Fractional Doses of Inactivated Poliovirus Vaccine in Oman


ABSTRACT

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BACKGROUND

We conducted a clinical trial of fractional doses of inactivated poliovirus vaccine administered to infants in Oman, in order to evaluate strategies for making the vaccine affordable for use in developing countries.

METHODS

We compared fractional doses of inactivated poliovirus vaccine (0.1 ml, representing one fifth of a full dose) given intradermally with the use of a needle-free jet injector device, with full doses of vaccine given intramuscularly, with respect to immunogenicity and reactogenicity. Infants were randomly assigned at birth to receive either a fractional dose or a full dose of inactivated poliovirus vaccine at 2, 4, and 6 months. We also administered a challenge dose of monovalent type 1 oral poliovirus vaccine at 7 months and collected stool samples before and 7 days after administration of the challenge dose.

RESULTS

A total of 400 infants were randomized, of whom 373 (93.2%) fulfilled the study requirements. No significant baseline differences between the groups were detected. Thirty days after completion of the three-dose schedule, the rates of seroconversion to types 1, 2, and 3 poliovirus were 97.3%, 95.7%, and 97.9%, respectively, in the fractional-dose group, as compared with 100% seroconversion to all serotypes in the full-dose group (P = 0.01 for the comparison with respect to type 2 poliovirus; results with respect to types 1 and 3 poliovirus were not significant). The median titers were significantly lower in the fractional-dose group than in the full-dose group (P<0.001 for all three poliovirus serotypes). At 7 months, 74.8% of the infants in the fractional-dose group and 63.1% of those in full-dose group excreted type 1 poliovirus (P = 0.03). Between birth and 7 months, 42 hospitalizations were reported, all related to infectious causes, anemia, or falls, with no significant difference between vaccination groups.

CONCLUSIONS

These data show that fractional doses of inactivated poliovirus vaccine administered intradermally at 2, 4, and 6 months, as compared with full doses of inactivated poliovirus vaccine given intramuscularly on the same schedule, induce similar levels of seroconversion but significantly lower titers. (Current Controlled Trials number, ISRCTN17418767.)
IN 1988, THE WORLD HEALTH ASSEMBLY RESOLVED TO ERADICATE POLIOMYELITIS BY THE YEAR 2000.1 Substantial progress toward this goal has been made, although eradication remains elusive. One poliovirus serotype, wild poliovirus type 2, has apparently been eradicated, with the last isolation reported in India in October 1999.2 The number of countries in which the presence of wild poliovirus was never interrupted decreased to 4 in 2009 (from more than 125 polio-endemic countries in 1988), and the number of cases of poliomyelitis decreased by more than 99% during the same period.3,4

As the eradication efforts accelerated, the preparations for the posteradication era intensified in parallel. A critical decision to stop the routine use of oral poliovirus vaccine was proposed in 19975 and was endorsed in 2004 by the Advisory Committee on Polio Eradication (ACPE).6 The pre-requisites for cessation of the use of the oral poliovirus vaccine have been elaborated,7 the vaccination options have been identified,8 and the risks for paralytic disease after cessation of the use of the oral poliovirus vaccine have been quantified.9

In 2007, the ACPE added to the list of pre-requisites a requirement for an “affordable inactivated poliovirus vaccine” that would be appropriate for use in developing countries.10 The current weighted average purchase prices per dose of vaccine, when purchased by the United Nations Children’s Fund (UNICEF), are $0.15 for the trivalent oral poliovirus vaccine and approximately $3 for the inactivated poliovirus vaccine. To realize an affordable inactivated poliovirus vaccine, a number of strategies are being pursued, including a schedule reduction (the administration of fewer doses in a routine schedule); a reduction of the antigen dose (i.e., fractional-dose inactivated poliovirus vaccine); the use of adjuvants, resulting in a decreased need for antigen; optimization of production processes (i.e., increasing cell densities, creating new cell lines, or using alternative inactivation agents); and the development of an inactivated poliovirus vaccine produced from Sabin strains that would be appropriate for production in developing countries. Undoubtedly, the most important of these options in the near term is the development of an inactivated poliovirus vaccine produced from Sabin strains.11-13

