PERSPECTIVE

India's Last Battle in the War Against Polio

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Type 2 vaccine virus is the predominant cause of Vaccine-derived poliovirus and Vaccine-associated paralytic poliomyelitis. Therefore, World Health Organization recommends global synchronized switching from trivalent to bivalent Oral polio vaccine. To prevent the risk of type 2 poliovirus re-emergence, atleast one dose of Inactivated polio vaccine is recommended at 14 weeks of age in routine immunization, before the switch. To protect immunocompromised children and those under 14 weeks of age, an additional dose must be given at 6 weeks of age. Mass campaigns of Injectable polio vaccine in states with poor Routine immunization coverage, before the trivalent to bivalent Oral polio vaccine switch, will reduce risk of Vaccine-derived poliovirus by covering all under-immunized pockets. The additional costs are justified as it is our ethical obligation to eliminate any iatrogenic risk.

Keywords: *Oral polio vaccine, Inactivated polio vaccine, Vaccine associated poliomyelitis.*

India completed three years without a case of Wild poliovirus (WPV), subsequent to which South East Asia Region, WHO was declared polio-free in March 2014. However, since 2009, India has witnessed 41 cases of Vaccine-derived poliovirus (VDPV), including two such cases in 2014 [1]. In settings with low immunization coverage, live vaccine virus used in Oral polio vaccines (OPV) can multiply for long and undergo mutations to gain neuro-virulence. This VDPV can cause paralysis and circulate in the community to cause outbreaks [2,3]. Another concern, Vaccine-associated paralytic polio (VAPP) is a rare but serious adverse event following OPV administration [4]. VAPP tends to occur in both OPV recipients and their unimmunized contacts.

VDPV AND VAPP: GROWING CONCERNS

Currently, two types of polio vaccines are mainly used in National health programs in India. The trivalent OPV (tOPV) contains live attenuated polioviruses of all three serotypes delivered through Universal immunization program (UIP) and pulse polio national immunization day (NID) campaigns. Other vaccine, the bivalent OPV (bOPV) contains two serotypes of live attenuated poliovirus (type 1 and 3) and delivered through Pulse polio, Sub-national immunization day (SNID) campaigns. Similar to the global situation, more than 90% VDPV cases in India were caused due to type 2 virus [1]. Cases of VDPV also occur with type 1 and type 3 poliovirus. These viruses are further subdivided into 3 categories: (*a*) circulating VDPVs (cVDPVs), when evidence of person-to-person transmission in the community exists; (*b*) immunodeficiency-associated VDPVs (iVDPVs), which are isolated in rare cases from people with primary B-cell and combined immunodeficiencies who have prolonged VDPV infections; and (*c*) ambiguous VDPVs (aVDPVs), which are either clinical isolates from persons with no known immunodeficiency, or sewage isolates of unknown source [5]. In 2013, seven countries reported cases of paralytic poliomyelitis caused by circulating VDPV (cVDPV), all associated with Sabin 2, of which Pakistan reported the greatest number (n=44) [6]. Recent experience from Nigeria, Egypt and USA indicates that cVDPVs can become endemic [7,8], and cause outbreaks in under-vaccinated community even in a developed country (Amish community, USA) [8]. Fortunately, none of the VDPVs reported in India after 2010 have been of the circulating type [9].

It has been estimated in developed countries that VAPP cases occur at a frequency of 2-4 cases/million birth cohort per year in countries using OPV, 40% of which is caused by OPV2 [10]. Using the above incidence rate, about 50-100 children are estimated to suffer from VAPP every year in India. Though India and other developing counties lack reliable data on VAPP, some reports in previous years suggest that cases could be much higher in India as 181, 129 and 109 VAPP cases were reported in 1999, 2000 and 2001, respectively [4,11]. The above discrepancy demonstrates that risk of VAPP per child is higher in India than the developed countries. This is contrary to what some studies report when they compare risk of VAPP per OPV dose, where the risk is lower in India because of higher number of

OPV doses. In 1999, overall risk in India was estimated to be 1 case per 4.6 million OPV doses. The risk of first-dose recipient VAPP (1 case per 2.8 million doses) was higher than the risk of subsequent-dose recipient VAPP (1 case per 13.9 million doses) [4]. Government of India does not count VAPP as polio with the justification that VAPP is sporadic and poses little or no threat to the community at large [12].

GLOBAL CONSENSUS ON ELIMINATION STRATEGY

Despite higher risks of VAPP and VDPV, OPV was preferred over IPV for public health programs during pre-eradication period, mainly due to its lower costs and ease of implementation. However, in the present era, VAPP and VDPV overwhelmingly outnumber polio due to WPVs, and therefore OPV has to be discontinued as early as feasible, for ethical reasons [13]. Though, studies from US and Australia have shown that switching from OPV to IPV may not be cost-effective [13,14], it is our imperative to eliminate the iatrogenic risk of VAPP at any cost, (in line with the principle of first do no harm). World Health Organization (WHO) has rightly recommended a global synchronized withdrawal of OPV starting with OPV type 2 (by switching from tOPV to bOPV) accompanied by strengthening of routine immunization. However, there is an increased risk of emergence of cVDPVs during the withdrawal of trivalent OPV as the immunity level against type 2 poliovirus will decrease. To prevent such an emergence of VDPV, it is recommended that before this switch population immunity against type 2 polio virus be boosted by introduction of at least one dose of Inactivated Polio Vaccine (IPV) in the UIP [15].

