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HEAD TO HEAD

Should India launch a national immunisation programme against rotavirus? No

India is considering including rotavirus vaccine in its national childhood immunisation programme. **Johnie Rose** and **Umesh Parashar** (doi:10.1136/bmj.e7818) support the move, but **Jacob Puliyel** and **Joseph Mathew** question the evidence used to support vaccination

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The programme to immunise all the world's children with the rotavirus vaccine is based on mistaken assumptions. Careful evaluation of available evidence does not support the launch of the programme in India. It will divert funds from more life saving interventions and could cause harm.

Inappropriate extrapolations

The World Health Organization recommended universal rotavirus vaccination well before regional evidence of its effectiveness was collected. This is a distortion of the standard procedure whereby recommendations are made based on local evidence. The distortion came about in two stages. In 2007, the WHO committee looking at rotavirus vaccination for developing countries decided that efficacy data from one population can be extrapolated to other populations that are in an "equivalent child mortality strata."[1] This presumes that the prevalent virus strains are the same in different regions with similar socioeconomic status and mortality rates. There is no scientific evidence to support this assumption. Following this in 2009, using data from Malawi (one of the poorest regions in the world),[2] Nicaragua, and a handful of developed countries, WHO recommended rotavirus vaccine for all regions of the world.[3]

Rationale

According to the GAVI Alliance, which funds vaccination for children in poor countries, rotavirus vaccination is a key step towards lowering child mortality and achieving the millennium development goal for reduction of deaths among children under 5 years of age.[4] Worldwide, rotavirus is said to cause 527 000 deaths. [5] In India it is estimated to cause 122 000 to 153 000 deaths annually.[5] It is hoped that the vaccine will reduce diarrhoeal deaths by 40% and the overall mortality rate of children under 5 by 5%.[6]

The estimate of deaths from rotavirus was arrived at by multiplying the mean rotavirus detection rate in a country by the diarrhoea case fatality rate, assuming a uniform mortality rate for all causes of diarrhoea.[7] This is inappropriate for two reasons. Firstly, deaths from rotavirus infection can be prevented by simple measures to correct dehydration.[8] Bacterial diarrhoea, on the other hand, is more often associated with sepsis and systemic complications and is likely to have a higher mortality. Secondly, in up to 58% of cases positive for rotavirus there is coinfection with other pathogens. Attributing all deaths to rotavirus whenever the virus is isolated overestimates rotavirus mortality.[9]

Natural infections not protective in India

Data from Mexico show that two successive, naturally occurring rotavirus infections protect against subsequent infections.[10] Although these data pertain to protection against natural infections of rotavirus strains prevalent in the area, it was projected as evidence that any rotavirus vaccine (the monovalent RV1 or pentavalent RV5) would provide similar protection against all strains of the infection and in every part of the world.[11]

The local rotavirus strains in India are different from those in other regions.[12] Furthermore, new strains are continuously emerging through reassortment between animal and human strains.[12] Studies have shown that two episodes of natural infection in India, unlike in Mexico, afford little protection against subsequent infections,[13] perhaps because of the rapidly evolving strains. Given that these data contradict the Mexico data that was used as evidence for launching universal vaccination, urgent reappraisal of the recommendation is warranted.

No reduction in mortality

No studies have looked at the efficacy of the vaccine in India, but studies from Bangladesh and Vietnam show vaccine efficacy

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against rotavirus diarrhoea is 48%.[14] This is much lower than in the West, where efficacy is around 90%.[15 16] The main reason given for advocating immunisation is that it would reduce childhood mortality. However there was no significant reduction in deaths among the 1009 receiving the vaccine (four deaths) compared with the 1007 placebo recipients (three deaths).[14] A Cochrane meta-analysis (55 704 vaccine recipients and 44 813 placebo recipients) found mortality was marginally higher in the vaccinated group than the placebo group (174 *v* 106 deaths; absolute risk increase=0.00312, number needed to harm=1333).[17] These analyses show that the vaccine is unlikely to become a major lifesaving intervention or help in achieving the millennium development goal.

Faulty cost-benefit projection for India

Two analyses specifically evaluating the Indian context have concluded that the vaccine is cost effective. One study suggests that at a price of $0.15/dose (8 rupees; £0.09; €0.12) the vaccine would save 44 000 lives and be cost saving.[18] The market price is $50/dose in middle income countries.[19]

Rose and colleagues used more sophisticated Markov modelling techniques,[20] pegging the cost of vaccine at $7/dose. Incidentally, this is the price negotiated by Brazil.[21] Using efficacy data from the West they suggested that the vaccine would prevent 41 000 deaths (avoiding one death for every 470 children immunised) and would cost $164 per disability adjusted life year saved.

Both studies extrapolated data acquired elsewhere. If the findings of the Cochrane meta-analysis showing absence of reduction in mortality were incorporated into the calculations, the projected cost per life saved and cost per life year gained would have been substantially higher.

To promote the uptake of expensive vaccine, GAVI often supplies vaccines to developing countries at highly subsidised rates for a limited period. Later, the subsidy is withdrawn and poor countries have to pay the full market price. In this manner they are often unfairly lured into a debt trap.[22] Developing countries must estimate affordability and cost-benefits of vaccines against the market price at which it will be available to them in the long term.

In India, vaccinating the birth cohort of 25 million with a vaccine that costs $14/child (two doses) would cost $350m. The entire immunisation budget for 2011-12 was $240m.[23] Only 52% of the population receives three doses of the diphtheria-tetanus-pertussis (DPT) vaccine.[24] The cost for all three doses of DPT is $0.30/child. Logically, the country's first priority must be to reach inexpensive established vaccines to its rural poor who are unvaccinated at present.

Inclusion of rotavirus vaccine in the national immunisation programme is a long term and binding commitment. It must be based on hard nosed, pragmatic evaluation of the evidence. The commercial interests of the manufacturers must not be allowed to influence decision making. Unfortunately the existing evidence does not support the inclusion of current rotavirus vaccines into the immunisation programme in India.

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