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Complex task to estimate immune responses to various poliovirus vaccines and vaccination schedules

Khalequ Zaman,

International Centre for Diarrhoeal Disease Research Bangladesh, Dhaka 1212, Bangladesh

Abhijeet Anand

US Centers for Disease Control and Prevention, Atlanta, GA, USA

Since licensing of the first poliovirus vaccine in 1955, multiple types of live attenuated oral poliovirus vaccines (OPVs) and inactivated poliovirus vaccines (IPVs) have been tested or licensed for routine childhood vaccination schedules. IPVs have been manufactured by inactivating the three serotypes of different poliovirus seed strains, either the wild or the Sabin polioviruses, the latter of which is used for manufacturing OPVs.[1] IPVs have also been used with different routes of administration and doses, and have been given at different ages.

WHO's Strategic Advisory Group of Experts (SAGE) on immunisation provides global recommendations for routine poliovirus vaccination. However, technical advisory committees of individual countries have often recommended alternative schedules with variations in the age of administration, number of doses, and combinations with other vaccines. Therefore, there is wide variation in routine poliovirus vaccination schedules.[2] This discrepancy has led to the need for trials that test the immunogenicity of poliovirus vaccines in different combinations and using different vaccination schedules. In low-income countries, where poliovirus transmission is largely faecal–oral, it is important for children to develop both robust intestinal immunity, which prevents transmission of polioviruses, and humoral immunity, which protects them from paralytic poliomyelitis. Therefore, the review of poliovirus vaccines by Grace Macklin and colleagues[3] in *The Lancet Infectious Diseases* that reports on humoral and intestinal mucosal immunity is comprehensive.

Multiple reviews and meta-analyses[4,5] have studied the immunogenicity of different combinations of poliovirus vaccines and strains under different vaccination schedules. The review by Macklin and colleagues is a valuable addition to the scientific literature because it applies the innovative network meta-analysis methodology to estimate the immunogenicity of different OPV and IPV schedules. Network meta-analysis allows indirect comparisons of interventions that have not been included in head-to-head comparisons, and thus should be helpful to assess the immunogenicity of the wide variety of vaccines and schedules in the literature on poliovirus vaccines.

kzaman@icddrb.org .

We declare no competing interests.

Overall, the results reported by Macklin and colleagues summarise those reported by others,[3] including the inability of IPVs to induce intestinal mucosal immunity in the absence of previous exposure to live poliovirus. The average proportion of individuals who developed intestinal mucosal immunity to type 2 poliovirus was similar following three doses of bivalent OPV (bOPV) with types 1 and 3 (30%) to that of three doses of bOPV with IPV (25%). Additional IPV doses did not enhance intestinal mucosal immunity. This finding is relevant for outbreak-response vaccination, particularly for outbreaks of type 2 vaccine-derived poliovirus. Type 2 OPV was withdrawn from routine vaccination in April, 2016, and is now maintained in a global stockpile for outbreak response. Although countries have used IPVs for responding to outbreaks of type 2 vaccine-derived poliovirus,[6] the use of IPVs should be planned considering possible previous vaccination with type 2 OPV, as IPV does not induce intestinal immunity, which is important for reducing faecal-oral transmission.

Macklin and colleagues also reported that a single IPV dose improves humoral immunity against serotype 2, with small additive value of a second IPV dose. The policy implications of this finding are unclear,[7,8] as other studies have reported opposing results.[9] After administration of one IPV dose, few participants show evidence of seroconversion, but more of them are primed to express a rapid immune response when challenged by another dose of poliovirus vaccine.[3] This effect mimics a possible scenario when a person vaccinated with a single dose of IPV is immunologically challenged by wild poliovirus.[7,8] However, it is not certain if IPV priming is protective; an investigation[9] done during a poliovirus outbreak showed a large difference in the effectiveness of one versus two IPV doses, which is not consistent with priming being immunologically equivalent to seroconversion. Furthermore, research in macaques has shown that the potential immunological effect of a single IPV dose might be time-limited.[10] Although both a single intramuscular full IPV dose and an intradermal one-fifth fractional IPV dose led to the formation of memory B cells, no circulating memory B cells could be detected after 5 months. Multiple IPV doses were essential to form memory B cells that could be detected for at least 16 months.

Macklin and colleagues reported that there are small differences in the immunogenicity of different types of IPVs, including those from alternative seed strains or that use different doses or routes of administration. This finding should be reassuring to countries that are considering two doses of fractional intradermal IPV instead of two full IPV doses. Uptake of fractional (one-fifth of the full dose) intradermal IPV has been slow and restricted to a few countries (eg, India, Bangladesh, Nepal, and Sri Lanka), despite a SAGE recommendation affirming the immunogenicity of two doses of fractional intradermal IPV. Unforeseen IPV production challenges lead to global IPV supply shortages. Intradermal IPV offers a much-needed alternative to stretch short IPV supplies to vaccinate more children.

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