord, and infant sera for IgG anti-Vi and for IgG antibodies to Hib CP and the diphtheria, tetanus, and pertussis toxins at 7, 12, and 13 months. Even though high cord IgG anti-Vi levels partially suppressed infant responses to Vi-rEPA, the researchers determined that the vaccine was safe, induced protective anti-Vi levels, and was compatible with other EPI vaccines. Vu Dinh Thiem et. al.[11] reasoned that immunization for Typhoid Fever added to the EPI vaccines along with improving water quality would have avoided the tragedy that befell Tajikistan public health officials in 1996 when drinking water became contaminated with fecal material, resulting in 8,901 typhoid cases and 95 deaths. The results of Vu Dinh Thiem et. al.[11] are encouraging to support incorporating Vi-rEPA into routine Expanded Program of Immunization to reduce the morbidity and mortality associated with Typhoid Fever in endemic areas. There are many studies regarding the development of a novel vaccine for *S. typhi*. For example, the recent emergence of *S. paratyphi* has induced newer strategies to develop *Paratyphi* vaccination programs as no vaccines are currently available[12].

Even though the overdue strategy seems fading from the lack of political will, Vi-based Vaccines for Asia Initiative (VIVA) had helped in the use of Vi polysaccharide vaccine in high risk areas of Nepal through school-based vaccination program and tourism-sector vaccination[13]. This introduces a new hope towards the fight against Typhoid Fever. Currently, the best possible approach is to integrate the Typhoid vaccination into the Expanded Program of Immunization (EPI) until an improved sanitation and sewage disposal system is attained. We must acknowledge that this approach is not definitive until sufficient political and economic attention is received from all stakeholders including Government of Nepal – Ministry of Health in liaison with GAVI Alliance, World Health Organization, USAID and UNICEF.

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