GLOBAL TASK FORCE ON
CHOLERA CONTROL

CHOLERA VACCINE RESEARCH PRIORITIES

OCV Working Group
2019

A REVIEW OF CURRENT EVIDENCE AND KNOWLEDGE GAPS

Oral Cholera Vaccine (OCV) SAGE Recommendations and WHO Position Paper, 2017

GTFCC OCV Working Group Meeting, 2017

Stakeholder Consultation on Preferred Product Characteristics for Cholera Vaccines, 2017

Ongoing consultations with countries and partners

Wellcome Trust/ DFID GTFCC Research Agenda Scoping meeting, 2018

2017, 92, 477–500 No 34

World Health Organization
Organisation mondiale de la Santé

Weekly epidemiological record
Relevé épidémiologique hebdomadaire

25 AUGUST 2017, 92th YEAR / 25 AOÛT 2017, 92e ANNÉE
No 34, 2017, 92, 477–500
http://www.who.int/wer

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Cholera vaccines: WHO position paper – August 2017

Introduction

In accordance with its mandate to provide guidance to Member States on health policy matters, WHO issues a series of regularly updated position papers on vaccines and combinations of vaccines against diseases that have an international public health impact. These papers are concerned primarily with the use of vaccines in large-scale immunization programmes. They summarize essential background information on diseases and vaccines and conclude with the current WHO position on the use of vaccines worldwide.

The papers are reviewed by external experts and WHO staff, and reviewed and endorsed by the WHO Strategic Advisory Group of Experts (SAGE) on immunization (http://www.who.int/immunization/sage/en). The GRADE methodology is used to systematically assess the quality of the available evidence. The SAGE decision-making process is reflected in the evidence-to-recommendation tables. A description of the processes followed for the development of vaccine position papers is available at: http://www.who.int/immunization/position_papers/position_paper_process.pdf

The position papers are intended for use mainly by national public health officials and managers of immunization programmes. They may also be of interest to international funding agencies, vaccine advisory groups, vaccine manufacturers, the medical community, the scientific media, and the general public.

This position paper replaces the 2010 WHO position paper on cholera vaccines.[1] It incorporates recent developments in the field of cholera and provides revised guid-

[1] See No. 13, 2010, pp.117–128.

Vaccins anticholériques: Note de synthèse de l'OMS – août 2017

Introduction

Conformément à son mandat qui est de donner aux États Membres des conseils sur les questions de politique sanitaire, l'OMS publie une série de notes de synthèse régulièrement actualisées sur les vaccins et les associations vaccinales contre les maladies ayant un impact sur la santé publique au niveau international. Ces notes portent essentiellement sur l'utilisation des vaccins dans le cadre de programmes de vaccination à grande échelle. Elles résument les informations essentielles sur les maladies et les vaccins et présentent en conclusion la position actuelle de l'OMS concernant l'utilisation des vaccins dans le contexte mondial.

Ces notes sont examinées par des experts externes et des membres du personnel de l'OMS, puis évaluées et approuvées par le Groupe stratégique consultatif d'experts sur la vaccination (SAGE) de l'OMS (http://www.who.int/immunization/sage/fr). La méthodologie GRADE est utilisée pour évaluer de manière systématique la qualité des données disponibles. Le processus de décision du SAGE est reflété dans les tableaux des données à l'appui des recommandations. Une description des processus suivis pour l'élaboration des notes de synthèse sur les vaccins est consultable à l'adresse: http://www.who.int/immunization/position_papers/position_paper_process.pdf

Les notes de synthèse de l'OMS s'adressent avant tout aux responsables nationaux de la santé publique et aux administrateurs des programmes de vaccination. Toutefois, elles peuvent également présenter un intérêt pour les organismes internationaux de financement, les groupes consultatifs sur les vaccins, les fabricants de vaccins, le corps médical, les médias scientifiques et le grand public.

