



Safety and Efficacy Oral Cholera Vaccine (OCV) in Hodeidah, Yemen

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Abstract

Background : A national Oral Cholera Vaccine (OCV) campaign was launched in Hodeidah, in response to the first outbreak in Hodeidah ,Yemen , May 2017. **Objectives:** Therefore. the study aimed to monitor the efficacy and determine the incidence of adverse events following immunization (AEFI) with OCV among the Hali District , Hodeidah peoples of Yemen. .

Methodology: The study was designed in two phases, the phase I, a cross sectional survey was designed to monitor the safety (AEFI) of OCV where the study was carried out between 6th May 2018 and 30th August 2018. The study included 210 participants that were administrated the vaccine orally. The adverse events were reported after 24 – 72 hours from administration of vaccine. The phase II, a cohort study was designed after three months of OCV vaccination campaign that included 151 cholera patients in diarrhea treatment center (DTC) with reporting of vaccination status and vaccine efficacy (VE) of OCV was measured based on two methods , the first was rapid measurement method and the second was cohort study . **Results:** A total of 210, 40 % of males and 60 % of females, aged from 10 years to 60 years. 50 % of participants was children , 30 % of young and 20 % of elderly. The incidence of AEFI of OCV among participants was reported in 20 participants (9.52 %). While, non-serious were reported in 190 participants (90.48 %). The major adverse events were reported as the following: loss appetite (9.52%), vomiting (7.14%), diarrhea (4.29%), abdominal pain (1.92%), and fever (0%). On the other hand, the VE of OCV was 96.72% according to rapid estimation method and 98.65 % based on cohort study. **Conclusion:** Our findings concluded that OCV was highly safe and effective. Additionally, monitoring AEFIs during emergency cholera outbreak campaigns supports the favorable safety profile of OCV.

Keywords : Cholera , OCV , Vaccine , Safety , AEFI , Efficacy , Hodeidah, Yemen

1. Introduction

Cholera continues to pose a major global public health challenge, especially in areas lacking access to clean water and adequate sanitation. Characterized by acute watery diarrhea, the disease can be fatal in 25–50% of untreated cases and remains endemic in countries like Yemen [1–3], Iraq [4], Lebanon [5], Sudan [6], and parts of eastern India [7]. Frequent outbreaks also occur in areas with poor sanitation, including refugee camps. In response to the burden of cholera in endemic and high-risk areas, oral cholera vaccines (OCVs) have become an important public health tool [8] alongside water, sanitation, and hygiene (WASH) interventions [9,10]. Over the past 50 years, several OCVs have been developed and evaluated for safety, efficacy, and effectiveness [11]. In October 2017, the World Health Organization (WHO) launched a global strategy to eliminate cholera by 2030 [9]. However, achieving this goal has been hindered by a limited global supply of OCVs, a challenge exacerbated by an increase in cholera outbreaks since 2021. To address this, a WHO-prequalified OCV was introduced to expand vaccine availability [12,13]. Post-marketing studies are essential in assessing the real-world impact of OCVs at both individual and population levels. Since the 1980s, a range of killed and live oral cholera vaccines have undergone evaluation. Although study outcomes have varied, OCVs have generally shown greater effectiveness in public health settings than in clinical trials, primarily due to herd immunity. This paper focuses on reviewing the safety and efficacy of killed oral cholera vaccines, with an emphasis on their role in reducing cholera burden in vulnerable populations [14].

2. Methodology

2.1. Study setting and designs

The study was accrued out in Hodeidah ,Yemen and designed in a two phases, the phase I , a cross sectional survey was designed to monitor the safety / Adverse Events Following Immunization (AEFI) of OCV where the vaccination campaign was

carried out between 6th May 2018 and 15th May 2018. While the study was carried out between 6th May to 30th August 2018. The study included 210 participants that were administrated the vaccine orally. The adverse events were reported after 24 – 72 hours from administration of vaccine. The phase II was designed in a cohort study after three months of OCV vaccination campaign .

2.2. Participants

The study included 361 participants aged 1– 60 years old in Al Hali district, Hodeidah, Yemen. This district was chosen as high incidence of cholera. OCV was not yet introduced into this country's routine immunization program [15,16]

- **Phase I :** 210 participants received OCV and screened after 24 – 72 hours, participants met the eligibility criteria and were enrolled. Participants met the eligibility criteria and were enrolled and aged from 1 – 60 years. A random sampling technique was used in this phase
- **Phase II :** 151 patients after 3 months were confirmed with cholera in diarrhea treatment center (DTC) in Authority of Public AL Thawara Hospital of Hodeidah, Yemen. Participants met the eligibility criteria and were enrolled and aged from 1 – 60 years .

