Review: rotavirus vaccines moderately reduce rotavirus diarrhoea in children

Soares-Weiser K, Goldberg E, Tamimi G, *et al*. Rotavirus vaccine for preventing diarrhoea. *Cochrane Database Syst Rev* 2004;(1):CD002848.

Clinical impact ratings Paediatrics ★★★★★★☆ Tropical medicine ★★★★★☆☆ Infectious disease ★★★★☆☆☆

Q In children and adults, are rotavirus vaccines effective for preventing rotavirus diarrhoea?

METHODS

Data sources: Cochrane Infectious Diseases Group's trials register, Medline, EMBASE/Excerpta Medica, LILACS, Biological Abstracts (all up to October 2003), Cochrane Central Register of Controlled Trials (2003, Issue 3), bibliographies of relevant articles, and contact with researchers and a rotavirus manufacturer (Merck Sharp & Dohme).

Study selection and assessment: randomised controlled trials (RCTs) in any language that compared rotavirus vaccines with placebo, no vaccination, or a different rotavirus vaccine in children or adults. Study quality was assessed for method of allocation, allocation concealment, blinding, sample size, exclusions after randomisation, and follow up period.

Outcomes: rotavirus diarrhoea, all cause diarrhoea, all cause mortality, and adverse events.

MAIN RESULTS

63 RCTs of children (age range newborns to 12 years) and 1 small safety study of 10 adults (21–30 years of age) met the selection criteria. Main types of vaccines evaluated included bovine (13 RCTs), human (2 RCTs), rhesus (32 RCTs), and the combined bovine and human rotavirus vaccines (4 RCTs). All but 1 RCT were placebo controlled. Meta-analyses were done using a random effects model. Fewer children in the bovine, human, and rhesus vaccine groups than in the corresponding placebo groups had rotavirus diarrhoea (table). Furthermore, fewer children in the rhesus and bovine vaccine groups had all cause diarrhoea than in the placebo groups (table). However, the human vaccine and placebo groups did not differ for rate of all cause diarrhoea. For other outcomes where sufficient data were reported, the rhesus rotavirus vaccines group and placebo group did not differ for rate of all cause mortality (table). For adverse effects, only the rhesus rotavirus vaccines were associated with an increased incidence of fever (table).

CONCLUSION

In children, rotavirus vaccines are effective for reducing the rate of rotavirus diarrhoea.

Commentary

Rotaviruses are responsible for one third of all hospital admissions for diarrhoea worldwide and for approximately 600 000 deaths per year.[1] This rotavirus associated mortality represents approximately 25% of all diarrhoeal deaths and 6% of all deaths of children <5 years of age. In the US, UK, and Australia, it has been estimated that 1 in 57, 1 in 40, and 1 in 24 children, respectively, are admitted to hospital with rotavirus infection in the first 5 years of life. Rotavirus infection represents a health burden for children similar in magnitude to measles, pertussis, mumps, and varicella before routine vaccination.

A licensed vaccine against rotavirus became available in North America in 1998, but it was associated with a high risk of intussusception and was voluntarily withdrawn. The Centers for Disease Prevention and Control subsequently estimated this risk to be increased 20–30 fold over the expected risk in the 2 weeks following first vaccination (ie, 1 or 2 patients with intussusception among each of the 10 000 infants vaccinated).[2] The review by Soares-Weiser *et al* shows that vaccines are very effective in preventing rotavirus diarrhoea. In underdeveloped countries, mortality remains a major issue, and the potential benefits of a vaccination programme against rotavirus may far outweigh any risks. Unfortunately, in addition to unresolved safety concerns, barriers to immunisation include the high cost of the vaccine and the fact that the relatively few trials in poor countries have suggested lower efficacy than in economically advantaged societies. This review found that results for mortality and safety of rotavirus vaccines were scarce and incomplete. Trials of newer generation vaccines will be of most importance in those countries with the highest burden of diarrhoeal disease and must include comprehensive follow up data on adverse outcomes.

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1 Barnes G. Rotavirus vaccine. *J Paediatr Gastroenterol Nutr* 2000;**30**:12–7.
2 CDC National Immunization Program. http://www.cdc.gov/nip/diseases/rota/intussusception.htm

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Rhesus, bovine, and human rotavirus vaccines *v* placebo in children at ⩽4 years*

Outcomes	Number of RCTs (n)	Comparisons	Weighted event rates	RRR (95% CI)	NNT (CI)
Rotavirus diarrhoea	20 (13 305)	Rhesus v placebo	11% v 19%	41% (30 to 50)	13 (12 to 17)
	17 (5283)	Bovine v placebo	11% v 18%	41% (24 to 55)	15 (10 to 25)
	3 (2482)	Human v placebo	3% v 12%	58% (15 to 79)	12 (6 to ∞)
All cause diarrhoea	11 (7706)	Rhesus v placebo	54% v 63%	14% (8 to 20)	12 (9 to 20)
	11 (3309)	Bovine v placebo	28% v 37%	27% (11 to 40)	10 (6 to 25)
	1 (281)	Human v placebo	19% v 21%	9% (−44 to 43)	Not significant
All cause mortality	4 (6029)	Rhesus v placebo	0.16% v 0.18%	28% (−212 to 84)	Not significant
				RRI (CI)	**NNH (CI)**
Fever	32 (13 718)	Rhesus v placebo	35% v 23%	100% (51 to 164)	9 (7 to 15)

*RCTs = randomised controlled trials. Abbreviations defined in glossary; RRR, RRI, NNT, NNH, CI, and weighted event rates calculated from data in article using a random effects model.