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## News

# Indian rotavirus vaccine concern over intussusception is unfounded, say researchers

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## 116 E Rotavirus Vellore Study: Request for Vaccine Safety Data

The report contains a number of misleading assertions and a fundamental misunderstanding of statistics. These need to be corrected.

The Rotavirus 116E trial was registered with the Clinical Trials Registry ClinicalTrials.gov (NCT01305109) and was done at 3 centers. One of the outcomes measured was 'safety of ORV 116E for intussusception events in comparison to a placebo from day of 1st dose till the age of 2 years'. According to the study report (1) intussusception was 'suspected' from symptoms, if a child had three or more vomiting in an hour, or blood in stools or increase in abdominal girth by 2 cm or more in a 4 hour period or a abdominal mass palpable per abdomen. Such children were examined by a pediatrician and if they felt intussusception was 'possible', the baby had an ultrasound examination within 8 hours.

Aggregated data from the three centers has been published (1,2). This shows that the incidence rate of ultrasound-diagnosed-intussusceptions was 37.5/10,000 among the vaccinated and 26.3/10,000 among placebo recipients. There were 11/10,000 more intussusceptions among those who received the 116E vaccine. This is nearly 70 times higher than the risk of intussusceptions with the current, internationally licensed vaccine, Merck's RotaTeq.

The 116E trial also reported that was regional differences in the susceptibility to intussusceptions with the incidence in Vellore 20 times higher than in Delhi. Given this high susceptibility in Vellore, a request for disaggregated data on numbers with symptoms of intussusceptions and number of ultrasound diagnosed intussusceptions in each the three centers over the 2 year period, was made (3). It is understood that some intussusceptions are transient and may have resolve even before the ultrasound examination was performed.

Dr Kang told the BMJ that "it is misleading and statistically incorrect to use rates of intussusception from a 6800 child study to claim that the vaccine is risky" - as the study was not powered to look for rare events. This is a grave misunderstanding of the statistics involved. If statistical difference is seen in the 1000 vaccinated children in Vellore compared to 500 controls, it is evidence that the vaccine is unsafe in that population. As the incidence of intussusceptions is several folds higher with the 116E vaccine (than with RotaTeq) a smaller sample will show

statistical differences. If a statistical difference is demonstrated, it means the study was powered adequately and it is not wrong to declare that it is risky to use the vaccine in that community.

Dr Kang does not provide the data that will allow easy calculation of the risk in Vellore but she quotes the WHO reporting that “existing data on Rotavac do not point to an increased risk from intussusceptions”. The data, when provided, will speak for itself and we do not have to rely on the say-so of the WHO.

The authors have published aggregated data from the 3 centers where there was no statistically significant difference in intussusceptions in vaccine recipients and controls. Dr VijayaRaghavan of the Department of Biotechnology (DBT) under whom the multi-center trial was done, says that the disaggregated data has been provided to the National Technical Advisory Group on Immunization (NTAGI). As a member of this apex advisory body of the Government of India, I can say that I have requested this data and it has not been provided to the NTAGI as yet. Dr VijayaRaghavan goes on to say that in response to various queries that they have received he will ensure “data is available for analysis by a competent body, meeting the requirements of analytical rigor and transparency.” As the analytic skills needed here are very basic and the aggregated data is already in the public domain, it is not clear only a DBT-selected ‘competent body’ can be privy to the Vellore figures.

Dr Kang told the BMJ, “We are trying to be as responsible as possible” but she is not disclosing the data requested. The primary responsibility of the researchers is to protect children not the interest of vaccine manufacturers. Providing the data would be the responsible thing to do.

Jacob Puliyeel

[puliyeel@gmail.com](mailto:puliyeel@gmail.com)

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**Competing interests:** No competing interests

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Jacob M. Puliyeel

Pediatrician

St Stephens Hospital, Delhi, India.

St Stephens Hospital, Delhi, India.

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