A cluster randomized non-inferiority field trial on the immunogenicity and safety of tetanus toxoid vaccine kept in controlled temperature chain compared to cold chain

INTRODUCTION

Most vaccines are required to be kept cold (2-8°C) from manufacturer to beneficiaries. However, in cold chain hotspots, this can be an obstacle to vaccines delivery, especially in countries with limited cold chain infrastructure and electricity [1,2]. Several studies have shown the possibility of using vaccines outside the 2-8°C range, under control of temperature change (CTC) [3,11]. CTC allows vaccines to be kept outside the cold chain for a defined duration and temperature depending on the vaccine’s particular heat-stability profile [2,12].

The possibility of using vaccines in CTC started with the introduction of Vaccine Vial Monitor (VVM), a time-temperature indicator, to the market. The VVM contains a time-temperature sensitive square and an outer circle. The square changes color with exposure to heat indicating whether the vaccine is likely to have been damaged [13].

Immunogenicity of women with TT is a central strategy of the Material and Neontal Tetanus Elimination Initiative [16]. TT supplementary immunization activities (SIAs) target women of reproductive age in high-risk areas. The delivery of TT in CTC could remove one of the important barriers to reaching undererved and marginalized populations considered mostly affected by tetanus.

MATERIALS AND METHODS

Study design

Cluster randomized, non-inferiority trial conducted in three health zones of Moïssala district, Chad. In each health zone, a village was chosen at random in an indirect approach using EPI card. Clusters corresponding to a village or group of villages with 600-800 residents, were stratified according to distance to health centers (≤5 km and >5 km) and to infant vaccination activities taking place at village level [17].

All women 14-49 years of age were invited to participate. Eligible participants had received a maximum of one previous TT dose as determined by vaccination history, were eligible for vaccination according to national schedule and had no contraindication to TT vaccination. Clusters were assigned to received TT kept in cold chain or CTC with equal probability by stratum.

Prior to the study, in TT 10 dose-ials (Serum Institute of India Limited, Hyderabad, India) from three different batches were exposed to CTC conditions in Moïssala district, Chad. CTC vaccines were kept inside vaccine carriers without ice packs for 30 days and carried by teams during a national immunization campaign in Chad.

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Study population

A total of 2238 participants residing in 42 villages grouped in 34 clusters were enrolled into the study. SES Analysts completed the study in each group. The primary study’s aim was to examine the vaccine analysis included 1830 participants with pre- and post-vaccination antibody level result.

DISCUSSION

This study demonstrates the stability and immunogenicity of TT manufactured by Serum Institute of India limited kept in CTC at temperatures ≤40°C for up to 30 days. TT in CTC retained adequate potency with no significant differences in antibody responses compared to cold chain vaccines.

RESULTS

Table 1: Results of potency, pH and flocculation tests for vaccines kept in CTC and standard cold chain

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>CTC</th>
<th>Cold Chain</th>
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<tbody>
<tr>
<td>Potency (IU/ml)</td>
<td>29.0 (16.0)</td>
<td>29.0 (16.0)</td>
</tr>
<tr>
<td>pH</td>
<td>6.5 (2.3)</td>
<td>6.5 (2.3)</td>
</tr>
<tr>
<td>Flocculation</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 2: Exposure to temperatures and VMM status of the CTC and cold chain administered vaccines

<table>
<thead>
<tr>
<th>Study population</th>
<th>CTC</th>
<th>Cold chain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants' characteristics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>25.1 (11.2)</td>
<td>25.1 (11.2)</td>
</tr>
<tr>
<td>Pre-vaccination CTC</td>
<td>64 (5.7%)</td>
<td>71 (4.8%)</td>
</tr>
<tr>
<td>Number of pre-vaccination CTC</td>
<td>2.6 (9.14)</td>
<td>2.5 (9.07)</td>
</tr>
<tr>
<td>Number of pre-vaccination cold chain</td>
<td>392 (36.6%)</td>
<td>392 (36.6%)</td>
</tr>
<tr>
<td>Women last TT dose</td>
<td>4.8 (3.60)</td>
<td>4.8 (3.60)</td>
</tr>
<tr>
<td>Received a TT dose before inclusion</td>
<td>50 (49.5%)</td>
<td>54 (52.9%)</td>
</tr>
<tr>
<td>Baseline GMC in IU/ml (95%CI)</td>
<td>0.35 (0.33-0.36)</td>
<td>0.35 (0.33-0.36)</td>
</tr>
</tbody>
</table>

No adverse events were observed 30 min post-vaccination. A small number of participants (n=25) self-reported an adverse event occurring 7 days after vaccination (2 in CTC and 23 in cold chain). These were characterized by a local reaction at the injection site with pain and swelling in occasions accompanied by fever and headache.

REFERENCES