Protection against cholera from killed whole-cell oral cholera vaccines: a systematic review and meta-analysis

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Background

• Killed whole-cell oral cholera vaccines (kOCVs) are becoming a standard cholera control and prevention tool.

• However, vaccine efficacy and direct effectiveness estimates have varied, with differences in study design, location, follow-up duration, and vaccine composition posing challenges for public health decision making.

• We did a systematic review and meta-analysis to generate average estimates of kOCV efficacy and direct effectiveness from the available literature.

Methods

• Design
  – For this systematic review and meta-analysis, we searched PubMed, Embase, Scopus, and the Cochrane Review Library on July 9, 2016, and ISI Web of Science on July 11, 2016.
  – We included randomized controlled trials and observational studies that reported estimates of direct protection against medically attended confirmed cholera conferred by kOCVs.
  – We included studies published on any date in English, Spanish, French, or Chinese.
  – This study is registered with PROSPERO, number CRD42016048232.

• Data extraction
  – We extracted from the published reports the primary efficacy and effectiveness estimates from each study and also estimates according to number of vaccine doses, duration, and age group.

• Study outcomes
  – The main study outcome was average efficacy and direct effectiveness of two kOCV doses.

• Data analysis
  – We conduct the meta-analysis using a random-effect models.

Results

– Seven trials (with 695 patients with cholera) and six observational studies (217 patients with cholera) met the inclusion criteria.

– The average two-dose efficacy of 58% (95% CI 42-69, I2=58%) and effectiveness of 76% (62-85, I2=0) (Figure 2).

– Two-dose efficacy estimates of kOCV were similar during the first 2 years after vaccination, with estimates of 56% (95% CI 42-66, I2=45%) in the first year and 59% (49-67, I2=0) in the second year (Figure 3).

– The efficacy reduced to 39% (13 to 57, I2=48%) in the third year, and 26% (46 to 63, I2=74%) in the fourth year.

– Average two-dose efficacy in children younger than 5 years (30% [95% CI 15-42], I2=0%) was lower than in those 5 years or older (64% [58-70], I2=0%; p=0.0001) (Figure 5).

Conclusions

• Two kOCV doses provide protection against cholera for at least 3 years. One kOCV dose provides at least short-term protection, which has important implications for outbreak management. kOCVs are effective tools for cholera control.

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