



Seroprevalence comparison of different varicella vaccines among Turkish children

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We read with interest the paper by Umit et al.¹ about the comparison of seroconversion rates of different varicella vaccines among Turkish children aged 12–15 months. In the study, the authors claimed a higher seroconversion rate among Turkish children by vOka varicella vaccines than MAV/06 strain vaccines (82.7% vs. 64.3%, respectively). However, in this letter, we point out that the authors made a significant interpretational error of seroprevalence results as seroconversion ones. In addition, we discuss a critical methodological weakness in assessing antibody titers against varicella zoster virus (VZV) in the authors' study, which further likely undermines their claim. Furthermore, we would like to provide correct and updated information on the effectiveness of the varicella vaccine, including vOka and MAV/06 vaccines among Korean children, which was neither introduced nor discussed appropriately in the authors' paper.

First, the authors claimed that they examined and compared seroconversion rates of different varicella vaccines in their paper: "... Seroconversion rate was significantly higher in vOka group than MAV/06 group."^{1(p4190)} However, we think that what the authors actually assessed in their study was seroprevalence, not seroconversion in that the authors measured antibody titers against VZV only once, that is, after administration of varicella vaccines. There was no pre-vaccination assessment of antibody titers against VZV in the authors' study. About 5% of the infants included in a previous Turkish study² of 9-month-old infants were already seropositive against VZV before administration of varicella vaccines, even if infants with a history of varicella had been excluded from the previous study as in the authors' paper. Thus, we think that the authors' claim of the assessment of seroconversion in their paper is simply not tenable. For the same reason, the authors' discussion of their results in comparison with the previous seroconversion study³ among Korean children in which antibody titers against VZV were assessed twice (pre-vaccination and post-vaccination), is also misleading. We would like to emphasize that in two experimental studies^{3,4} among Korean children, the seroconversion rates of vOka-strain and MAV/06-strain varicella vaccines (63–99% vs. 74–98%, respectively) were very similar to each other.

Second, in the authors' study, the seropositivity after administration of varicella vaccines was assessed with an indirect immunofluorescence test (IIFT) kit (Anti-VZT IIFT IgG, Euroimmune, Germany), not the fluorescent antibody to

membrane antigen (FAMA) assay⁵ which has been known to be the gold-standard assay for assessing biologically-relevant neutralizing antibodies against VZV. However, in their paper, the authors neither provided any information on the sensitivity and specificity of the IIFT kit against the standard FAMA assay nor discussed the impact of the use of the IIFT kit on their results. We believe that the FAMA assay with a serum dilution of 1:4 (considered a standard cutoff point for evaluating the seropositivity before or after administration of varicella vaccines) would be more sensitive and specific to lower titers of neutralizing antibodies against VZV⁵ than the IIFT kit with a serum dilution of 1:10 used in the authors' paper. Some studies^{6,7} have also reported only moderate levels of correlation (e.g., .54–.68) in relatively lower anti-VZV antibody titers between the FAMA assay and IIFT. Furthermore, the aforementioned two Korean experimental studies with the FAMA assay have supported the comparable rates of seroconversion between vOka strain and MAV/06 strain vaccines. Taken all of the above together, we think that the results in the authors' study solely based on the IIFT kit should be reexamined and confirmed in future studies of using both the FAMA assay and the IIFT kit.⁸

Third, we think that the authors' discussions on Korean studies on the effectiveness of the varicella vaccine (Oka and MAV/06 strains) were heavily and selectively based on some erroneous Korean studies.^{9,10} A small case-control study by Lee et al.⁹ raised a question about the effectiveness of the varicella vaccine in Korea where a national varicella immunization program had started in 2005: the reported vaccine effectiveness was very low (13%). However, the case-control study has been criticized due to possible selection bias.^{11–13} A recent national birth-cohort study¹⁴ among Korean children confirmed that there is at least a moderate level (49.9–86.1%) of one-dose vaccine effectiveness against VZV, although it may have been underestimated.^{11,13} On the other hand, the same research group^{9,10} of the erroneous case-control study has continued to argue that the incidence rate of varicella cases in Korea has increased even after the national varicella immunization program. However, as we said elsewhere,¹¹ their argument has been based on data from the Korea National Notifiable Disease Surveillance System in which only varicella cases notified by medical doctors and other responsible persons are included and counted. In fact, their argument has been rebuked by us and other Korean researchers^{11,12,15,16} using or

in comparison with more nationally representative data. In addition, as expected, our recent study¹⁷ supported that the incidence of varicella cases with complications substantially decreased during 2010–2020 in Korea.

We agree with the authors that, given the current short history of MAV/06 varicella vaccines in Turkey, future epidemiological studies are warranted for evaluating the effectiveness of MAV/06 varicella vaccine among Turkish children. We hope that the authors will conduct a more well-designed immunogenicity study of different varicella vaccines among Turkish children in the future, with consideration of the interpretational and methodological shortcomings that we have discussed above and better understanding on the recent Korean studies on the comparative immunogenicity and effectiveness of the varicella vaccine.

Disclosure statement

In accordance with Taylor & Francis policy and our ethical obligation as researchers, we are reporting that we are employees of GC Pharma, a pharmaceutical company in Korea. The main aim of the submitted manuscript as a correspondence is to discuss interpretational and methodological issues in a Turkish children study on the seroprevalence comparison of different varicella vaccines. No specific product of GC Pharma was discussed in the submitted manuscript.

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