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Review Article

Rationale for introduction of one dose of Inactivated Polio Vaccine at 14 weeks in National Immunization Programme of India

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Abstract: India is a polio-free country since 2011, but immunization against polio has to continue because of continued endemicity in 2 countries, and capability of Sabin viruses to cause paralytic polio case and outbreaks. On the other hand, vaccination against polio has to cease eventually after the Wild Polio Viruses are eradicated. These contradictory situations make the road to final milestone of polio eradication rather tortuous. This article discusses the rationale behind the recent step taken by India in this direction i.e. addition of Inactivated Polio Vaccine in India's National Immunization Programme, and briefly mentions the future course of action i.e. introduction of bivalent OPV in place of trivalent OPV.
Keywords: Eradication, Inactivated Polio Vaccine, India, Oral Polio Vaccine, Poliomyelitis

INTRODUCTION

The eradication of polio is a top global health priority. Since the World Health Assembly (WHA) announced a goal to eradicate polio in 1988, thereby creating the Global Polio Eradication Initiative (GPEI), the number of polio cases has declined from 350,000 cases in 1988 to 359 in 2014[1]. To reach the final milestone, WHA in 2013 endorsed GPIE's *Polio Eradication and Endgame Strategic Plan 2013-2018* [2] which provides a detailed approach and concrete timeline for eradication of polio- an infection that that causes disease, deformity, disability, discrimination and even death. This plan is different from previous eradication plans because it deals with eradication of polio caused not only by wild viruses but also paralytic polio cases associated with Oral polio Vaccine (OPV) (Fig 1). To address risks associated with OPV use, the plan calls for a phased and synchronized withdrawal of OPV globally.

Fig-1: Unique features of Polio Eradication and Endgame Strategic Plan 2013-2018[3]

The Rationale for OPV Withdrawal:

OPV was developed in 1961 by Dr Albert Sabin. tOPV contains all three poliovirus serotypes (1, 2 & 3) that have been attenuated- a process greatly reducing their neurovirulence and transmissibility, but retaining immunogenicity. Live attenuated polioviruses replicate in the oral cavity, intestinal mucosa, lymphoid cells and lymph nodes that drain these organs. Vaccine viruses are excreted in the stools of recipients for up to 6 weeks, and may spread to contacts who upon exposure may be infected with vaccine virus and thus protected. The use of this vaccine has led to elimination of polio from four of the six WHO regions, and eradication of Wild Poliovirus 2 (WPV2). WPV 3 had its last victim in 2012, but the surveillance period is rather short to celebrate its global disappearance. OPV has been the primary vaccine of choice in the eradication effort because it is inexpensive, can be easily administered orally, induces humoral immunity to prevent infection of the nervous system as well as oral and intestinal mucosal immunity, and can spread to close contacts through secondary spread thus immunizing them or boosting their immunity[4]. However, the balance of benefit of OPV starts tilting against it as polio is eliminated from a country or region. This is because of very low but real risk of polio associated with OPV.

Vaccine Associated Paralytic Polio (VAPP):

Cases of VAPP are clinically indistinguishable from poliomyelitis caused by WPV. The incidence of VAPP has been estimated to be at 2-4 cases/million birth cohort per year in countries using OPV[5]. VAPP occurs both in vaccine recipients and their unimmunized contacts. All three viruses in tOPV are responsible for cases of VAPP, but Sabin Virus 2 causes 40% of cases[6]. Available data suggest differences in the epidemiology of VAPP in developing and industrialized countries. In developed countries, VAPP occurs mainly in early infancy associated with the first dose of OPV and decreases sharply (>10 folds) with subsequent OPV doses. However, in low- and middle-income countries including India the age of VAPP is higher (1-4 years) and largely associated with second or subsequent doses. The main factors responsible for this difference are considered to be lower immune responsiveness to OPV and higher prevalence of maternally-derived antibodies in populations in developing countries[7].

Vaccine-derived polioviruses (VDPVs):

The attenuated viruses in OPV vaccines may acquire the neurovirulence and transmissibility similar to WPV. They may then become circulating vaccine-derived polioviruses that cause case or outbreaks of paralytic poliomyelitis. These viruses are further sub-divided into 3 categories: (1) cVDPVs when evidence of person-to-person transmission in the community exists; (2) immunodeficiency-associated VDPVs (iVDPV) which are isolated from cases of primary B-cell and combined immunodeficiencies; and (3) ambiguous VDPVs (aVDPV) which are either clinical isolates from persons with no immunodeficiency, or sewage isolates of unknown source. The behaviour of cVDPVs can be similar to that of WPVs, with significant paralytic attack rates and sustained person-to-person transmission. Recent experience indicates that low vaccination coverage is a major risk factor for cVDPV outbreaks; cVDPVs have the ability to become endemic and can be imported & spread in an under-vaccinated community[8,9]. Although, cases of VDPVs also occur with type 1 and type 3, most outbreaks during 2012-2013 were due to type 2 Sabin virus[10]. Thus, continued use of OPV in a polio-free country creates a vicious cycle; where OPV itself becomes responsible for cases of paralytic polio in a community, country or region, but high herd immunity has to be ensured to prevent cases of VAPP and cVDPV, as well as importation of WPV from countries yet to reach the target. The answer lies in switching from OPV to Inactivated Polio Vaccine (IPV) which is a killed vaccine, and is not associated with VAPP or cVDPV.

Why Not Switch from OPV to IPV at one go?

