Conjugate Vaccine for Typhoid Fever - New Solution to an Old Problem

Today, in spite of having increased knowledge about causative agents of many infectious diseases, we are far behind from controlling many of these and in the development of an efficient vaccine. Typhoid fever is one such disease, which is caused by *Salmonella enterica* serovar *typhi*. Although salmonellosis is rare in developed and industrialized countries, it still remains a serious problem in most of the developing countries, especially Southeast Asian countries, Africa, and Latin America.[1]

From the time of introduction of a heat-killed phenol preserved and acetone-killed lyophilized injectable whole cell *Salmonella typhi* vaccine in England and Germany in 1896, many attempts have been made to refine the vaccine to reduce the incidence of adverse events and improve the efficacy. The Vi polysaccharide vaccine introduced by Felix *et al.* which showed that the presence of serological response against Vi polysaccharide in typhoid fever is another important milestone in the progress toward an effective vaccine for typhoid fever.[2,3] The recent data of the community vaccination in high-incidence areas of Kolkata, Karachi, and North Jakarta showed the cost-effectiveness of Vi polysaccharide vaccine in children.[4]

Due to the side effects and low effectiveness of the killed whole cell vaccine, a need for a more competent vaccine candidate emerged. With the knowledge that live attenuated strain elicits more immune response, attenuated *Salmonella* strains were considered for vaccine development. Ty21a was the first live oral attenuated *Salmonella* vaccine.[5] This strain lacks both functional galactose-epimerase (*galE*) gene and the Vi antigen and is highly attenuated. The Ty21a vaccine is licensed in 56 countries of Asia, Africa, USA, and Europe.[6]

Despite an adequate immune response and efficacy against typhoid fever, Ty21a has certain drawbacks. To obtain sufficient immunity, high numbers (10⁹) of bacteria are required for oral dose; its use is recommended for children only above 5–6 years of age. This vaccine is highly acid labile, and hence, stomach acidity has to be either neutralized or bypassed when Ty21a is to be fed orally. Several strains of *S. typhi* strains have been developed for oral vaccination for typhoid fever, but they were unable to maintain growth in mammalian tissue. The typhoid vaccines designed till date give best protection to children >2 years of age.[1]

In this context, the pre-qualification of a conjugate vaccine called Typbar-TCV® developed by an Indian pharmaceutical company Bharat Biotech by the WHO is a welcome development. The pre-qualification was based on the recommendation by the strategic advisory group of experts on immunization, for routine use in children over 6 months of age in typhoid endemic countries.[7]

With the introduction of this refined vaccine which has been developed keeping in mind the drawbacks of previous vaccines for typhoid fever, it is expected that we may be closer to finding a solution for an old problem.

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