Introduction of one dose of IPV prior to vaccination with OPV led to elimination of VAPP in Hungary. Countries with high routine immunization coverage that switch from OPV to IPV in their immunization programs consistently eliminate VAPP cases. Previous studies also suggest that a single dose of IPV will effectively close the immunity gap against poliovirus type 2 (and types 1 and 3) in previously tOPV vaccinated children. In addition, a recent study in India found that in infants and children (aged 6–11 months, 5 and 10 years) with a history of multiple doses of OPV, a single dose of IPV boosted intestinal mucosal immunity and reduced the prevalence of excretion of vaccine virus by 39% to 76%, after an OPV challenge, compared to no polio vaccination [15]. Global OPV2 withdrawal requires the absence of 'persistent' cVDPV2 for at least 6 months. Therefore, according to the Strategic Advisory Group of Experts on immunization, countries must complete the planning for introduction of IPV by end 2014, and introduce IPV by end 2015 [16]. If one dose of IPV is used, it should be given from 14 weeks of age (when maternal antibodies have diminished and immunogenicity is significantly higher), and can be co-administered with an OPV dose. To reduce VAPP risk, countries may consider alternative schedules based on local epidemiology, including the documented risk of VAPP prior to four months of age. The implementation of the new schedule (three OPV doses + one IPV dose) does not replace the need for supplemental immunization activities (SIAs), especially in countries such as India that have insufficient routine immunization coverage [15].

CHALLENGES FOR INDIA

Polio eradication in India has faced region-specific challenges and varying immune response of population in comparison to those living in other parts of the world. Thus launch of IPV and its timing must be tailor-made for Indian population. Issues that need serious consideration are:

Continuing poor coverage of Routine immunization (RI) and infrequent SNIDs: While the Pulse polio campaigns cover nearly all children upto five years of age, UIP reaches to only about 71.5 % of children. [17]. Threat of VDPV looms large on the remaining, poorly immunized population. With high annual growth rate, this population is vulnerable to extensive VDPV circulation as there is rapid influx of new susceptibles in the already under-vaccinated cohort [4]. In addition, as per the recommendations of India Expert Advisory Group for Polio Eradication (IEAG) [9], post-WPV eradication India has reduced the frequency of bOPV SNIDS. This may have already resulted in lower immunity levels to type 1 and 3 polioviruses, especially among newborns and infants, raising the risk of type 1 and 3 VDPV. When OPV is withdrawn, there will be a time overlap when children shedding vaccine viruses may transmit infection to immunity-naive infants and children, seeding the emergence of VDPV uninhibited by immunity. Such early lineages of VDPV will remain in silent circulation until conditions are right to cause outbreaks. By then, their containment would have become difficult [18].

Therefore, when IPV is introduced, its coverage must reach rapidly to more than 90% in all States with no pockets with poor immunity against any types of polio virus. It is unlikely that UIP would be able to achieve such high levels of coverage. Mass campaigns using IPV should be conducted in States with low vaccine coverage (<80%), like those done for Measles, based on Polio SIA microplans. Measles catch-up campaigns conducted across many large and backward states in India achieved high level of coverage (>90%) and demonstrated our capability to execute a mass campaign using an injectable vaccine.

Protecting Young and Immuno-compromised children: Infants could be at higher risk of VDPV as they may not have sufficient protection due to maternal antibodies. Risk of VAPP is documented to be about five times higher after first dose than after subsequent doses [4]. IPV administered only at 14 weeks would leave children younger than 14 weeks unprotected. In India, a large proportion of children (42.5%) under 5 years of age are underweight [19], and many of them may respond sub-optimally to IPV. This makes them susceptible for generation and circulation of VDPV. According to WHO Position Paper on Polio Vaccines, immunocompromised people usually develop immunity against polio only when they are given two doses of IPV [15].

Therefore, it is important to administer two doses of IPV, including an early dose, preferably at 6 weeks of age (even though efficacy at 6 weeks is only half of that at 16 weeks) [20], and second dose at or after 14 weeks of age (in addition to the routine OPV doses). Another benefit of giving two dose of IPV with an early first dose will be higher coverage so that more children will receive atleast one dose of IPV.

CONCLUSIONS

Post WPV eradication, VAPP and VDPV are the last formidable opponents in India's war against Polio. The Global strategy must be customized in line with our local considerations. Administration of additional early dose of IPV at 6 weeks of age (other than the mandatory dose at or after 14 weeks of age) will ensure an early, stronger and more widespread protection against the risks of VAPP and VDPV. Moreover, launch of mass IPV campaigns in states with poor routine immunization coverage before the tOPV-bOPV switch will help pre-empt any emergence of VDPV in susceptible populations. The additional costs of an extra IPV dose in the UIP and mass campaigns may be justified as it is an ethical obligation on us to eliminate the iatrogenic risk of VDPV.

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