One approach to stretching the available supplies of inactivated poliovirus vaccine and reducing the cost per vaccination, with a potential for rapid implementation, is antigen-sparing through intradermal delivery. The intradermal route of administration to improve immunogenicity and achieve a reduction in cost has been evaluated for many vaccines.14-19 The intradermal administration of inactivated poliovirus vaccine was first evaluated by Salk.20,21 More recently, in small studies conducted in India, fractional-dose inactivated poliovirus vaccine given intradermally resulted in seroconversion rates that were similar to those achieved with the full-dose vaccine.22-24

One potential problem associated with intradermal injection is the difficulty of administering the vaccine reliably with a needle and syringe. Several devices are in development to permit reliable intradermal delivery, and several needle-free devices are now available for investigational use. Inactivated poliovirus vaccine administered intramuscularly with the use of jet injectors has previously been shown to elicit satisfactory immune responses.25,26

Because the immunogenicity of inactivated poliovirus vaccine is greatly affected by the levels of maternally derived antibodies,27,28 a clinical study design was selected in which newborns were enrolled and were vaccinated at 2, 4, and 6 months of age with either fractional doses or full doses of inactivated poliovirus vaccine.

METHODS

STUDY OBJECTIVES AND PROTOCOL

The study had four objectives: to compare humoral antibody responses (seroconversion and antibody titer) after completion of a three-dose schedule of fractional-dose inactivated poliovirus vaccine with the responses after completion of a three-dose schedule of full-dose inactivated poliovirus vaccine; to evaluate the dose-specific immune responses; to assess mucosal immunity after a three-dose schedule of inactivated poliovirus vaccine; and to determine adverse events after vaccination with either fractional-dose or full-dose inactivated poliovirus vaccine.

Oral or written informed consent for the participation of the newborns was obtained from parents in accordance with ethical principles, including the Declaration of Helsinki. The study was approved by the Ministry of Health in Oman, the institutional review board of the Ministry of Health in Oman, and the ethics review committee of the World Health Organization (WHO) in Geneva and was carried out in compliance with...
Good Clinical Practice guidelines. GlaxoSmithKline donated the study vaccines, and Bioject provided the needle-free devices, disposables, and regulatory documents and assisted with the training of the study staff. Neither company had any role in the design of the study, the accrual or analysis of the data, or the preparation of the manuscript. All authors vouch for the completeness and accuracy of the data and analyses presented.

The field work of the study was conducted between March 1, 2007, and December 31, 2007, in five sites in Oman (Salalah, Dhofar Governorate; Sohar, North Batinah Governorate; Musanah and Rustaq, South Batinah Governorate; and Sur, Sharqiya Governorate).

STUDY DESIGN

Expectant mothers and prospective fathers were contacted during prenatal visits. They were provided information about the study and asked whether they were willing to participate. Newborns were eligible for participation if oral or written informed consent was obtained from the parents, if the infant’s Apgar score at 5 minutes was 9 or 10, if the infant’s birth weight was at least 2.5 kg, if the infant was healthy (not requiring hospitalization), and if the family was not planning to move out of the study area during the study period. Infants were excluded if a diagnosis or suspicion of immunodeficiency disorder in the infant or a family member was revealed.

Infants were randomly assigned to receive either the fractional-dose inactivated poliovirus vaccine (0.1 ml, representing one fifth of a full dose) or the full-dose inactivated poliovirus vaccine (0.5 ml) at 2, 4, and 6 months of age. Both vaccines were produced by GlaxoSmithKline and were formulated to contain at least 40 D-antigen units of poliovirus serotype 1 (Mahoney strain), 8 D-antigen units of poliovirus serotype 2 (MEF-1 strain), and 32 D-antigen units of poliovirus serotype 3 (Saukett strain). When the infants were 7 months of age, they were administered a challenge dose of monovalent type 1 oral poliovirus vaccine (GlaxoSmithKline) formulated to contain at least 10⁶ median cell-culture infectious doses (CCID₅₀) of Sabin poliovirus type 1. The vaccines were shipped under appropriate cold-chain conditions from the manufacturer to Muscat.²⁹

