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Decay of Sabin inactivated poliovirus vaccine (IPV)-boosted poliovirus antibodies

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ABSTRACT

Introduction: We conducted a follow-on study to a phase I randomized, controlled trial conducted in Cuba, 2012, to assess the persistence of poliovirus antibodies at 21–22 months following booster dose of Sabin-IPV compared to Salk-IPV in adults who had received multiple doses of oral poliovirus vaccine (OPV) during childhood.

Methods: In 2012, 60 healthy adult males aged 19–23 were randomized to receive one booster dose, of either Sabin-inactivated poliovirus vaccine (Sabin-IPV), adjuvanted Sabin-IPV (aSabin-IPV), or conventional Salk-IPV. In the original study, blood was collected at days 0 (before) and 28 (after vaccination), respectively. In this study, an additional blood sample was collected 21–22 months after vaccination, and tested for neutralizing antibodies to Sabin poliovirus types 1, 2 and 3.

Results: We collected sera from 59/60 (98.3%) subjects; 59/59 (100%) remained seropositive to all poliovirus types, 21–22 months after vaccination. The decay curves were very similar among the study groups. Between day 28 and 21–22 months, there was a reduction of $\geqslant$87.4% in median antibody levels for all poliovirus types in all study groups, with no significant differences between the study groups.

Conclusion: The decay of poliovirus antibodies over a 21–22-month period was similar regardless of the type of booster vaccine used, suggesting the scientific data of Salk IPV long-term persistence and decay may be broadly applicable to Sabin IPV.

1. Introduction

In 2008, the WHA recommended the WHO develop safer inactivated poliovirus vaccine (IPV) production technology using attenuated seed strains, such as Sabin polioviruses (Sabin-IPV) [1]. Sabin-IPV technology would partly address the biosafety risks associated with Sabin-IPV production, therefore allowing for production in developing countries [2,3].

The immunogenicity of Sabin-IPV administered in the primary series has been well-established in different clinical studies in China, Japan, Poland, and Cuba [4–7], some of which demonstrated that Sabin-IPV induced adequate neutralizing antibodies to both Sabin and wild poliovirus [6,8]. Sabin-IPV products are currently licensed in Japan and China, and are under development in many other countries [9]. As Sabin-IPV and adjuvanted Sabin-IPV (aSabin-IPV) are expected to be widely used in the near future, it is important to assess the medium and long-term persistence of Sabin-IPV boosted antibody response.

Several studies have demonstrated the long-term presence of neutralizing antibodies, induced by Salk IPV [10–13]. To date however, only one study has assessed the duration of immunity induced by Sabin-IPV. This was a phase III trial conducted in Japan, using tetravalent diphtheria-tetanus-acellular pertussis-Sabin-IPV vaccine (DTaP-Sabin-IPV), which demonstrated comparable immunity between Salk-IPV and DTaP-Sabin-IPV, 6–18 months after vaccination [5].

We conducted a follow-on study to the phase I Cuba study conducted in 2012. This study is the first to assess and compare the decay of neutralizing antibodies to poliovirus, between day 28 and 21–22 months, in adults who received multiple doses of oral poliovirus vaccine (OPV) during childhood, following a booster dose of either Sabin-IPV, aSabin-IPV, or Salk-IPV, in a tropical setting.

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2. Methods

In the phase I trial in Cuba conducted in 2012, sixty healthy male subjects aged 19–23 years, who had received polio vaccination with multiple doses of OPV during childhood, in accordance with the Cuban national immunisation program, and with no history of receiving poliovirus vaccine since the age of 9 years, were enrolled and randomized, to receive a booster dose of either conventional Salk-IPV, or Sabin-IPV, or aSabin-IPV (adjuvanted with Aluminum hydroxide), with the following formulations: Salk-IPV 40:8:32 D-antigen Units per dose (DU/dose), Sabin-IPV 20:32:64 DU/dose, and aSabin-IPV 10:16:32 DU/dose and 0.5 mg aluminum hydroxide, respectively [14]. All Sabin-IPV and Salk-IPV vaccines were provided by the Netherlands Vaccine Institute (NVI) (currently called Intravacc) [7].

In our follow-on study, all subjects were contacted at 21–22 months after initial vaccination, for blood collection. Sera were tested at the Institute Pedro Kouri, for neutralizing antibodies to Sabin poliovirus types 1–3, using standard micro-neutralization assay. The antibody titers were diluted to 1:65,536, above the standard 1:1024 because high titers were expected with a boosting dose of IPV. Seroconversion was defined as a $\geqslant$fourfold increase in reciprocal antibody titers.

We calculated the decay in antibody titers at day 28 and at 21–22 months, and the overall increase in antibody titers during day 0 and 21–22 months, by poliovirus type and study arm with 95% confidence intervals using bootstrapping sampling and estimation with 10,000 replications. We tested differences in antibody titers between the study groups, with Salk-IPV as the reference group, by poliovirus type, using Wilcoxon rank sum test with significance indicated by $p \leqslant 0.05$. All analyses were conducted using statistical application "R 3.1.2" [15].

