Humoral Immunity in Two Groups of Children Induced by Two Supplemental Doses of Oral Polio Vaccine, and in the Umbilical Cord Blood

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Summary

The immunogenicity of mass campaign doses of oral poliovirus vaccine (OPV) was evaluated by measuring serum neutralizing antibodies (NAs) in two groups of children. The first group included 215 children before and after two mass vaccination campaing conducted in 1994's national immunization days (NIDs) and the second, included 420 children after receiving two supplemental doses of OPV in 1996. In order to measure the NAs against poliovirus types, 1,2, and 3 transferred to the neonates 412 sera collected from umbilical cord blood and tested. Precampaign seroprevalences to the virus types were compared with those of the postcampaign in the first group. The titers of NAs against all three types of the virus had raised significantly in postcampaign serum samples. The NA prevalence against poliovirus types was also high in the serum samples collected from the second group. Four weeks after the second supplementary dose of OPV, 96%, 94% and 91% of these children had immune titers of NAs against poliovirus types 1,2 and 3 respectively. Of 412 umbilical cord blood samples, 82.3%, 80.8% and 68.9% showed NAs at dilution of >1:8 against poliovirus types 1,2, and 3 respectively. These findings suggest that NIDs should be continued to maintain the level of herd immunity at highest standard level, among susceptible and at risk hosts, against all three types of the virus.

Key words: polipvirus, neutralizing antibodies, National Immunization Days, seroprevalence.

Introduction

Poliomyelitis (polio) is the major cause of lameness in some developing countries. World Health Organization (WHO) estimates ~ 80.000 cases occurred in 1995(CDC 1994). Poliomyelitis occurs worldwide, except in areas where the virus has been eliminated, such as Western Hemisphere and most industrialized countries (CDC 1994). In 1988, the World Health Assembly (WHA) passed resolution WHA 41.28, which committed the WHO to the global eradication of poliomyelitis by the year 2000 (de Quadros *et al* 1992). In 1994 Iran adopted the goal of elimination of polio from the country by year 2000. Following the implementation of the three basic eradication strategies, including the achievement and maintenance of high routine immunization coverage with OPV, the use of supplemental immunization activities, including national immunization days and the development of sensitive systems of epidemiological and laboratory surveillance, including the use of the standard case definition, cases of polio in the country decreased rapidly. In order to eradicate the wild virus it is necessary to continue nationwide vaccination to hold the immunity of susceptible individuals against all three types of the poliovirus at highest standard level.

This study was designed to measure neutralizing antibody titers against poliovirus types 1, 2, and 3 among three different groups of populations consisting of 412 pregnant women residing in Tehran, 215 children from two villages of Mianeh, and 420 children residing in west Azarbyejan. Our findings are relevant to the need for continuing country wide vaccination campaigns as an important strategy of the polio eradication.

Materials and Methods

Source of samples. Three different sets of serum samples were studied. (i) 412 sera were collected from umbilical cord blood of pregnant women who had been referred to two hospital's maternity wards in Tehran in 1993, (ii) 215 children in two villages of Mianeh, east Azarbayejan province, who had received two supplemental doses of oral poliovirus vaccine on NIDs (15th April and 13th May 1994) were chosen as the

first group of the vaccinated children in this study. Paired sera were collected from them just before administration of the first vaccine and 4 weeks after the second, and (iii) 420 single serum samples were collected from children residing in the west Azarbayejan during mass vaccination conducted in NIDs in 1996. The sera were collected 4 weeks after the second supplemental OPV vaccine.

To examine maternal immunity transferred to neonates borne to the mothers under study, titers of NAs to poliovirus types 1, 2 and 3 were determined. To determine the immunogenicity of two mass campaign doses of OPV, the seroprevalence and titers of NAs to poliovirus types 1, 2 and 3 before the mass campaign were compared with those after the campaign in the first group of the children. To determine the herd immunity of the second group of the children, titers of NAs to the viruses were determined in sera collected after the second round of mass vaccination.

Serology. For determination of NA titers against poliovirus types 1, 2 and 3, all samples were first heat inactivated at 56C and then were tested in triplicate at the Virology Department, Tarbiat Modarres University, Tehran. A microneutralization test using serum dilutions ranging from 1:2 to 1:128 was used test was conducted at 37°C. Sera were considered to be positive if NAs were detected at dilution ?1:8.

Viruses. Attenuated poliovirus types 1, 2 and 3, received from Razi Institute were adapted to HeLa cells and 100 $TCID_{50}$ of each virus was used in the study. The cells were grown in minimum essential medium (MEM) supplemented with 5% inactivated calf serum.

