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Dear Editor,

We write with reference the recent article by Biggart et al[1] describing a lack of association between the use of rotavirus vaccine and seizures in the UK which contrasts with reports from the USA, Australia and Spain.[2–4] A weakness of that study was that it only examined inpatients rather than attendances to the emergency department, where convulsions are observed and most then discharged. It also proposed that the negative results could be due to the monovalent vaccine used in the UK. We now report re-application of the same method in a Portuguese paediatric emergency service population to help address these uncertainties and further explore the effectiveness of RV vaccines against childhood seizures.

METHODS

In Portugal both RV vaccines have been available since 2006 with gradual progressive uptake via the private market.[5] Coimbra Children's Hospital (Hospital Pediátrico de Coimbra) in central Portugal provides secondary and all out-of-hours pediatric primary care for the municipality with ≈28,000 emergency attendances per year for children less than 4 years old. We identified all hospital attendances between 2000 and 2014 with febrile or afebrile seizures aged 6 months to <4 years (ICD-9-CM codes: 780.3*/779.0*/333.2*/345*). Using the method described in Biggart et al[1] we performed an interrupted time series analysis of the rates of seizure attendance before and after vaccine introduction, fitting separate models for the number of febrile and afebrile seizure presentations against availability of vaccine with age and year as covariates and size of birth cohort as an offset. As this was an analysis of anonymised routine clinical data, formal ethical review was not required.

RESULTS

During the study period, rates of vaccine use rose from 16%(2006) to 44%(2014) and the birth rate in the central region of Portugal fell considerably from 23,441 to 15,556. The absolute number of presentations with convulsion was falling before vaccine introduction which continued with time although rates of convulsions remained constant. The peak age of febrile convulsion presentations was 1-2 years (370/100,000). In contrast, afebrile convulsion rates did not vary with age, with a rate of ≈80/100,000. Our model did not show evidence of a reduction in either febrile (OR 1.1 (95% CI 0.7-1.6) p=0.56) or afebrile (OR 0.8 (95% CI 0.5-1.3) p=0.37) seizures in association with vaccine introduction and use. Sub-analysis by age also failed to show any significant effect, with no apparent trends in the rates of either convulsion type. Performing a post-hoc power calculation based on our sample size, level of vaccine use and background seizure rate, we would expect to have been able to detect ($p<0.05$) a 40% change in the rate of seizures with 99% power and a 20% reduction with 75% power.

CONCLUSIONS

We analysed rates of seizure presentations to a regional paediatric Emergency Service, comparing 6 years before with 8 years following RV vaccine introduction. Seizure presentations were already falling, probably as a result of falling birth cohort sizes but no evidence of further vaccine-induced reductions were found. Although an observational study and prone to ecological bias, this report extends previous observations in inpatients to include the outpatient setting in a country where both vaccines are in use albeit at low coverage.[6] We plan to re-evaluate this association in a case-control study.

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