Abstract

Typhoid fever vaccines currently available are immunogenic and proven safe for immunizing children and adults. Research on polysaccharide vaccines carried out earlier by several scientific workers concluded that bacterial carbohydrate antigens are less immunogenic or ineffective in facilitating antibody responses in infants below 2 years of age group. This aspect remained a major problem in case of infants who are more prone to typhoid fever in endemic areas. Extensive research on bacterial polysaccharides revealed that polysaccharide antigens are T-cell independent in nature and hence polysaccharides are incapable to recruit T-cells for their antibody responses which resulted in poor immune responses and also, secondary memory responses do not occur. Vaccination against *Haemophilus influenzae* type b disease proved that polysaccharide-protein conjugates are capable to invade T-cells for the immune mechanism to be activated by converting T-cell independent polysaccharides as T-dependent. The same strategy was followed in the present study to develop an effective vaccine candidate against typhoid fever. Vi Polysaccharide of *Salmonella typhi* was isolated by fermentation and purification process and coupled to Tetanus toxoid under controlled conditions. Typhoid Vi-polysaccharide-Tetanus toxoid conjugates were characterized and final vaccine preparations are experimentally studied at preclinical level and in human clinical trials. The final lots of Typhoid Vi polysaccharide-protein conjugates
were studied in laboratory animals for abnormal, acute and systemic toxicity. A challenge study was conducted in mice to prove the protective efficacy and immunogenicity study was conducted in comparison with native polysaccharide vaccine and antibody evaluation was determined by ELISA testing. All these data supported the evaluation of the vaccine in humans. Vi polysaccharide-protein conjugate vaccines were tested for immunogenicity in the age groups of 13-17 years, 6-12 years with (single dose) and in 2-5 years with two doses. A native Vi polysaccharide vaccine is used as reference vaccine. The immunogenicity of test and reference vaccine was bridged statistically and results obtained proved that experimental ViPs-TT conjugate vaccines provided significantly more protection than currently available native polysaccharide vaccines against typhoid fever. This experimental study was followed up and optimized at production scale. This vaccine was tested in the field by carrying out human clinical trials and found to be safe and effective in both children and adult age group. Also the Vi polysaccharide-Tetanus toxoid vaccine developed found to be superior or effective than the native polysaccharide vaccine.