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Letter to the Editor

Intussusception risk with 116E rotavirus vaccine in Vellore, South India

We congratulate John and colleagues for their surveillance of intussusception during the 116E rotavirus vaccine trial [1]. They point out that it is critical to be vigilant to the risk of intussusception "to determine if there are safety signals of a larger magnitude than currently expected that may preclude licensure".

Rotasheild was licensed after a trial involving 14,687 patients. In this trial there was an excess of 3 cases of intussusception per 10,000 children vaccinated. All the intussusceptions were among infants who received the second or third dose of the vaccine [2]. Post-licensure, after 9 cases of intussusceptions were reported, analysis revealed an excess risk of 1–2 intussusceptions per 10,000 vaccinated. Rotasheild was then withdrawn from the market [3].

After Rotasheild was withdrawn, the US FDA approved another rotavirus vaccine – RotaTeq based on results of a much larger trial among 72,324 infants. No excess in intussusception was noted in the RCT but post-marketing surveillance revealed a small increase in risk of intussusception of 0.15/10,000 [4].

In the study reported by John [1] the vaccine was tested in only 6719 infants (4532 received vaccine; 2187 were controls). Ultrasound evidence of intussusception was found in 17 who had received the 116E vaccine (3.75/1000 or 37.5/10,000) and in 6 babies receiving placebo (2.636/1000 or 26.36/10,000). There was an excess of 11 cases of intussusception per 10,000 vaccinated. This is 5–10 times higher than the risk of intussusception with Rotasheild vaccine (which was withdrawn from the market) and nearly 70 times higher than the risk of intussusception with the current, internationally licensed vaccine, RotaTeq.

Intussusception rates varied in the different regions studied by John and colleagues [1]. In Vellore it was 581/100,000 child-years and in Delhi it was much lower – 27.7/100,000 child-years. The regional differences in intussusception rates could mean that it may be more risky to use the vaccine in some areas. The authors however do not provide disaggregated data on numbers of ultrasound-diagnosed intussusception among the vaccinated and the controls in Vellore. We request they do so in response to this letter, so that the risk in this area may be calculated meaningfully.

Intussusception is difficult to diagnose and treat in rural India in the absence of qualified doctors. Where there is lack of health-care facilities, children have an increased risk of mortality. Meier reports that children with intussusception treated at a hospital in a developing country had a mortality of 18% [4]. Many in India will not even reach a surgical center before they die. This is the milieu in which the vaccine will be used. There is need to evaluate the risk of intussusception carefully before using the vaccine in rural India.

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