Successful study of Swedish vaccine candidate against diarrhea

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University of Gothenburg researchers have reported the first successful results of an oral, inactivated vaccine candidate ETVAX against enterotoxigenic E. coli diarrhea in a placebo-controlled phase I/II study in infants and children from six months to five years of age in Bangladesh.

All predefined primary endpoints for the study were achieved, showing that the vaccine candidate was safe and broadly immunogenic, stimulating immune responses to all key vaccine components.

Only a few mild to moderate adverse reactions were observed among participants; the vaccine induced impressive serum and intestinal immune responses in young children and infants, with 80–100 percent of children two to five years of age and 50 to 80 percent of infants six to 11 months of age responding to all key vaccine antigens.

Giving the vaccine together with an adjuvant enhanced the magnitude, breadth and kinetics of the intestinal immune responses in infants. Results are presented in this week´s issue of *The Lancet Infectious Diseases*.

Children and travelers

Enterotoxigenic E. coli (ETEC) bacteria are a primary cause of diarrhea, leading to substantial illness and death in children in low- and middle-income countries (LMICs) as well as in travelers to LMICs. Currently, there is no ETEC vaccine available on the market for use in either children or travelers to ETEC high-risk areas, and ETEC vaccine development is a World Health Organization priority.

An oral ETEC vaccine candidate, ETVAX, was developed at University of Gothenburg in collaboration with Scandinavian Biopharma, Stockholm. ETVAX consists of inactivated E. coli bacteria expressing high levels of protective antigens and the ETEC-based B subunit protein LCTBA.

This clinical study examined the administration of ETVAX, given alone or together with different doses of an adjuvant, double-mutant heat-labile toxin (dmLT), to assess the vaccine's safety and immunogenicity in 450 children.

Descending age groups of children two to five years, one to two years and six to 11 months were given two doses of vaccine in one of three fractionated dose levels (i.e., one-eighth, one-fourth and one-half) of a full adult dose with or without different doses (2.5 to 10 micrograms) of the dmLT adjuvant or buffer alone (placebo) as a drink two weeks apart in a double-blind manner.

Confirm promising data

In addition to safety analyses, immune responses were determined by measuring the amount of antibodies produced in the intestine (feces) as well as antibodies secreted by lymphocytes circulating in blood to the intestine.

The results confirm and extend the promising data previously reported from ETVAX trials in Swedish and Bangladeshi adults. Based on the results of this trial, studies were initiated in September 2019 to further test safety, immune responses and protection of ETVAX (including dmLT) in African children six to 23 months of age. A study evaluating the protective efficacy of ETVAX in Finnish travelers to Africa will be completed by the end of the first quarter of 2020.

More information: Firdausi Qadri et al. Safety and immunogenicity of the oral, inactivated, enterotoxigenic Escherichia coli vaccine ETVAX in Bangladeshi children and infants: a double-blind, randomised, placebo-controlled phase 1/2 trial, *The Lancet Infectious Diseases* (2019). DOI: 10.1016/S1473-3099(19)30571-7

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