Vaccines for preventing rotavirus diarrhoea: vaccines in use (Review)

Soares-Weiser K, MacLehose H, Bergman H, Ben-Aharon I, Nagpal S, Goldberg E, Pitan F, Cunliffe N

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2012, Issue 11

http://www.thecochranelibrary.com

WILEY

[Intervention Review]

Vaccines for preventing rotavirus diarrhoea: vaccines in use

Karla Soares-Weiser[1], Harriet MacLehose[2], Hanna Bergman[1], Irit Ben-Aharon[3], Sukrti Nagpal[4], Elad Goldberg[5], Femi Pitan[6], Nigel Cunliffe[7]

[1]Enhance Reviews Ltd, Wantage, UK. [2]Cochrane Editorial Unit, The Cochrane Collaboration, London, UK. [3]Enhance Reviews, Kfar-Saba, Israel. [4]Liverpool School of Tropical Medicine, Liverpool, UK. [5]Department of Medicine E, Beilinson Hospital, Rabin Medical Center, Petah Tikva, Israel. [6]Chevron Corporation, Lagos, Nigeria. [7]Institute of Infection and Global Health, Faculty of Health and Life Sciences, University of Liverpool, Liverpool, UK

Contact address: Karla Soares-Weiser, Enhance Reviews Ltd, Central Office, Cobweb Buildings, The Lane, Lyford, Wantage, OX12 0EE, UK. karla@enhance-reviews.com. ksoaresweiser@gmail.com.

Editorial group: Cochrane Infectious Diseases Group.
Publication status and date: New search for studies and content updated (no change to conclusions), published in Issue 11, 2012.
Review content assessed as up-to-date: 10 May 2012.

Citation: Soares-Weiser K, MacLehose H, Bergman H, Ben-Aharon I, Nagpal S, Goldberg E, Pitan F, Cunliffe N. Vaccines for preventing rotavirus diarrhoea: vaccines in use. *Cochrane Database of Systematic Reviews* 2012, Issue 11. Art. No.: CD008521. DOI: 10.1002/14651858.CD008521.pub3.

ABSTRACT

Background

Rotavirus results in more diarrhoea-related deaths in children less than five years of age than any other single agent in countries with high childhood mortality. It is also a common cause of diarrhoea-related hospital admissions in countries with low childhood mortality. Currently licensed rotavirus vaccines include a monovalent rotavirus vaccine (RV1; Rotarix, GlaxoSmithKline Biologicals) and a pentavalent rotavirus vaccine (RV5; RotaTeq, Merck & Co., Inc.). Lanzhou lamb rotavirus vaccine (LLR; Lanzhou Institute of Biomedical Products) is used in China only.

Objectives

To evaluate rotavirus vaccines approved for use (RV1, RV5, and LLR) for preventing rotavirus diarrhoea.

Search methods

We searched MEDLINE (via PubMed) (1966 to May 2012), the Cochrane Infectious Diseases Group Specialized Register (10 May 2012), CENTRAL (published in *The Cochrane Library* 2012, Issue 5), EMBASE (1974 to 10 May 2012), LILACS (1982 to 10 May 2012), and BIOSIS (1926 to 10 May 2012). We also searched the ICTRP (10 May 2012), www.ClinicalTrials.gov (28 May 2012) and checked reference lists of identified studies.

Selection criteria

We selected randomized controlled trials (RCTs) in children comparing rotavirus vaccines approved for use with placebo, no intervention, or another vaccine.

Data collection and analysis

Two authors independently assessed trial eligibility, extracted data, and assessed risk of bias. We combined dichotomous data using the risk ratio (RR) and 95% confidence intervals (CI). We stratified the analysis by child mortality, and used GRADE to evaluate evidence quality.

Main results

Forty-one trials met the inclusion criteria and enrolled a total of 186,263 participants. Twenty-nine trials (101,671 participants) assessed RV1, and 12 trials (84,592 participants) evaluated RV5. We did not find any trials assessing LLR.

RV1

Children aged less than one year: In countries with low-mortality rates, RV1 prevents 86% of severe rotavirus diarrhoea cases (RR 0.14, 95% CI 0.07 to 0.26; 40,631 participants, six trials; high-quality evidence), and, based on one large multicentre trial in Latin America and Finland, probably prevents 40% of severe all-cause diarrhoea episodes (rate ratio 0.60, 95% CI 0.50 to 0.72; 17,867 participants, one trial; moderate-quality evidence). In countries with high-mortality rates, RV1 probably prevents 63% of severe rotavirus diarrhoea cases (RR 0.37, 95% CI 0.18 to 0.75; 5414 participants, two trials; moderate-quality evidence), and, based on one trial in Malawi and South Africa, 34% of severe all-cause diarrhoea cases (RR 0.66, 95% CI 0.44 to 0.98; 4939 participants, one trial; moderate-quality evidence).