Inactivated poliovirus vaccine was administered either intradermally with the use of a needle-free device (Biojector 2000, Bioject) or intramuscularly with the use of an auto-disable syringe and needle. The needle-free device was approved by the Food and Drug Administration for intramuscular and subcutaneous administration and on a case-by-case basis for investigational intradermal administration with the use of a spacer.³⁰-³⁵ Parents were aware of the study-vaccination assignment of their children.

After vaccination, study personnel observed the infants for 30 minutes to monitor immediate adverse events. The infants were administered liquid paracetamol, and instructions were given to parents to administer 50 mg every 8 hours for 3 days. Infants were evaluated for adverse events through home visits conducted at 24 hours after each vaccination by qualified medical staff members who were aware of the study-vaccination assignments. In addition, a hospital discharge survey was conducted to capture all hospitalization events in the study population. All other routine antigens (diphtheria and tetanus toxoids, pertussis, Haemophilus influenzae type b, and hepatitis B) were administered concurrently, with the use of a pentavalent combination vaccine.

At 7 months of age, all the infants received a dose of monovalent type 1 oral poliovirus vaccine. Stool samples were collected before and 7 days after administration of the monovalent type 1 vaccine. Because one site stored the stool samples in the refrigerator instead of the freezer for some time, we excluded those samples from the analyses. Stool samples were analyzed according to WHO guidelines at the National Institute for Public Health and the Environment, Bilthoven, the Netherlands.

Blood specimens were collected at birth (cord blood) and at 2, 4, 6, and 7 months. An automated single-use heel-stick device (Tenderfoot, International Technidyne) was used to collect the blood specimens from the infant. After coagulation, the serum was separated, frozen, and stored at the study site (or at the central stores in the capital) at −20°C until shipment to the Centers for Disease Control and Prevention (CDC). The specimens were tested in triplicate with the use of modified neutralization assays for antibodies to types 1, 2, and 3 poliovirus by laboratory staff who were unaware of the vaccination group of the infants whose specimens they were analyzing. The initial dilution was a reciprocal titer of 8. Seropositivity was defined as a reciprocal titer of at least 8. Seroconversion was defined as an increase by a factor of 4 in the antibody titer over the
expected decline in the titer of maternally derived antibodies in a successive specimen. In addition, if an infant did not undergo seroconversion according to this definition, the infant was also evaluated for seroconversion after all three doses had been administered (at 2, 4, and 6 months) or after any two consecutive doses (doses administered at 2 and 4 months or at 4 and 6 months). The half-life of antibody decay was assumed to be 28 days. In the case of infants who were seronegative, a change to seropositive in a successive specimen was considered to indicate seroconversion.

At the end of the study, the parents of infants assigned to the fractional-dose group were administered a brief questionnaire that inquired whether they preferred a needle and syringe or a needle-free injection device for the administration of a vaccine.

STATISTICAL ANALYSIS

We calculated that with a minimum sample size of 139 infants in each of the two study groups, the study would have the power to determine the noninferiority of the fractional-dose inactivated poliovirus vaccine as compared with the full-dose inactivated poliovirus vaccine, with a noninferiority threshold of an absolute value of 20%, at a two-sided alpha level of 0.05 and a beta level of 0.10.

Statistical analyses were performed with the use of the R and SAS statistical software packages. Comparisons of the proportion of infants in each group who underwent seroconversion were performed with the use of Yates-corrected chi-square tests. The differences in the distribution of antibody titers were tested with the use of the Kolmogorov–Smirnov nonparametric method. We calculated the 95% confidence intervals around the median values.

