Sabin Vaccine in Poliomyelitis Eradication: Achievements and Risks

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Abstract

Poliomyelitis eradication using the oral polio vaccine (OPV), also known as the Sabin vaccine, has been a major medical achievement led by the World Health Organization (WHO) and various countries. The OPV has been administered over 10 billion times to three billion children and has prevented over 13 million polio cases. With the more recent appearance of OPV-related complications, especially the vaccine-derived poliovirus (VDPV) and vaccine-associated polio paralysis, it is important to reconsider the role of this vaccine in polio eradication. Since 2014, the number of VDPV cases has exceeded the number of wild polio virus cases. Given that OPV is the only source of VDPV, an established phased plan to withdraw OPV from use and switch to an inactivated polio vaccine (IPV) was determined. Therefore, countries that still use the OPV in their national immunization programs need to develop adequate plans for supplying IPV in an effective and affordable manner. IPV provides protection against polio, but is insufficient for protection against poliovirus circulation when administered alone. Genetically engineered stabilized, live vaccines are being developed and guarantee the profit of Sabin OPV without the risk.

Keywords: Oral polio vaccine (OPV), wild polio virus, vaccine-associated polio paralysis (VAPP), vaccine-derived poliovirus (VDPV).
INTRODUCTION

After decades of being administered to several billion children globally as well as being credited as primarily responsible for the eradication of poliomyelitis, the Sabin vaccine is now being considered for withdrawal from use. The history of the vaccine, its impact on human health, the rationale for its withdrawal, the alternative use of inactivated polio vaccine (IPV), and associated risks of this substitution are discussed in this short communication.

History of Sabin vaccine

Albert Sabin published an article in 1960 describing the effects of the new trivalent oral polio vaccine (tOPV) when administered to approximately 26,000 children in Cuba. The new vaccine was licensed in the USA after 1961 due to its superior level of antibody production and sufficiently rare neurotropic effects on monkeys. Cuba was the first country to conduct a polio vaccination campaign on a national level. Sabin provided his investigational data and strains of polio to Chumakov, a Soviet microbiologist, in 1956. Chumakov later started organizing the production of the OPV for his state, and only some million children in the Soviet Union were administered this vaccine by 1959. The success of Chumakov’s efforts later led to the licensing of the OPV.

The OPV consists of three strains of live attenuated poliovirus. This vaccine was easier to administer compared to its injectable counterpart and resulted in a so-called herd effect. It also offered longer-lasting immune protection, which included systemic, humoral, cellular, and mucosal immunity (OPV was the superior choice over IPV for global eradication for three main reasons; lower production cost, ease of administration and its ability to induce mucosal immunity)

OPV was preferred over IPV as the vaccine for global eradication due to its capacity to induce mucosal immunity, its lesser production price, and easiness of administration.

Sabin donate his vaccine strains in 1972 to the World Health Organization (WHO) to allow the vaccine to reach more people in developing countries. As a result of this donation, the percentage of children worldwide who received the full course of OPV increased from 5% to 80% in only two decades.

Eradication of poliomyelitis

A proposal to eradicate polio was made in 1988 by the WHO. A strategic plan outlined the requirements for achieving this goal, which included certification-indicating eradication for regions, as well as two phases: an OPV ending phase and a post-OPV phase. The plan mandated vaccination coverage of more than 80% amongst children, with additional vaccine doses provided during national vaccine days. One dose of the vaccine leads to 50% of children developing immunity against the strains; three doses lead to 95% or more. Several surveillance systems for polio were also set in place, as were containment protocols.

Wild poliovirus

Of the three strains of wild poliovirus, the type 2 strain was last reported to cause poliomyelitis in 1999 and was formally certified as eradicated since 2015. The type 3 strain was last reported in 2012 in Nigeria. Since 2012, every case of poliomyelitis has been attributed to the type 1 strain and has occurred in one of only three countries: Nigeria, Pakistan, and Afghanistan. There has been steady progress in both Pakistan and Afghanistan. In 2016, Pakistan reported 20 cases of poliomyelitis; in 2017, there were only 5 reported cases. Similarly, in Afghanistan, a total of 13 cases were reported in 2016, with only 6 reported cases in 2017 (Circulating vaccine-derived poliovirus type 2 – Nigeria). There are three countries in the globe with current wild poliovirus spread, namely, Nigeria, Afghanistan, and Pakistan. These countries are also affected by circulating vaccine-derived poliovirus type 2 (cVDPV2) outbreaks.