Le présent document remplace la note de synthèse de l'OMS sur les vaccins anticholériques publiée en 2010.[1] Il intègre les faits récents dans le domaine du choléra et fournit

[1] Voir No. 13, 2010, pp.117–128.

WORLD HEALTH ORGANIZATION Geneva
ORGANISATION MONDIALE DE LA SANTÉ Genève

Annual subscription / Abonnement annuel Sw. fr. / Fr. s. 346.–
08.2017
ISSN 0049-8114
Printed in Switzerland

CURRENT KNOWLEDGE GAPS

Impact of vaccination on disease transmission and trends (outbreak, endemic, humanitarian settings)

- Standard methodologies and indicators
- Optimal timing for prevention and control
- Newer delivery strategies

Vaccine characteristics – including among children 1 – 5 years old

- Overall: longer term duration of protection (>3 years), herd effects, booster dosing, dosing duration
- Children 1 – 5 years: immunogenicity and effectiveness, primary dosing

Integration

- WaSH + OCV: design and evaluation of WaSH + OCV interventions
- Design and evaluation of synergies with immunization programs: coadministration with other vaccines during campaigns or routine immunization (polio, measles & measles-rubella, typhoid, others)

Economics

- Costing and cost-effectiveness in different settings, including delivery strategies

RESEARCH PRIORITIES (SHORT- TO MEDIUM-TERM, 1 – 5 YEARS)

RESEARCH TOPICS	SETTING	COLLABORATIONS
Appropriate targeting of OCV use for maximum impact on disease transmission, trends, morbidity and mortality • Selection of the target populations • Selection of delivery strategy(ies) • Optimal timing for vaccination in outbreak settings	Outbreak Endemic	Surveillance (Epi & Lab) WG
Vaccine impact measurement • Development of standardized indicators and appropriate methodologies (selection of comparison groups, laboratory surveillance methods, others)	Outbreak Endemic	Surveillance (Epi & Lab) WG
Vaccine effectiveness and duration of protection • Understanding the immune response kinetics and effectiveness of dosing schedules and intervals, including booster dosing especially among young children (1 – 5 years)	Outbreak Endemic	Lab WG Cholera research collaborators

RESEARCH PRIORITIES (SHORT- TO MEDIUM-TERM, 1 – 5 YEARS)… CONTINUED

RESEARCH TOPICS	SETTING	COLLABORATIONS
OCV and WaSH • Design effectively timed and targeted WaSH + OCV intervention package(s) to ensure maximum synergy • Evaluate cost, operational feasibility, cost-effectiveness and impact	Outbreak Endemic	WaSH WG Surveillance (Epi & Lab) WG
Integration with other immunization programs (polio, MCV, MR, typhoid, others) • Evaluate immune interference • Understand costs and operational feasibility	Outbreak Endemic	Lab WG Other stakeholders (EPI programs, SAGE, RITAGs, NITAGs)
Understanding newer delivery strategies • Design newer delivery strategies to improve coverage, especially among hard-to-reach populations • Evaluate cost, operational feasibility, cost-effectiveness and impact	Endemic Outbreak	Surveillance (Epi & Lab) WG

RESEARCH PRIORITIES (MEDIUM- TO LONGER-TERM, 3 YEARS AND BEYOND)

RESEARCH TOPICS	COLLABORATIONS
Newer vaccine development and research Development of newer vaccines with simplified product characteristics such as, • Are simpler and cheaper to manufacture (to facilitate technology transfer to developing country manufacturers) • Have schedules (single dose) and presentations (thermostable, tablets etc.) • Have a longer duration of protection • Have better immunogenicity and protection, including among younger children	Manufacturers Donors Other stakeholders