RESULTS

STUDY POPULATION

A total of 400 parents consented to have their infants enrolled in the trial. Cord blood was collected from all 400 newborns. A total of 13 infants were withdrawn from the study between birth and the first vaccination visit at 2 months of age because the parents refused to have their infants continue in the study (12 infants) or because the family moved out of the study area (1). Another 14 were withdrawn or excluded during the remain-
order of the study period because of a protocol violation (12 infants, of whom 1 received an incorrect vaccine and 11 were replacements for other infants who had left the study and were therefore not allowed to be included in the protocol analysis), because the family moved out of the study area (1), or because an insufficient amount of serum was collected (1). A total of 373 infants (93.2%) completed all the study requirements (Fig. 1).

**Baseline Characteristics and Seroprevalence**

After random assignment to either the fractional-dose group or the full-dose group, the infants in the two groups did not differ significantly with respect to baseline characteristics, seroprevalence, or titers of poliovirus antibodies. Seroprevalence was 97.9% in the fractional-dose group and 98.4% in the full-dose group for type 1 poliovirus; 95.7% and 96.8%, respectively, for type 2 poliovirus; and 82.9% and 78.0%, respectively, for type 3 poliovirus (Table 1).

**Seroconversion**

The rates of seroconversion to types 1, 2, and 3 poliovirus after completion of the three-dose inactivated poliovirus vaccine schedule were 97.3%, 95.7%, and 97.9%, respectively, in the full-dose group, as compared with 100% for all serotypes in the fractional-dose group; the only significant difference was for seroconversion to type 2 (P = 0.01) (Table 2). Among infants who underwent seroconversion, there were significant differences in median titers according to serotype or study treatment (Table 2). At the end of the study, the overall median reciprocal titers in the fractional-dose group were less than half those in the full-dose group (Fig. 2). The dose-specific seroconversion rates according to treatment group are shown in Table 3.

The presence of maternally derived antibodies was a risk factor for failure to undergo seroconversion to all three poliovirus serotypes in the fractional-dose group, as compared with 100% for all serotypes in the full-dose group; the only significant difference was for seroconversion to type 2 (P = 0.01) (Table 2). Among infants who underwent seroconversion, there were significant differences in median titers according to serotype or study treatment (Table 2). At the end of the study, the overall median reciprocal titers in the fractional-dose group were less than half those in the full-dose group (Fig. 2). The dose-specific seroconversion rates according to treatment group are shown in Table 3.

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### Table 1. Baseline Characteristics of the Infants Enrolled in the Study, According to Study Group.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Fractional Dose (N = 187)</th>
<th>Full Dose (N = 186)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex — no./total no. (%)</td>
<td>94/187 (50.3)</td>
<td>98/186 (52.7)</td>
</tr>
<tr>
<td>Birth weight — kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>3.19</td>
<td>3.17</td>
</tr>
<tr>
<td>95% CI</td>
<td>3.12–3.29</td>
<td>3.10–3.23</td>
</tr>
<tr>
<td>Interval from birth to study vaccine administration — days</td>
<td>62</td>
<td>62</td>
</tr>
<tr>
<td>Type 1 poliovirus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seroprevalence at birth — %†</td>
<td>97.9</td>
<td>98.4</td>
</tr>
<tr>
<td>Reciprocal titer — median (95% CI)</td>
<td>228 (181–287)</td>
<td>325 (205–456)</td>
</tr>
<tr>
<td>Type 2 poliovirus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seroprevalence at birth — %†</td>
<td>95.7</td>
<td>96.8</td>
</tr>
<tr>
<td>Reciprocal titer — median (95% CI)</td>
<td>144 (91–181)</td>
<td>144 (114–228)</td>
</tr>
<tr>
<td>Type 3 poliovirus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seroprevalence at birth — %†</td>
<td>82.9</td>
<td>78.0</td>
</tr>
<tr>
<td>Reciprocal titer — median (95% CI)</td>
<td>29 (23–36)</td>
<td>23 (23–36)</td>
</tr>
</tbody>
</table>

* None of the differences between the groups were significant at the 0.05 level. CI denotes confidence interval. † Seroprevalence refers to a reciprocal antibody titer of 8 or higher.