Achievements of oral polio vaccine

The OPV has been administered over 10 billion times to three billion children and has prevented over 13 million cases of polio and has led to a 99% reduction in polio incidence.

In 1988,350,000 cases of paralytic polio cases were reported worldwide in 125 endemic countries at a moment in time when the World Health congregation was trying to eradicate polio.

In 2018, only 29 cases of wild polio paralysis have been reported worldwide; these cases have all been reported from three endemic countries, namely, Afghanistan, Nigeria, and Pakistan (Fig. 1).
Risks of oral polio vaccine

Vaccine-associated paralytic poliomyelitis (VAPP)

Although OPV contains weakened polio strains, these strains can still result in poliomyelitis in one per 2.7 million recipients\(^\text{10}\). This is known as vaccine-associated paralytic poliomyelitis (VAPP), which is caused by a genetically modified virus that is formed in the small intestine after the administration of the vaccine. VAPP not only affects those who have been vaccinated, but also the unvaccinated or non-immune close contacts.

In children with healthy immune systems, the incidence of VAPP is an estimated one in 750,000 doses; this rate is one in 6.9 million for subsequent doses\(^\text{11}\). Even though the type 3 strain is the most widespread cause of VAPP\(^\text{12}\), the type 2 strain has been associated with poliomyelitis in the close contacts of those who have received the vaccine.

Vaccine-derived poliovirus (VDPV)

Vaccine-derived polioviruses (VDPVs) are uncommon strains of poliovirus that have genetically mutated from the strains enclosed in the OPV.

The live attenuated vaccine-virus may no longer be similar to the original vaccine-virus as it has genetically altered throughout replication in the intestine\(^\text{13}\). If the virus circulates for 12–18 months, an individual may reacquire neurovirulence. These viruses are called circulating vaccine-derived polioviruses (cVDPV). The survival of these viruses is inversely comparative to the population immunity; the more they replicate, the more they transform, and exchange genetic material with other enteroviruses as they spread through the population\(^\text{14}\).

The low rate of vaccination coverage is the main problem for development of vaccine-derived poliovirus, more than the vaccine itself. If a community is entirely immunized, they will be protected against both the vaccine-derived and wild polioviruses\(^\text{15}\).

Vaccine derived polioviruses have recently started to appear worldwide and are genetically different\(^\text{16,17,18,19}\) from previous strains of polioviruses.

Types of VDPVs

There are three types of VDPVs: circulating VDPV, immunodeficiency-related VDPV, and ambiguous VDPV.

Circulating cVDPV

Outbreaks of circulating vaccine-derived poliovirus are uncommon. During the period 2000-2011 – a time in when over 10 billion doses of OPV were administered worldwide – 20 cVDPV outbreaks registered, leading to 580 polio cases. In the similar time, without vaccination with OPV, around six million children would have been paralyzed by poliovirus.

A total of 108 cases of cVDPV2 cases were reported from 2016 to 2018. These cases were related to 8 outbreaks in 5 countries (Somalia, Fig. 1. Map of polio distribution, past and present
Nigeria, Congo, Pakistan, and Syria). Most of the cases were reported in Syria20.

Immunodeficiency-related VDPV

A few cases have been reported where lengthened reproduction of VDPVs have been noted in people with severe immune deficiency. The lack of an effective immune response leads to the inability of clearing the intestinal infection, which is normally supposed to be cleared within 6-8 weeks. Therefore, they continue to expel immunodeficiency-related VDPVs (iVDPVs) for expanded periods.