GTFCC RESEARCH AGENDA MEETING (WELLCOME/DFID), JULY 2018

PRE-IMPLEMENTATION	IMPLEMENTATION	POST IMPLEMENTATION / M&E

Burden of disease and identification of hotspots:
• Description of existing hotspots to inform the definition of hotspots:
  • Quantification: laboratory confirmation, sero-surveys
  • Characterization: changing incidence and timing, WASH conditions, transmission (in and out)
• Accessible laboratory confirmation methods in hotspots
• Develop and pilot an assessment tool – hotspot vs at risk (using a tier approach), including lab capacity
• Improve estimates of mortality and where it occurs
 	
Transmission dynamics:
• Macro level analysis: laboratory data, Whole Genome Sequencing, epidemiological data
• Community/household level: environmental reservoir vs human to human transmission, Social science
• Disease modelling for outbreak short term prediction
	Optimization of interventions at the community level:
	• Rapid Diagnostic Tests
	• Use of antibiotic (targeted prophylaxis)
	• WASH package (short medium and long term)
	• Delivery strategies for OCV including new cholera vaccines, use in "controlled temperature chain" (CTC)
	• Behavior change
	
	Operational research on cholera vaccine:
	• co-administration with other vaccines, vaccine duration of protection, simplification of delivery
	
	Synergies of interventions: OCV and WASH
	
	Cholera And Severe Acute Malnutrition (SAM)
		Effectiveness:
		• Outcomes and process for continuous improvement
		• Improve targeting and use of interventions in country
		
		Change in attitude:
		• Political will
		• Lessons learnt to be documented

CROSS-CUTTING
Social sciences • Country engagement: policy drivers, determinants and barriers • Documenting success stories through case studies – to be linked to advocacy efforts **Impact**: • Level of WASH coverage needed to stop transmission, • Role of disease estimate modelling to support countries in defining control plans • Impact of outbreak response (including OCV reactive campaigns) and endemic cholera control activities **Cost effectiveness/value for money**

Survey:Question

- Please list the top three short term research questions (in the next 1-3 years)

- Please list the top three medium term research questions (in the next 3-5 years)

Vaccine effectiveness and duration of protection

- Improving understanding of dose interval strategies 2 weeks interval or longer.
- Level of protection of breastfeeding infants in mothers who have received OCVs
- Duration of protection at the community level following mass vaccination campaign in different settings (high endemicity, outbreak prone hotspot...)
- Understanding when to use a single dose rather than two doses
- Opportunities for 1-dose schedule of vaccination instead of 2-dose

OCV and WASH integration

- Vaccine demand estimation for next 10 years aligned with WASH activities
- Barriers to WASH investment at scale to compliment OCV use.
- Value added of wash interventions at time of OCV administration

Other topics

- Comparative effectiveness of CATI (case-area targeted intervention) vs. OCV
- OCV in emergency and insecurity zones: What strategies are effective?
- can seroepidemiology be used to define hotspots in countries with poor microbiological surveillance capacity
- Maximizing the efficiency and benefits using CTC with OCV out of the cold chain.
- Vaccine market research and price-determining factors
- What OCV Fails to deliver in long-term cholera elimination
- Barriers to OCV acceptance in some cultures/contexts
- Delivery approaches for routine OCV - eg self-administration, epi
- can seroepidemiology be used to define hotspots in countries with poor microbiological surveillance capacity

Medium term

- Development and testing of a long term protection and heat resistant OCV
- Evaluation of the local OCV production capacity
- level of protection against cholera in low and high risks areas of cholera
- alternative delivery strategies that will maintain population immunity without repetitive mass vaccination campaigns
- Optimal ways to synergize vaccine and wash interventions
- vaccines with higher efficacy in children under 5 and longer duration of protection
- Making a cheaper heat stable vaccine with increased manufacturing potential
- How to develop "national stockpiles" that can be used quickly during outbreaks? (Global stockpiles generally are not available sufficiently quickly).
- Maximizing the benefits of case based interventions - vaccinations around the case integrated with WASH around the case.
- Vaccine delivery strategies, especially among children