**Poliovirus Excretion after Challenge Dose**

At 7 months of age, all infants received a challenge dose of monovalent type 1 oral poliovirus vaccine. Virus isolation data are summarized in Table 4. The stool excretion data presented here include data from 312 infants from three governorates. All the poliovirus isolates in this study were vaccine-related poliovirus. Before the challenge with monovalent type 1 oral poliovirus vaccine, a total of four infants excreted poliovirus (in the fractional-dose group, one infant excreted type 2 and one excreted type 3; in the full-dose group, one excreted a mixture of types 1 and 3, and one excreted type 2). At day 7 after administration of the monovalent type 1 oral poliovirus vaccine, 74.8% of the infants in the fractional-dose group excreted type 1 poliovirus, as compared with 63.1% in the full-dose group (P = 0.03).

**Adverse Events after Vaccination**

A total of 42 serious adverse events (all requiring hospitalization) were recorded in the study population — 18 in the fractional-dose group and 24
in the full-dose group (P = 0.40). The events were related to infectious causes (39 events, of which the vast majority were diarrhea or upper respiratory infection, with no significant differences between the groups), anemia (1), and falls (2). Five hospitalizations (11.9% of the events) occurred when the infants were between birth and 2 months of age, before the administration of any study vaccine. There were no significant between-group differences in serious adverse events. Other than the 42 hospitalizations, there were no adverse events of any degree of severity that were considered to have been related to participation in the study.

**Assessment of Treatment Preference**

The parents of infants enrolled in the study were administered a questionnaire during the last study visit. Of 187 eligible parents, 185 (98.9%) responded. When asked about their preference with respect to the method of administration of the next vaccination, 8 parents (4.3%) preferred vaccination with the use of needle and syringe, 172 (93.0%) preferred the needle-free device, and 5 (2.7%) expressed no preference.

**Discussion**

This trial in Oman represents a large-scale evaluation of fractional-dose inactivated poliovirus vaccine administered intradermally at 2, 4, and 6 months of age with the use of a needle-free device. Our findings suggest that fractional-dose inactivated poliovirus vaccine given intradermally with the use of a needle-free device results in rates of seroconversion to all poliovirus serotypes that are similar to those achieved with full-dose inactivated poliovirus vaccine given intramuscularly; however, the median titers were significantly lower in the fractional-dose group than in the full-dose group. In addition, after a challenge with monovalent type 1 oral poliovirus vaccine, a significantly higher proportion of infants in the fractional-dose group than in the full-dose group excreted virus. Both routes of administration were well tolerated, and no adverse events were attributable to the trial intervention.

These results confirm earlier findings that suggested that intradermal administration of fractional doses could result in high seroconversion rates. Although the median titers in both groups were high, the median titers in the fractional-dose group were less than half those in the full-dose group. These titers were achieved despite a routine policy in Oman of providing vaccinated infants with paracetamol, a drug that was shown in one study to blunt the effect of the vaccine. Since any detectable titer would be expected to prevent paralytic disease, and the median titers in the fractional-dose group are similar to those reported in previous studies of full-dose inactivated poliovirus vaccine, it is unlikely that the differences in titer between the two groups in our study would have practical implications.

A somewhat higher proportion of infants in
the fractional-dose group than in the full-dose group excreted poliovirus type 1 after the administration of a challenge dose of monovalent type 1 oral poliovirus vaccine. The practical implications of this finding are unclear.

Nevertheless, in terms of antigen content used (a factor that greatly affects the production cost), three fractional doses add up to 0.3 ml, representing three fifths of a full dose. Even if we were to aim for 100% seroconversion with four fractional doses instead of three full doses, the cost per infant vaccinated with inactivated poliovirus vaccine would be less than $3 with the fractional-dose vaccine, as compared with $9 for the full-dose vaccine, a savings of $6 per vaccinated infant. The cost for a four-dose fractional inactivated poliovirus vaccine would still be substantially higher than that of a three-dose trivalent oral poliovirus vaccine schedule (which is approximately $0.45). However, in order to achieve in the developing world levels of seroconversion with trivalent oral poliovirus vaccine that are the same as those achieved with inactivated poliovirus vaccine, supplemental doses of trivalent oral poliovirus vaccine

