Effectiveness of one dose of oral cholera vaccine in response to an outbreak: a case-cohort study

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Summary

Background **Oral cholera vaccines represent a new effective tool to fight cholera and are licensed as two-dose regimens with 2–4 weeks between doses. Evidence from previous studies suggests that a single dose of oral cholera vaccine might provide substantial direct protection against cholera. During a cholera outbreak in May, 2015, in Juba, South Sudan, the Ministry of Health, Médecins Sans Frontières, and partners engaged in the first field deployment of a single dose of oral cholera vaccine to enhance the outbreak response. We did a vaccine effectiveness study in conjunction with this large public health intervention.**

Methods **We did a case-cohort study, combining information on the vaccination status and disease outcomes from a random cohort recruited from throughout the city of Juba with that from all the cases detected. Eligible cases were those aged 1 year or older on the first day of the vaccination campaign who sought care for diarrhoea at all three cholera treatment centres and seven rehydration posts throughout Juba. Confirmed cases were suspected cases who tested positive to PCR for *Vibrio cholerae* O1. We estimated the short-term protection (direct and indirect) conferred by one dose of cholera vaccine (Shanchol, Shantha Biotechnics, Hyderabad, India).**

Findings **Between Aug 9, 2015, and Sept 29, 2015, we enrolled 87 individuals with suspected cholera, and an 898-person cohort from throughout Juba. Of the 87 individuals with suspected cholera, 34 were classified as cholera positive, 52 as cholera negative, and one had indeterminate results. Of the 858 cohort members who completed a follow-up visit, none developed clinical cholera during follow-up. The unadjusted single-dose vaccine effectiveness was 80·2% (95% CI 61·5–100·0) and after adjusting for potential confounders was 87·3% (70·2–100·0).**

Interpretation **One dose of Shanchol was effective in preventing medically attended cholera in this study. These results support the use of a single-dose strategy in outbreaks in similar epidemiological settings.**

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Introduction

Oral cholera vaccines are a feasible and effective tool for cholera outbreak response.[1,2] Currently, there are three WHO-prequalified oral cholera vaccines; one primarily for travellers (Dukoral, Janssen, Beerse, Belgium), and two that are better adapted for delivery through mass campaigns in outbreaks, Shanchol (Shantha Biotechnics, Hyderabad, India, prequalified in November, 2012) and Euvichol (EuBiologics, Seoul, South Korea, prequalified in December, 2015). Two doses of any of these killed whole-cell vaccines provide high levels of direct protection probably lasting at least 5 years and some herd protection.[2–6]

In 2015, fewer than 4 million doses of oral cholera vaccine were produced, with most purchased by the global oral cholera vaccine stockpile, managed by the International Coordinating Group, comprised of Médecins Sans Frontières, UNICEF, the International Federation of the Red Cross and Red Crescent Societies, and WHO.[7] Although production will probably have increased in 2016, global availability will continue to be dwarfed by the more than 2 billion people at risk of cholera.[8] Delivery of two oral cholera vaccine doses separated by at least 2 weeks presents logistical challenges for achieving adequate coverage in areas at most risk where populations are highly mobile and the epidemic focus might rapidly shift.

Epidemiological evidence, although minimal, suggests that one oral cholera vaccine dose might provide moderate protection from cholera.[2,4,9,10] Immunogenicity studies also suggest that a single dose of oral cholera vaccine elicits a similar (vibriocidal) antibody response to two doses provided 2–4 weeks apart.[11,12] Modelling results suggest that when vaccine supply is limited, vaccinating twice the number of people with a single dose will often save more lives than providing the full two-dose regimen to a smaller population during an outbreak.[13] The global shortage of oral cholera vaccine, which will probably persist for years, coupled with the challenges of delivering two doses in some settings, might make a single dose, if effective, an attractive regimen.