Children aged up to two years: In countries with low-mortality rates, RV1 prevents 85% of severe rotavirus diarrhoea cases (RR 0.15, 95% CI 0.12 to 0.20; 32,854 participants, eight trials; high-quality evidence), and probably 37% of severe all-cause diarrhoea episodes (rate ratio 0.63, 95% CI 0.56 to 0.71; 39,091 participants, two trials; moderate-quality evidence). In countries with high-mortality rates, based on one trial in Malawi and South Africa, RV1 probably prevents 42% of severe rotavirus diarrhoea cases (RR 0.58, 95% CI 0.42 to 0.79; 2764 participants, one trial; moderate-quality evidence), and 18% of severe all-cause diarrhoea cases (RR 0.82, 95% CI 0.71 to 0.95; 2764 participants, one trial; moderate-quality evidence).

RV5

Children aged less than one year: In countries with low-mortality rates, RV5 probably prevents 87% of severe rotavirus diarrhoea cases (RR 0.13, 95% CI 0.04 to 0.45; 2344 participants, three trials; moderate-quality evidence), and, based on one trial in Finland, may prevent 72% of severe all-cause diarrhoea cases (RR 0.28, 95% CI 0.16 to 0.48; 1029 participants, one trial; low-quality evidence). In countries with high-mortality rates, RV5 prevents 57% of severe rotavirus diarrhoea (RR 0.43, 95% CI 0.29 to 0.62; 5916 participants, two trials; high-quality evidence), but there was insufficient data to assess the effect on severe all-cause diarrhoea.

Children aged up to two years: Four studies provided data for severe rotavirus and all-cause diarrhoea in countries with low-mortality rates. Three trials reported on severe rotavirus diarrhoea cases and found that RV5 probably prevents 82% (RR 0.18, 95% CI 0.07 to 0.50; 3190 participants, three trials; moderate-quality evidence), and another trial in Finland reported on severe all-cause diarrhoea cases and found that RV5 may prevent 96% (RR 0.04, 95% CI 0.00 to 0.70; 1029 participants, one trial; low-quality evidence). In high-mortality countries, RV5 prevents 41% of severe rotavirus diarrhoea cases (RR 0.59, 95% CI 0.43 to 0.82; 5885 participants, two trials; high-quality evidence), and 15% of severe all-cause diarrhoea cases (RR 0.85, 95% CI 0.75 to 0.98; 5977 participants, two trials; high-quality evidence).

There was no evidence of a vaccine effect on mortality (181,009 participants, 34 trials; low-quality evidence), although the trials were not powered to detect an effect on this end point.

Serious adverse events were reported in 4565 out of 99,438 children vaccinated with RV1 and in 1884 out of 78,226 children vaccinated with RV5. Fifty-eight cases of intussusception were reported in 97,246 children after RV1 vaccination, and 34 cases in 81,459 children after RV5 vaccination. No significant difference was found between children receiving RV1 or RV5 and placebo in the number of serious adverse events, and intussusception in particular.

Authors' conclusions

RV1 and RV5 prevent episodes of rotavirus diarrhoea. The vaccine efficacy is lower in high-mortality countries; however, due to the higher burden of disease, the absolute benefit is higher in these settings. No increased risk of serious adverse events including intussusception was detected, but post-introduction surveillance studies are required to detect rare events associated with vaccination.

PLAIN LANGUAGE SUMMARY

Vaccines for preventing rotavirus diarrhoea: vaccines in use

Rotavirus infection is a common cause of diarrhoea in infants and young children, and can cause mild illness, hospitalization, and death. Rotavirus infections results in approximately half a million deaths per year in children aged under five years, mainly in low- and

middle-income countries. Since 2009, the World Health Organization (WHO) has recommended that a rotavirus vaccine be included in all national immunization programmes.

This review evaluates a monovalent rotavirus vaccine (RV1; Rotarix, GlaxoSmithKline Biologicals) and a pentavalent rotavirus vaccine (RV5; RotaTeq, Merck & Co., Inc.). These vaccines have been evaluated in several large trials and are approved for use in many countries. No trials of the Lanzhou lamb rotavirus vaccine (LLR; Lanzhou Institute of Biomedical Products) were found; this vaccine is used in China only. The review includes 41 trials with 186,263 participants; all trials compared a rotavirus vaccine with placebo. The vaccines tested were RV1 (29 trials with 101,671 participants) and RV5 (12 trials with 84,592 participants). The trials took place in a number of worldwide locations.

In the first two years of life, RV1 prevented more than 80% of severe cases of rotavirus diarrhoea in low-mortality countries, and at least 40% of severe rotavirus diarrhoea in high-mortality countries. Severe cases of diarrhoea from all causes (such as any viral infection, bacterial infections, toxins, or allergies) were reduced after vaccination with RV1 by 35 to 40% in low-mortality countries, and 15 to 30% in high-mortality countries.

In the first two years of life, RV5 reduced severe cases of rotavirus diarrhoea by more than 80% in low-mortality countries, and by 40 to 57% in high-mortality countries. Severe cases of diarrhoea from all causes were reduced by 73% to 96% in low-mortality countries, and 15% in high-mortality countries, after vaccination with RV5. Diarrhoea is more common in high-mortality countries, so even modest relative effects prevent more episodes in this population. The vaccines when tested against placebo gave similar numbers of adverse events such as reactions to the vaccine, and other events that required discontinuation of the vaccination schedule.