<table>
<thead>
<tr>
<th>Type 1 poliovirus</th>
<th>Seroconversion Fractional Dose</th>
<th>Full Dose</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before first vaccination at 2 mo</td>
<td>3/187 (1.6)</td>
<td>4/186 (2.2)</td>
<td>NS</td>
</tr>
<tr>
<td>After vaccination</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose 1</td>
<td>19/184 (10.3)</td>
<td>40/182 (22.0)</td>
<td>0.005</td>
</tr>
<tr>
<td>Dose 2</td>
<td>110/165 (66.7)</td>
<td>125/142 (88.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dose 3</td>
<td>48/55 (87.3)</td>
<td>17/17 (100)</td>
<td>NS</td>
</tr>
<tr>
<td>Other†</td>
<td>2/7 (28.6)</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>None</td>
<td>5/184 (2.7)</td>
<td>0/182 (0)</td>
<td>NS</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Type 2 poliovirus</th>
<th>Seroconversion Fractional Dose</th>
<th>Full Dose</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before first vaccination at 2 mo</td>
<td>2/187 (1.1)</td>
<td>6/186 (3.2)</td>
<td>NS</td>
</tr>
<tr>
<td>After vaccination</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose 1</td>
<td>31/185 (16.8)</td>
<td>57/180 (31.7)</td>
<td>0.001</td>
</tr>
<tr>
<td>Dose 2</td>
<td>103/154 (66.9)</td>
<td>106/123 (86.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dose 3</td>
<td>43/51 (84.3)</td>
<td>17/17 (100)</td>
<td>NS</td>
</tr>
<tr>
<td>Other†</td>
<td>0/8 (0)</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>None</td>
<td>8/185 (4.3)</td>
<td>0/180 (0)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Type 3 poliovirus</th>
<th>Seroconversion Fractional Dose</th>
<th>Full Dose</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before first vaccination at 2 mo</td>
<td>1/187 (0.5)</td>
<td>3/186 (1.6)</td>
<td>NS</td>
</tr>
<tr>
<td>After vaccination</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose 1</td>
<td>17/186 (9.1)</td>
<td>82/183 (44.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dose 2</td>
<td>117/169 (69.2)</td>
<td>93/101 (92.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dose 3</td>
<td>48/52 (92.3)</td>
<td>8/8 (100)</td>
<td>NS</td>
</tr>
<tr>
<td>Other†</td>
<td>0/4 (0)</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>None</td>
<td>4/186 (2.2)</td>
<td>0/183 (0)</td>
<td>NS</td>
</tr>
</tbody>
</table>

* Seroconversion was defined as an increase by a factor of 4 in the antibody titer over the expected value given the decline in the titer of maternally derived antibodies of a successive specimen. NS denotes not significant.
† Other indicates seroconversion after doses 1 and 2, 2 and 3, or 1, 2, and 3.
would be needed, thus narrowing the differences in vaccine costs between the two approaches.

The intradermal administration of fractional doses of inactivated poliovirus vaccine appears to be safe and preferred by parents and health care providers. A questionnaire administered to parents of infants in the fractional-dose group reported a strong preference for this route of administration. When the parents were asked why they preferred intradermal administration, the vast majority of parents responded with a comment that “the baby does not cry.” The number of hospitalizations recorded during the course of our study probably reflects a sensitive health care system that errs on the side of being conservative and hospitalizes infants with minor ailments.

Our study has several limitations. First, we did not evaluate whether a fractional-dose inactivated poliovirus vaccine given intramuscularly would have yielded results similar to those seen with the fractional-dose given intradermally. Second, although we captured serious adverse events, we were not able to capture local or systemic adverse events that occurred after the home visit that took place 24 hours after the vaccination (unless these resulted in hospitalization); in another study, a combination of redness and induration (mostly <5 mm) developed in some infants after intradermal administration of the vaccine.46 Finally, we cannot exclude the possibility that some infants enrolled in the study were exposed secondarily to trivalent oral poliovirus vaccine, which is used routinely in Oman. However, as indicated by both seroconversion data between birth and 2 months of age and the prechallenge viral isolation data, the level of such exposure was probably low and would have affected both study groups equally and thus should not substantially affect the interpretation of the results.

