Typhoid conjugate vaccine use on adults and children

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Research for the development of a new typhoid conjugate vaccine has made a significant progress in recent years. A Phase I Clinical Trial of Vi-DT typhoid conjugate vaccine (made by SK Chemicals Korea) has shown promising results. This typhoid vaccine was shown to be safe and immunogenic in the clinical study conducted in Manila, the Philippines. An important observation of the research study was that all the participants (100 percent) showed significant immune response upon vaccination with Vi-DT.

Typhoid fever, an invasive bacterial infection caused by Salmonella enterica serovar Typhi (S. Typhi), is an important public health problem in the world, especially in developing countries of Africa and Asia. Susceptible human hosts usually ingest S. Typhi through contaminated food or water, so the long-term solution for typhoid prevention is provision of safe water, sanitation infrastructure development, and hygiene interventions.

However, the development of infrastructure for water supplies and sanitation needs huge investment and may take decades to materialize. Hence WHO recommends use of typhoid vaccine as a control measure in the short-to-intermediate term. Additionally, typhoid vaccines are valuable for travellers, food workers (including street vendors), household contacts of typhoid carriers, and laboratory workers. Although typhoid as a disease is amenable to antibiotics treatment, increasing frequencies of multi-drug resistance among the invasive isolates is posing a serious threat and limiting the effectiveness of such treatments. Multidrug-resistant Salmonella typhi has become a major public health problem, as more people are prescribed antibiotics for even common fever in developing nations.

Currently, three types of typhoid vaccines are available in the market - Ty21a (a live vaccine given by mouth), Vi capsular polysaccharide vaccine (ViPS) (an injectable subunit vaccine); and typhoid conjugate vaccine (TCV). The Ty21a vaccine, a live oral vaccine, is available as an enteric-coated capsule or liquid formulation. It is given in three doses every other day and is not approved for use in children at less than five years of age. It elicits protection that starts 10 to 14 days after the third dose.

Travellers should be revaccinated annually, and those living in disease endemic areas every three years. The Vi polysaccharide vaccine is given as a single parenteral dose. Protection begins seven days after injection, and maximum protection is reached 28 days after injection, when the highest antibody concentration is attained (Carmody 2002). This vaccine is approved for persons two years of age and older. Re-vaccination every three years is recommended. Both the Ty21a and Vi polysaccharide vaccines have major limitations, like the need to administer multiple doses, short-lived protection and most importantly, neither vaccine is amenable to use in children younger than two years of age. So, these vaccines cannot be used in routine childhood vaccination programs and do not protect younger children who are most vulnerable. Hence there was a desperate need for the typhoid conjugate vaccine, as these are expected to have a longer duration of protection, can be given to children as young as 6 weeks of age and elicit booster response to subsequent doses.

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Three TCVs are expected to have a longer duration of protection, can be given to children as young as 6 weeks of age and elicit booster response to subsequent doses. The Vi-DT vaccine, a conjugate vaccine made by conjugating S. typhi Vi-polysaccharide to the Diphtheria toxoid (DT), was a randomized, observer-blinded Phase I study to assess the safety and immunogenicity of the Vi-DT vaccine.
immunogenicity of Vi-DT compared to Vi polysaccharide vaccine, conducted in Manila, Philippines. Participants were enrolled in an age de-escalation manner, adults followed by adolescents and finally children. Enrolled participants were randomly divided between the test group and the comparator group equally. Participants in the test group received Vi-DT (25?μg) at 0 and 4 weeks and participants in the comparator group received Vi polysaccharide vaccine (Typhim Vi®) and flu vaccine (Vaxigrip®) at 0 and 4 weeks.

A total of 144 participants were enrolled (48 by age strata, 24 in test and comparator groups each). No serious adverse event was reported in either group. Solicited and unsolicited adverse events were mild or moderate in both groups except for a four-year old girl in test group with grade 3 fever which resolved without sequelae. All participants in test group seroconverted after first and second doses of Vi-DT while the proportions in the comparator group were 97.1 per cent and 97.2 per cent, after first dose of Typhim Vi® and second dose of Vaxigrip®, respectively. Vi-DT showed 4-fold higher Geometric Mean Titers (GMT) compared to Typhim Vi® (adjusted for age strata, p<0.001). No further increase of GMT was detected after the second dose of Vi-DT.

New chapter in typhoid control about to begin

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