SUPPLEMENT ARTICLE

Progress and Challenges in Using Oral Cholera Vaccines to Control Outbreaks: The Médecins Sans Frontières Experience

Iza Ciglenecki,[1] Andrew S. Azman,[1,2] Christine Jamet,[1] Micaela Serafini,[1] Francisco J. Luquero,[3] and Jean-Clement Cabrol[1]

[1]Médecins Sans Frontières, Geneva, Switzerland; [2]Department of Epidemiology, Johns Hopkins University, Baltimore, Maryland; and [3]Epicentre, Paris, France

The use of oral cholera vaccine (OCV) has increased since 2011, when Shanchol, the first OCV suitable for large-scale use, became available. Médecins Sans Frontières considers OCVs an essential cholera outbreak control tool and has contributed to generating new evidence on OCV use in outbreaks. We showed that large-scale mass campaigns are feasible during outbreaks, documented high short-term effectiveness and showed that vaccines are likely safe in pregnancy. We found that a single-dose regimen has high short-term effectiveness, making rapid delivery of vaccine during outbreaks easier, especially given the on-going global vaccine shortage. Despite progress, OCV has still not been used widely in some of the largest recent outbreaks and thousands of cholera deaths are reported every year. While working towards improving our tools to protect those most at-risk of cholera, we must strive to use all available effective interventions in efficient ways, including OCV, to prevent avoidable deaths today.

Keywords. oral cholera vaccines; cholera; epidemics.

The use of killed oral cholera vaccine (OCV) has increased since 2011, when Shanchol, the first OCV suitable for large-scale use, became available and was prequalified by the World Health Organization (WHO) [1]. The creation of an OCV stockpile in 2013, together with funding for the vaccines and implementation costs, further facilitated vaccine use. Doubts about feasibility, timeliness, and acceptability of OCV, and the fear of diverting resources from other preventive interventions, which predominated discussions and discouraged reactive OCV use in the past [2], have been mostly put to rest by successful OCV field implementations. However, timeliness of reactive OCV campaigns, the logistic complexities of delivering the vaccine, and the persistent global shortage continue to hinder widespread OCV use.

Médecins Sans Frontières considers OCV to be an essential outbreak control tool, complimenting case management and water/sanitation/hygiene interventions. In 2012, we assisted the Guinea Ministry of Health in organizing a reactive vaccination campaign, targeting over 200 000 people. We demonstrated that reactive mass campaigns are feasible, and that even in remote rural villages high coverage can be reached (eg, >90% having received at least 1 dose and 76% 2 doses) [3, 4]. We documented high short-term vaccine effectiveness (86.6%; 95% confidence interval [CI], 56.7%–95.8%) and showed that the vaccine is likely safe in pregnancy [5, 6].

One important challenge for reactive use of current OCVs is the recommended 2-dose schedule. With evidence that a single OCV dose provides some short-term protection at the individual level [7] and may prevent more cases in an outbreak than providing 2 doses to half of the people [8], we assisted the Ministry of Health in Juba, South Sudan with adopting this single-dose strategy during a 2015 epidemic when only limited OCV was available. We demonstrated high short-term single-dose vaccine effectiveness of 87.3% (95% CI, 70.2%–100%) [9]. Less than a year later, when cholera broke in Zambia's capital Lusaka, after several years of absence, a similar situation involving a large urban population at risk and limited amount of vaccines appeared. With the same 1-dose strategy we reached almost half a million people, and were able to confirm the short-term effectiveness of this regimen (88.9%; 95% CI, 42.7%–97.8%) in a population where cholera had not been reported for more than 4 years [10]. As it is unclear how long protection from a single dose may last, the campaign was followed with a second dose 8 months later, when more vaccine was available. Current immunologic evidence suggests that the recommended 14-day interval is suboptimal, though more work is needed to define when booster doses should be provided [11].

Although OCVs are known to be thermostable, the vaccine package inserts require storage in the cold chain. This, coupled with the bulkiness of the vaccines, presents a major logistic challenge in organizing large-scale campaigns. In agreement with respective ministries of health, we opted for off-label vaccine use in most of our campaigns. Taking advantage of demonstrated

OCV heat stability [12], we kept vaccines stored in the central cold chain, but did not use passive cold chain (ie, cold boxes and vaccine carriers) on the day of vaccination, greatly reducing cold chain needs and related resources and costs. The above described vaccine effectiveness estimates were obtained from campaigns using this out-of-cold-chain strategy. Our example has so far not been widely followed, and most of the other OCV campaigns, even in the countries with previous experience of using the vaccines out-of-cold-chain, have been conducted with strict cold chain use [5, 9, 10]. Fortunately, Shanchol recently received WHO prequalification for controlled cold chain use, allowing the vaccine to be used with up to 14 days at ambient temperature not exceeding 40°C [13], and its bioequivalent, Euvichol, expected to get approval soon.

Optimal reactive use of OCV is hindered by delays in recognizing, confirming, and declaring cholera epidemics [14]. Improving surveillance systems will be essential in fight against cholera. But many of the recent large nationwide epidemics were protracted and even delayed campaigns would save many lives. More cholera cases have been reported to the WHO in 2017 than in any other year since the start of the seventh cholera pandemic, with unprecedented epidemics in war-torn Yemen and in eastern and central Africa [15, 16]. With only a few exceptions, despite great advances, OCVs have not been used in the major epidemics of 2017. The shortage of vaccines remains the biggest obstacle, even with recent increases in production. It forces health authorities to choose which populations will benefit from the vaccine and which cannot—a particularly difficult task with large populations at risk. Even if allocation decisions are epidemiologically justifiable, they may not be politically acceptable. Alternative, more targeted strategies, such as those focused on neighbors of cases [17, 18] or mobile high-risk groups [19], are rarely explored. Not every cholera outbreak is the same: an evidence-based "menu" of standardized intervention packages based on local epidemiology could greatly facilitate decision-making processes.

While long-term cholera control or elimination will likely depend on tackling cholera in areas with persistent transmission, it is during epidemics that the cholera burden is most devastating [20]. In the 21st century, with means available to both prevent and treat cholera, we should not accept thousands of cholera deaths reported every year. OCVs might not be a perfect outbreak response tool, but we must strive to use all available effective interventions and explore innovative ways to deliver them to those most at risk to prevent avoidable deaths today.

Notes

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