2.3. Safety of OCV

Data collection was carried out using a structured, interviewer-administered questionnaire. The questionnaire was specifically designed to address the study's objectives, with several items adapted from the WHO Global Manual on Surveillance of Adverse Events Following Immunization. It underwent multiple revisions and expert reviews. The final draft was pretested with 105 parents (both mothers and fathers of children aged 10 to 18) in their homes, in accordance with ethical considerations. Insights from the pretest were used to refine the tool. The finalized questionnaire consisted of four sections. The first section gathered demographic information, including the participant's sex and age. The second section explored participants' perceptions of AEFI.

2.4. Vaccine Efficacy of OCV

2.4.1. Rapid estimation method

This is the simplest initial method for identifying potential issues with vaccine effectiveness and determining the need for further evaluation. Whenever possible, use vaccination coverage data from surveys for calculations. If survey data is unavailable, rely on estimated administrative vaccination coverage. The effectiveness is assessed based on the proportion of the population vaccinated (cholera vaccination coverage) and the percentage of vaccinated individuals among cholera cases.

$$VE (\%) = \frac{PPV - PCV}{PPV \times (1 - PCV)} \quad \text{Equation (1)}$$

VE : Vaccine efficacy ; PCV : Percentage of cases vaccinated ; PPV : Percentage of the population vaccinated [18,19]. **Note one** : an vaccination coverage survey showed that 59 % of the target population was vaccinated (PPV = 39 % , 20 % , 59%, See Table 1) . **Note 2** : two cases of them were vaccinated during the campaign (PCV = 1.32 %) [17,18] .

2.4.2. Based on cohort study

This method enables a comparison of attack rates between vaccinated (VAR) and unvaccinated (NVAR) individuals, allowing for the calculation of relative risk—indicating the change in disease risk associated with vaccination. The formula is as follows:[17,18]:

$$RR = \frac{VAR}{NVAR}$$

$$VE (\%) = 1 - RR \quad \text{Equation (2)}$$

Table 1. OCV 1st and 2nd dose round in AL Hali district , Hodeiadh ,Yemen , 2018

Target people reached	(n , %)
Target population	247,812
Doses distribution	194,401
1 dose received only	95,581
2 doses received	49,410
OCV 1 dose	39 %
OCV 2 dose	20 %
OCV with at least one dose	59 %
OCV : Oral Cholera Vaccine [18]	

3. Results

3.1. Safety of OCV " Phase I"

3.1.1. Sex and age

A total of 210 AEFIs were reported, which corresponded to 20 cases reports. 40 % of males and 60 % of females, 105 participants (50%), aged from 10 to 18 years , 70 participants (30%) , aged from 19 to 50 and 35 participants (20%) that were more than 50 years old (Table 2) .

3.1.2. AEFI of OCV

The incidence of AEFI of OCV among participants was very low during the first 24 hours 20 cases (9.52 %). While, non-serious (AEFI) for 190 participants (90.48 %) were reported (Figure 1). On the other hand, the major adverse events were reported the AEFIs as the following: loss appetite (9.52%), vomiting (7.14%), diarrhea (4.29%), abdominal pain (1.92%), and fever (0%) (Figure 2).

Table 2. Demographic data and common AEFI of OCV (n:210)

Variables	n	%
Sex		
- Males		60
- Females		40
Age		
- 10 – 18 years		50
- 19 – 50 years		30
- More than 50 years		20
Adverse events		
- Loss appetite	20	9.52
- Abdominal pain	15	7.14
- Vomiting	09	4.29
- Diarrhea	04	1.90
- Fever	0.0	0.00

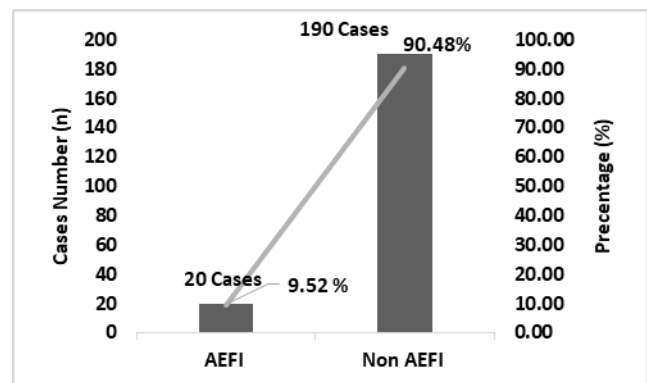


Figure 1. AEFI of OCV (N: 2010)

