Inappropriately Small Sample for Studying Adverse Events Following Immunization

We refer to the study of common illnesses before and after vaccination [1]. The authors looked for symptoms like constipation, rash, wheeze, rhinitis and watering of eyes in 1602 children in the week after immunization, and found the frequency was same as in the week prior to immunization (except for fever). It was sought to imply that most adverse events following immunization (AEFI) are explained by the background rate. The study was seriously flawed as the sample size selected was inadequate. The authors noted that no child had hypotonic hyporesponsive episode (HHE), seizures, pruritus, difficulty in breathing or breath holding, either during the pre- or post- vaccination period, and these are the AEFI described by the Brighton Collaboration (with their specific case definitions) [2].

Incidence of these AEFI is rare. As per WHO surveillance data, HHE occurs less than 1/1000, seizures in less than 0.5/1000 and anaphylaxis and shock incidence in one per million doses [3]. Thus, a sample size of 1602 is woefully inadequate to detect real AEFI. The authors have selected sample size so small that vaccine-related AEFI (other than fever) was unlikely to be picked up, and all they would see are routine symptoms unrelated to vaccination. With these figures, they concluded erroneously that AEFI can be explained or background rates.

In vaccine trials, randomized controls are used to look at the background rate. If there is a statistically significant increase in any adverse effect among the vaccinated, it is likely to be AEFI caused by the vaccine.

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Author's Reply

We agree that our study [1] was not powered to detect rare adverse events following immunization. Our study was powered to detect illnesses with a 1% or higher prevalence. This was sufficient to detect the increased risk of fever after vaccination. We also extended the study to examine the common childhood illnesses before and after immunization using a risk interval approach. Given that there is no description of these conditions following immunization visits with multiple vaccines in routine clinical practice, we believe that our data is useful for the community of practicing pediatricians and those interested in immunization.

We also appreciate the editorial that accompanied our paper which highlighted that "the study could be an appropriate starting point for more research to generate comparable data from public and private sector and different geographic locations in the country" [2].

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