3. Results

3.1. Study population

In the previous study, there were no significant differences between the three groups, in baseline characteristics of age, height, weight, time since receiving last OPV dose, or, baseline titer of neutralizing antibodies to Sabin poliovirus types 1–3 [7].

In our study, a total of 59/60 (93.1%) subjects were followed-up at 21–22 months (654–675 days). One subject in the aSabin-IPV arm was lost to follow-up, and one subject in the aSabin-IPV group had moved to Havana, where their blood was collected.

3.2. Antibody decay (day 28 to 21–22 months)

In the previous study, there were no differences in immunogenicity to Sabin poliovirus types 1–3 between the study groups during day 0 and day 28, with all subjects seroconverting or boosted by day 28 [7]. At day 28, median antibody titers were highest for poliovirus type 1 in the Sabin-IPV study group, and for poliovirus types 2 and 3 in the aSabin-IPV group (Fig. 1).

In our study, at 21–22 months, all subjects had detectable antibody titers for all Sabin poliovirus types, with median antibody titers highest for poliovirus types 1 and 2 in the Sabin-IPV study group, and for poliovirus type 3, in aSabin-IPV group. Median titers were lowest for all poliovirus types in the Salk-IPV group. We did not find any significant differences in median antibody titers between the study groups for all poliovirus types (Fig. 1, Table 1).

There were no statistically significant differences in the decay of antibody titers during day 28 and 21–22 months, between Salk-IPV, Sabin-IPV and aSabin-IPV groups, with relative reduction as a percentage decline in median antibody titers by poliovirus type: 92.1%, 92.1%, 87.4% for poliovirus type 1 ($p = 0.54$; $p = 0.61$, respectively); 96.0%, 95.0%, 95.0% for poliovirus type 2 ($p = 0.66$; $p = 0.93$, respectively); 93.7%, 92.1%, 93.7% for poliovirus type 3 ($p = 0.67$; $p = 0.50$, respectively) (Table 2).

3.3. Antibody increase (day 0 to 21–22 months)

There were no statistically significant differences in the relative increase in antibodies from day 0 to 21–22 months between Salk-IPV, Sabin-IPV and aSabin-IPV study groups by poliovirus type: 1121.3%, 1028.5%, 893.0%, for poliovirus type 1 ($p = 0.53$; $p = 0.40$, respectively); 458.7%, 694.7%, 402.8% for poliovirus type 2 ($p = 0.71$; $p = 0.95$, respectively); 320.5, 450.0, 566.0, for poliovirus type 3 ($p = 0.72$; $p = 0.54$, respectively) (Table 2).

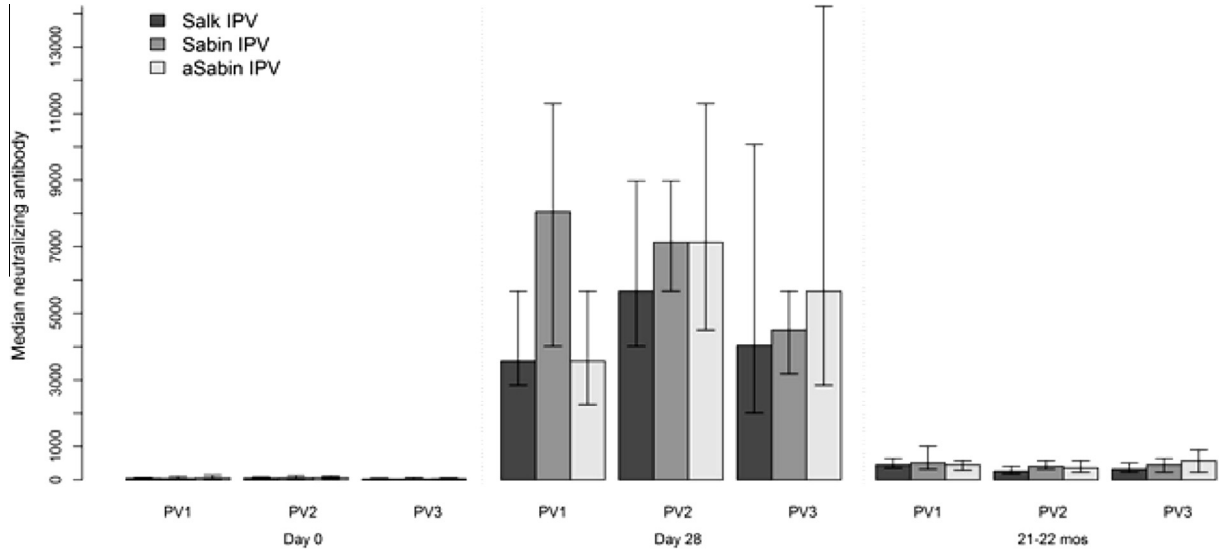

Fig. 1. Median antibody titers ($\log_2$) to poliovirus types 1–3, on day 0, day 28, and 21–22 months, by study group; 95% confidence intervals calculated using bootstrapping with 10,000 replications.