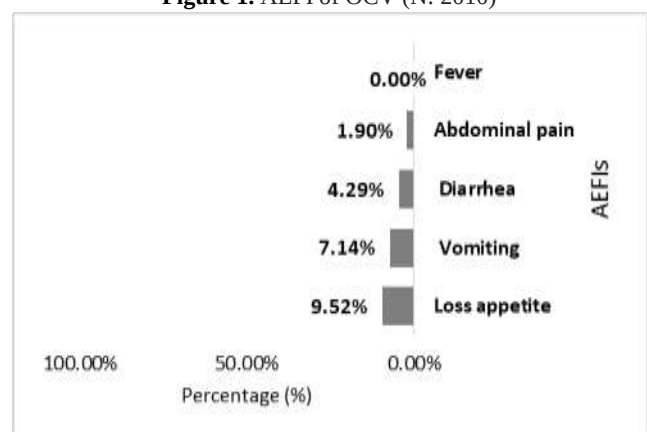


Figure 2. Major AEFI of OCV (n: 10)

3.2. Vaccine Efficacy (VE) " Phase II"

3.2.1. Sex and age

Table 3 presents the distribution of participants (total = 151) by sex and age group in a study assessing the VE of OCV. The males were 44% of the participants (66 cases). While the females were 56% of the participants (85 cases). The age groups were distributed , 16.50% (25 participants) were from 1–5 years. 28.50% (43 cases). Were from 6–18 years , 36.00% (54 cases) were from 18–50 years. The age of 19.00 % (29 cases) were more than 50 years .

3.2.2. Vaccination status

Among the 151 patients infected with cholera, 149 patients (98.68%) were unvaccinated, while only 2 patients (1.32%) had received the vaccine (Table 3) .

3.2.3. VE of OCV

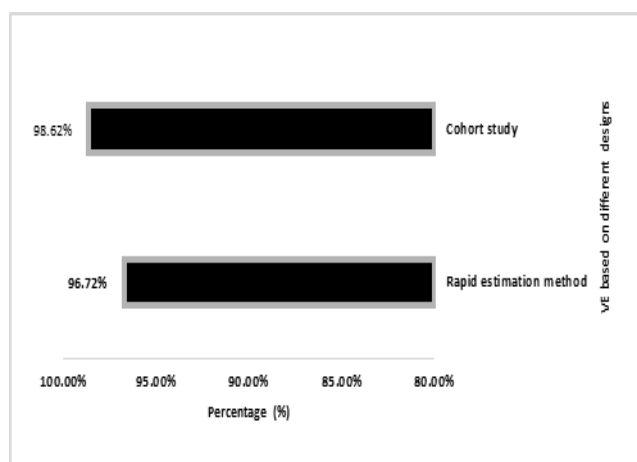
Table 4 presents the VE estimation derived from two different methodological approaches using data from 151 cases. The rapid estimation method reported a VE of 96.72%, while the cohort study approach showed a VE of 98.65% .

Table 3. Sex and age of participants in of VE of OCV (n:151)

Variables	n	%
Sex		
- Males	66	44
- Females	85	56
Age		
- 1 – 5 years	25	16.50
- 6 – 18 years	43	28.50
- 18 – 50 years	54	36.00
- More than 50 years	29	19.00
Vaccination status		
- Vaccinated	149	98.67
- Unvaccinated	2	1.32

Table 4. VE based on different designs (n:151)

Method	VE (%)
- Based on rapid estimation method	96.72
- Based on cohort study	98.65

**Figure 3.** VE based on different designs

4. Discussion

A total of 210 individuals, comprising 40% males and 60% females, aged between 10 and 60 years, participated in the study. Among them, 50% were children, 30% were young adults, and 20% were elderly. AEFIs were reported in 9.52 % of the participants. The main reported AEFIs included loss appetite (9.52%), vomiting (7.14%), diarrhea (4.29%), abdominal pain (1.92%), and fever (0%). Most of these cases (90.48%) were classified as non-serious. Our study agreed with previous study . In Lebanon, 46 case reports of AEFIs were recorded. The three most frequently reported AEFIs were fever (39.13%), diarrhea (30.43%), and vomiting (30.43%). The majority of reported cases (82.6%) were classified as non-serious [19]. In Iraq, 21% of respondents reported experiencing adverse events within 14 days of receiving either the first or second dose of the oral cholera vaccine (OCV). The majority of these events were mild, with abdominal pain (9%), fever (5%), vomiting (3%), and diarrhea (2%) being the most frequently reported. Only one case of rash was documented, and no serious adverse events were observed [20].

