Influenza is a major cause of respiratory disease leading to hospitalization in infants and young children. Since the Second World War, influenza has been prevented through annual administration of inactivated vaccines. In infants and young children, however, trivalent inactivated vaccines (TIVs) have been shown to be poorly immunogenic and less effective. Recent efforts to improve immunogenicity for these age groups include the development of live-attenuated vaccines and the modification of TIVs through addition of adjuvants and increasing amounts of antigen. Also, various routes of administration have been tested.

A single lineage of influenza B virus dominated in global circulation until the 1990s. In most recent seasons since 2001–2002, however, both lineages of the influenza B virus have co-circulated each season at varying levels. For the last 40 years, inactivated vaccines have consistently been formulated with two influenza A subtypes (A/H3N2 and A/H1N1) and one influenza B lineage, failing to take account of the two distinct genetic lineages of the influenza B virus (Victoria and Yamagata). The antigenic distinction of the lineages means vaccines containing only one would provide little protection against disease caused by the other. Lacking the ability to predict which lineage predominates in any particular influenza season, “mismatches” between vaccine and circulating B strains have occurred in 5 of 10 influenza seasons between 2001–2010 in the United States. Therefore, to prevent such “mismatches,” there has been a need to develop a quadrivalent inactivated vaccine (QIV) containing 2 A subtypes (A/H3N2 and A/H1N1) and 2 B lineages (Victoria and Yamagata).

In this issue, Lee et al.2 carried out a clinical trial on the safety and immunogenicity of a Korean egg-cultivated quadrivalent split-virion influenza vaccine in healthy children and adolescents aged 3–18 years. The study demonstrated that, compared to TIV recipients, the QIV recipients’ immune responses to common vaccine components were not inferior, and their immune responses to B lineage viruses present only in the QIV vaccines were superior. Both vaccines showed similar safety profiles. Prior to this study, another representative trial has also shown that addition of the fourth component increased immune responses to the B lineage component contained only in the QIV.3


Although less extensive than that caused by influenza A, the burden of influenza B is nonetheless substantial. It has been responsible for both severe disease and outbreaks, particularly in children and adolescents. One study estimated the impact of vaccine mismatch on the epidemiology of influenza B during 12 recent outbreaks of influenza in Finland between 1999–2012. Approximately 40% of the occurrences of influenza B in these outbreaks was mismatched with the genetic lineage of that contained in the TIVs, accounting for approximately 10% of influenza illness in the population, with the greatest impact of the vaccine mismatch on children and adolescents. In most recent seasons, both lineages of the influenza B virus have been co-circulating, but variations in the circulation of B lineages by season can be expected to influence the potential net impact of QIV on influenza-associated outcomes. Despite this variation, replacing TIVs with QIVs could lead to modest reductions in illness, hospitalizations, and deaths in the United States.

In Korea, the current national immunization program recommends TIVs for children aged 6 to 59 months. Other than that, there are no preferential recommendations for specific vaccines. As of the time of publication, there has been no indication from the Korea Advisory Committee on Immunization Practices as to whether it will recommend QIVs for the 2018–2019 season, but the limitations and potential costs of using TIVs are now clear: simply, TIVs, containing only one lineage of the influenza B virus, offer no protection against influenza caused by the second lineage. However, a recommendation to replace TIVs with QIVs can only be made after determining the benefits of doing so. Rigorous clinical trials directly comparing the efficacies of TTVs and QIVs are required. Despite the relationship between antibody responses and vaccine efficacy being well established, further data will improve our understanding of vaccine efficacy and effectiveness, especially in children. Finally, a detailed cost-benefit analysis will be required for key stakeholders, with the increased cost and the potential healthcare savings being two major determinants in estimating the benefit of replacing TIVs with QIVs.

REFERENCES


