

Interim Immune Response to a Delayed Second Dose of Oral Cholera Vaccine: A randomized, controlled, non-inferiority and immunogenicity trial in Conakry, Guinea

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Background

Oral cholera vaccines (OCVs) are important tools in outbreak control. Manufacturers recommend a 7- to 14-day interval between two doses. Adherence to this schedule for mass vaccinations in emergency situations can be operationally challenging. Recent evidence suggests that longer intervals between doses may trigger robust immune responses. Demonstrating non-inferiority of extended intervals between doses could allow more flexibility of OCV delivery strategies.

Methods

We aimed to evaluate the non-inferiority of the humoral immune response of a second dose of Euvichol-Plus® administered 6 or 12 months after the initial dose, compared to the standard 2-week interval. From 2022 to 2024, we conducted an open-label, randomized, controlled, non-inferiority trial in Conakry, Guinea, enrolling 456 healthy participants aged 1 to 39 years. Participants were randomized into three groups receiving the second OCV dose after a 2-week (control), 6-month, or 12-month interval. The primary endpoint was the geometric mean titer (GMT) of the serum vibriocidal antibodies (O1 Inaba and O1 Ogawa) 14 days after the second dose, with a non-inferiority margin of 0.67 on the GMT ratio (GMT of the intervention arm/GMT of the control arm).

Results

Baseline serum vibriocidal GMTs were similar across study arms. In the modified intention-to-treat and per-protocol populations, 14 days after the administration of the second OCV dose, the lower limit of the two-sided 97.5% confidence interval

of the serum vibriocidal antibody GMT ratio was greater than 0.67, for V. cholerae O1, Ogawa and Inaba serotypes. The prespecified non inferiority criterion was also met in children (1-4 years and 1-9 years).

Conclusion

The results demonstrate that two-dose OCV schedules with extended intervals of 6-month and 12-month are immunologically non-inferior to the standard 2-week interval against V. cholerae O1. This provides strong evidence in favor of more flexible two-dose OCV vaccination strategies, with extended intervals, without compromising longer-term immune protection.

Two-dose OCV schedules with 6-month and 12-month intervals are immunologically non-inferior to standard 2-week interval against V. cholerae O1, supporting flexible vaccination strategies without compromising longer-term immunity.