Theoretically, if VAPP/cVDPV is the issues in a polio-free India, the best answer is to stop OPV and switch to IPV which is safe, effective and not associated with vaccine-associated polio cases. We already have a vaccination schedule in place that is immunizing infants with DPT/Pentavalent vaccine at 6, 10 and 14 weeks. Addition of IPV in the schedule is not logistically impossible for a democratic country that is now emerging as a major economy. However, the reasons are not only financial, although economics do play its role in the decision making. The most important reason why India should not switch directly to IPV (and stop OPV) is that, although we are a polio-free nation, it does not mean that we are vaccinating 100% of birth cohorts. Moreover, all who are vaccinated are not protected because vaccines, in general are not 100% effective. Thus, there are infants and children who are susceptible, but these children do not get infected because of herd immunity, or/and capacity of Sabin viruses to spread from the vaccinated to close contacts. Thus introducing IPV, and stopping OPV altogether, simultaneously is epidemiologically unwise because it is fraught with danger of spread of cVDPV or imported WPV among the susceptible children. This is a weakness of IPV, as it is a killed vaccine that protects only the vaccinated and not close contacts. The answer lies in introduction of IPV and gradual cessation of OPV, one step at a time i.e. from trivalent to bivalent before complete cessation (Fig 2).

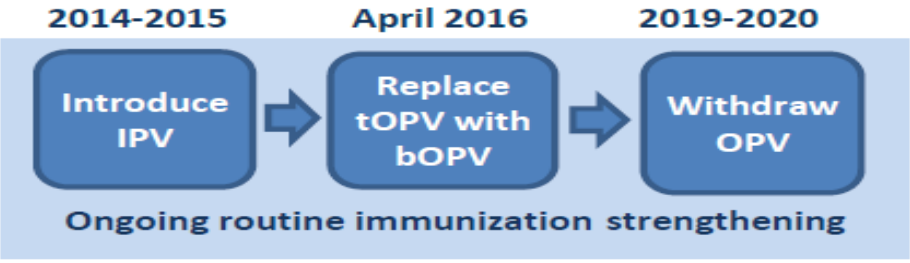

Fig-2:Timeline for introduction of IPV, switch from tOPV to bOPV and complete withdrawal of OPV[11]

Role of one dose of IPV in polio eradication and control:

Although, WPV 2 is considered eradicated, protection against type 2 cannot be withdrawn at present, because cVDPV2 is in circulation. Hence, immunization against Type 2 virus has to be maintained for the time being. The principal reason of adding one dose of IPV to the schedule is to prevent cases of paralytic polio due to Type 2 virus when the switch is made from tOPV to bOPV that does not include OPV2. In addition to this primary aim, IVP will boost the immunity against Type 1 and 3, thus facilitating faster march towards eradication, and it will also decrease VAPP and cVDPV cases due to all three viruses[12].

Why IPV at 14 weeks?

It is proven that addition of IPV before OPV eliminates vaccine related polio cases[11]. Therefore, the best time to add IVP should be at the earliest possibility in life (i.e. 6 week) because it will take care of almost all cases of VAPP (except due to 0 doses). However, India has added IPV at 14 weeks (OPV 1st dose at 6, OPV 2nd dose at 10, and OPV 3rd dose +IPV at 14 weeks of age) because in India (like in many countries dependent on OPV) maternal-transferred antibodies interfere in effectiveness of IPV in early infancy[12]. Hence, addition of IPV at 14 weeks is the best bargain as it will take care of Type 2 virus, which is its primary role, and also decrease cases of vaccine associated polio that are usually occurring after infancy in India.

Future Actions: The Switch from tOPV to bOPV: Why and When?

Although maximum cases of paralytic polio were caused by WPV 1, it was OPV 2 that proved most *notorious* in the vaccine. Firstly, because of its higher immunogenicity, it prevented development of effective immunity against WPV 1 and 3 among those vaccinated with tOPV[13]. Secondly, recent estimates have found that approximately 90% of cVDPV cases and 40% of VAPP cases were associated with the type 2 component of tOPV[14]. Moreover, no case of paralytic polio due to WPV 2 has been detected since 1999. Thus, omission of Type 2 from tOPV makes epidemiological sense, as it improves immunogenicity of bOPV against WPV 1 and 3. This advantage of bOPV was illustrated in a 2008 study conducted in India which showed that after two doses of bOPV, seroconversion was 80.3% against type 1 polio virus which was much higher than the 53.2% for tOPV[12]. Levels of seroconversion against type 3 show similar differences. The better performance of bOPV has played a key role in the potential disappearance of WPV type 3, the last case of which was reported in Nigeria in November 2012.

As Eradication of Polio is a global effort, the switch from tOPV to bOPV has to be universal and synchronized[15]. After the switch to bOPV the population immunity to type 2 polioviruses will decrease, and bOPV-vaccinated populations would become vulnerable to introductions of type 2 vaccine viruses including VDPV2 importations. If a country switches early, its population will be at increased risk of paralytic polio due to cVDPV2. If a country or region delays the switch, they will put others at risk[16]. Another epidemiological consideration is that the switch must occur during the low season of polio virus circulation (January through May) in order to further mitigate the risk of re-emergence of cVDPV2[12]. Keeping these issues in context, the type 2 component of OPV (OPV2) is planned to be phased out from all immunization activities in a globally coordinated manner in a two-week timeframe in April 2016[15].

Conclusion:

In summary, introduction of IPV at 14 weeks in Universal Immunization Programme of India[17] will boost immunity against the viruses; decrease vaccine associated paralytic polio cases, and prepares grounds for switch from tOPV to bOPV, in the most cost-effective manner. Thus, it is a step in our march towards eradication of poliomyelitis from our planet. Eradication of polio will be a heritage that, we will be proud to gift to our future generation, and they will be grateful to receive.

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