Studies from 25 countries (49 published manuscripts) from January 1960 to November 2012 reported 68 iVDPV cases. The VDPV represent a challenge to the worldwide polio eradication as it may serve as a source of the virus even after the eradication of wild-type21.

Ambiguous VDPV

Ambiguous VDPV is understood to be VDPV isolated from persons without identified immunodeficiency. A VDPV isolate is considered “ambiguous” when further investigations have excluded that it is part of an continuing chain of transmission, i.e. a cVDPV, or derived from an iVDPV22.

Management of vaccine-derived polioviruses

The current recommendation is to vaccinate every child several times with OPV to end polio spread, in spite of whether the virus is wild or vaccine-derived. VDPVs appear to be not as much transmissible as the wild poliovirus, and outbreaks of VDPV are typically self-limiting or quickly blocked with 2–3 rounds of high-quality supplementary immunization activities. Nowadays, the quantity of polio cases due to OPV is greater than that related to the wild virus.

Provided that OPV is used, VDPVs creates a threat of causing poliomyelitis in vulnerable individuals, which makes eradication difficult. Inactivated poliovirus vaccine (IPV) solves this problem since VDPV would not be able to form from an inactivated virus. However, economic and logistical barriers make switching to IPV difficult23.

What will occur following the removal of oral polio vaccine and the use of IPV only?

Several developed countries, which have better sanitation and smaller family sizes, have preserved polio elimination through the use of IPV24,25,26. This is because IPV alone does not have the risk of spreading the virus in the stool.

Although IPV has been included in routine vaccination around the world between 2014 and 201627, it is anticipated that IPV alone will not be sufficient to protect against the virus in all settings. Improvements in sanitation, as well as better IPV supplies25 will also be necessary.

Currently, genetically engineered live vaccines are being developed, this will hopefully maintain the benefits of the Sabin OPV without the associated risks28,29,30, and adjuvant IPV may supply a complementary route to a new effective vaccine31. We believe these new types of vaccines will be necessary to insure polio eradication.

Mass immunization with OPV remains the most efficient intervention to eliminate poliovirus transmission25, because in spite of the challenges mentioned, Sabin vaccination is clearly preferable to natural infection by wild polio virus or cVDP.

CONCLUSION

Polio is an extremely communicable viral disease that can spread quickly through person-to-person contact leading to everlasting paralysis. At present three types of wild poliovirus but only type 1 still in circulation nowadays. OPV vaccine is inexpensive and efficient at reducing polio spread in developing countries but carries a danger of VAPP and VDPV; therefore, all use of OPV have to end for the humanity to be entirely polio-free. IPV is being introduced to afford defense against all three serotypes, at the same time as OPV is being phased out.

Therefore, the countries that still use this vaccine (OPV) in their national immunization programs need to develop adequate plans for supplying IPV in an effective and affordable manner. The IPV provides protection against polio but alone is not enough to defend against poliovirus transmission.

To secure polio eradication for the future, genetically stabilized, engineered live vaccines are in progress and pledge the profit of the Sabin OPV with no risks.

The WHO has stated that poliomyelitis (polio) is on the way to turn into the next human disease forever to be eradicated as only 29 cases of wild poliovirus have been detected thus far in 2018 in Afghanistan, Nigeria, and Pakistan, the three lasting endemic countries.
At the same time as a 99.9% decrease in polio cases globally, the World Health Organization (WHO) said tackling the remaining 0.01% of polio cases has demonstrated to be difficult and warned that immunization efforts have to continue.

In spite of the risks fully discussed in this article, Sabin OPV immunization is for all time preferable to get the disease by wild polio virus or cVDPV. Mass immunization with OPV remains therefore the most efficient intervention to stop poliovirus transmission.

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CONFLICT OF INTEREST
The authors declare that there are no conflict of interest.

REFERENCES
15. World Health Organization, Regional Office for Africa. "Circulating vaccine-derived poliovirus type 2 (cVDPV2) Key messages". https://afro.who.int/node/9733 (June 6, 2018).
26. Pebody R. Polio vaccination in Europe: the shift from