Our study shows that intradermal administration of a fractional-dose inactivated poliovirus vaccine could serve as a dose-sparing strategy when used in a primary routine vaccination schedule in which doses are administered at 2, 4, and 6 months of age. Other approaches to lowering the production cost of vaccination (i.e., optimization of the production process, the use of alternative inactivation agents, and the use of adjuvants) or decreasing the number of doses of inactivated poliovirus vaccine (e.g., a two-dose schedule) should continue to be evaluated.

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Potency data were provided by GlaxoSmithKline and the national regulatory authority in Belgium. GlaxoSmithKline donated the study vaccines and Bioject, Portland, Oregon, provided the needle-free devices, disposables, and regulatory documents and assisted with the training of the study staff.

We thank the study staff from the field sites of Rustaq (Musannah), Sohar, Salalah, and Sur hospitals and polyclinics; the Oman families who participated in this study; Mr. Salem Al Mahrooji and the staff from the Expanded Program on Immunization and Central Vaccine Store in the Department of Communicable Disease Surveillance and Control; Debbie Moore, Barbara Anderson, and Naomi Dyhahl-Sissokko at the Centers for Disease Control and Prevention, Atlanta, for performing the serology tests; and Sabine van der Sanden, Ran Zhang, Gokhan Uslu, Edin Jusuc and Ron Altena at the National Institute for Public Health and the Environment, Bilthoven, the Netherlands, for conducting the stool isolation.

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**Table 4. Excretion of Poliovirus Serotypes and Nonpolio Enteroviruses, before and after a Challenge with Monovalent Oral Poliovirus Vaccine, According to Study Group.**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Type 1 Poliovirus</th>
<th>Type 2 Poliovirus</th>
<th>Type 3 Poliovirus</th>
<th>Nonpolio Enteroviruses</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>number/total number (percent)</td>
<td>number/total number (percent)</td>
<td>number/total number (percent)</td>
<td>number/total number (percent)</td>
<td>number/total number (percent)</td>
</tr>
<tr>
<td>Before challenge</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fractional dose</td>
<td>0/156 (0.6)</td>
<td>1/156 (0.6)</td>
<td>27/156 (17.3)</td>
<td>127/156 (81.4)</td>
<td></td>
</tr>
<tr>
<td>7 Days after challenge</td>
<td>116/155 (74.8)</td>
<td>1/155 (0.6)</td>
<td>7/155 (4.5)</td>
<td>31/155 (20.0)</td>
<td></td>
</tr>
<tr>
<td>Full dose</td>
<td>1/159 (0.6)</td>
<td>1/159 (0.6)</td>
<td>28/159 (17.6)</td>
<td>128/159 (80.5)</td>
<td></td>
</tr>
<tr>
<td>Before challenge</td>
<td>99/157 (63.1)</td>
<td>1/157 (0.6)</td>
<td>0</td>
<td>43/157 (27.4)</td>
<td></td>
</tr>
<tr>
<td>7 Days after challenge</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* All the poliovirus isolates in this study were vaccine-related poliovirus.
† There was a significant difference between the groups in the proportion of infants who excreted type 1 poliovirus at 7 days after the challenge (P=0.03).
‡ One infant excreted both type 1 and type 3 poliovirus.
§ One infant excreted both type 1 and type 2 poliovirus.
References


38. Biedenbender RD, Petjeian S, Dorsch K, et al. Reactogenicity following influenza vaccination by double-blind (DB), randomized placebo controlled (RPC) intradermal (ID) needleless jet injector (Biojet) compared to intramuscular (IM) injection in institutionalized frail elderly volunteers. Presented at the American Geriatrics Society Annual Scientific Meeting, Washington, DC, May 8-12, 2002 (poster).