In Nebal, pyrexia was the most common adverse event, occurring in 3.5% of Euvichol-S recipients and 3.7% of Shanchol recipients. No serious adverse events were considered vaccine-related [21]. A total of 777 adults and 486 children participated in the study, all of whom were healthy. No serious adverse reactions were reported in either vaccine group. Following the administration of two doses of Euvichol, vibriocidal antibody responses to *V. cholerae* O1 Inaba were non-inferior to those induced by Shanchol in both adults (82% vs. 76%) and children (87% vs. 89%). Similar results were observed for O1 Ogawa, with response rates of 80% vs. 74% in adults and 91% vs. 88% in children [22]. On the other hand, the VE of OCV was high, estimated at 96.72 %

using a rapid estimation method and 98.65 % based on a cohort study which aligns with confidence interval of several previous studies conducted worldwide such as Guinea (87%; 95% CI: 57–96%), Also differs with other observational studies conducted in Mozambique (78%; 95% CI: 39–92%), Zanzibar (79%; 95% CI: 47–92%). And differs with other studies such as Haiti (63%; 95% CI: 8–85%), and India (69%; 95% CI: 15–89%). The mean effectiveness across these studies was 76% (95% CI: 62–85%) [23]. OCV is now recommended as a supplementary public health measure alongside water, WASH interventions in cholera-endemic regions and areas at risk of outbreaks. The newer generation of OCV has demonstrated strong safety and effectiveness in older children and adults, though its protective efficacy appears to be limited in children under five years of age [24].

According to the U.S. Centers for Disease Control and Prevention (CDC), the manufacturer of Vaxchora reported that the vaccine reduces the risk of moderate to severe diarrhea by 90% within 10 days of vaccination and by 80% at three months in individuals aged 18 to 45 years. However, the duration of protection beyond three months remains unknown [25].

Finally , according to Médecins Sans Frontières (MSF) , if the estimated vaccine VE is $\geq 80\%$, it can generally be concluded that there is no significant issue with the vaccine's performance. This threshold is considered acceptable for operational decision-making in the field. However, if the VE is found to be $< 80\%$, this raises concerns about potential problems with the vaccine's effectiveness. In such cases, a more precise evaluation method, such as rapid measurement , a cohort study or a case-control study, is recommended to obtain a more reliable estimate and identify any underlying issues affecting vaccine performance. This approach ensures that decisions are based on robust epidemiological evidence [17].

The limitation study : Our study in phase II included 151 patients infected with cholera, 149 cases (98.68%) were unvaccinated, while only 2 patients (1.32%) were vaccinated. This stark disparity underscores the potential protective effect of vaccination against cholera. Although the number of vaccinated individuals in this cohort is small, the markedly lower infection rate among them suggests that vaccination may substantially reduce the risk of cholera infection. Further analysis, ideally with a larger vaccinated population, would help to more accurately estimate vaccine effectiveness and support broader immunization efforts in cholera-prone areas.

5. Conclusion

The study concluded high safety and efficacy of OCV. The study reported minor adverse events such as loss of appetite, vomiting, diarrhea, and abdominal pain, occurred in a few individuals less than 10 %. In addition , the VE was reported more than 90 %. Ultimately, vaccination remains a vital component of public health policies aimed at controlling infectious diseases. Vaccination programs have successfully contributed to the regional controlling and eradication of certain infectious diseases and have played a significant role in reducing both the incidence and mortality associated with numerous infections.

Data Availability

No data were used to support this study.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Acknowledgments

This work was conducted during our work at CTMID – Al Thawara Public Hospital Authority , Hodeidah ,Yemen .

Ethical Approval

The studies involving human participants were reviewed and approved by Ethics Committee of Tropical Medicine and Epidemiology Studies of Hodeidah University (CTMES-HU) Hodeidah, Yemen .

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