Hyperimmune sera. Positive control serum against each type of the virus was prepared in rabbit.

Vaccines. Both mass campaign OPV doses were prepared at Razi Institute.

Results

Immune status of umbilical cord blood against the virus types. Table 1 presents NA titers against three poliovirus types detected in the umbilical cord blood samples. As shown the titers are distributed within the range of <1:2 to 1:32. Overall

seroprevalence of acceptable NA titers against types 1, 2 and 3 of poliovirus were 82.3%, 80.8% and 68.7% respectively.

Immune status 4 weeks after receipt of 2 supplemental doses of OPV among the first group of children. Of 215 children in the study population before vaccination, only 90.5%, 84%, and 73.5% had acceptable titer (≥8) of neutralizing antibody against types 1, 2 and 3 of the virus respectively. The rates of seropositiveness 4 weeks after second vaccination rose to 99.5%, 100%, and 91.9% against poliovirus types 1, 2 and 3 respectively. Seroconversion rates for poliovirus types 2 and 3 were higher than that for type 1 poliovirus. Reciprocal of NA titers against poliovirus types 1, 2 and 3 are written for blood samples collected just before the first vaccination and 4 weeks after second one, separately.

Table 1. *NA titers against poliovirus types 1, 2 and 3 among the umbilical cord blood samples*

Reciprocal Of NA titers	Type 1 Poliovirus	Type 2 poliovirus	Type 3 Poliovirus
<2	1.46	3.88	9.22
2	2.91	3.15	2.42
4	13.34	12.13	19.66
8	33.73	37.62	34.46
16	31.06	27.18	24.27
32	17.47	16.01	9.95
GM	10.74	51.90	7.57
SD	2.14	8.60	2.51

The rates of the children having no detectable Nas against the poliovirus types 1, 2 and 3 before vaccination were 1.5%, 4.7% and 12.7%, respectively. These rates were converted to zero after second supplemental vaccination. Rates of secondary increase in antibody titers after second vaccination in the children are recorded for all three poliovirus types (Table 2).

Seroprevalences among the second group of children who had received two supplemental doses of OPV during 1996. Table 3 summarizes the neutralizing antibody titers against poilovirus types 1, 2 and 3 among the second group of the

Table 2. *Neutralizing titers of paired sera against three poliovirus types after the second supplemental doses of OPV in the first group of children*

Reciprocal of NA titers	Prevaccination			Postvaccination		
	Type 1	Type 2	Type 3	Type 1	Type 2	Type 3
<2	1.50	4.70	12.70	0.00	0.00	0.00
2	3.60	3.30	3.30	0.00	0.00	5.00
4	4.40	8.00	10.50	0.50	0.00	3.00
8	38.50	37.50	33.50	1.40	2.10	7.10
16	38.20	34.30	32.90	13.30	15.50	32.20
32	12.00	11.50	6.10	41.70	46.40	42.70
64	1.80	0.70	1.00	36.00	30.30	10.00
128	0.00	0.00	0.00	7.10	5.70	0.00
GM	11.40	9.99	7.62	39.97	37.47	20.44
SD	2.05	2.28	2.68	1.83	1.79	2.24

children who had received two supplemental doses of polio vaccine on national immunization days in 1996. Of the 420 children 4%, 6%, and 9% did not show detectable neutralizing antibodies against poliovirus types 1, 2 and 3 respectively. As shown in the table 4 96%, 94%, and 91% of the children had neutralizing antibodies at >1:8 serum dilutions against the viruses respectively.

Table 3. *Neutralizing antibody titers against three poliovirus types among the second group of children receiving two supplemental doses of polio vaccine*

Reciprocal Of NA titers	Type 1	Type 2	Type 3
<4	4	6	9
8	6	8	11
16	9	6	8
32	49	60	61
64	32	20	11
GM	30.8	26.7	21.82
SD	2.2	2.3	2.50

Discussion

In May 1988, the WHA committed the WHO to achieving the goal of global eradication of poliomyelitis by the year 2000 (de Quadros *et al* .1992). From 1988 through 1995 reported cases of paralytic polio declined by 80%, from 35,251 cases in 1988 to 7024 cases in 1995 (CDC 1994), preliminary data for 1996 suggested a further decrease by >50% compared with 1995. One of the key strategies for polio eradication is the administration of supplemental doses of OPV during nationwide mass campaigns known as NDIs (CDC 1994). NIDs provide two supplemental doses of OPV to all young children (generally those <5 years of age), regardless of their previous immunization status. The two rounds of NIDs are conducted during the low season for poliovirus transmission, with an interval of 4-6 weeks between rounds.

Vaccination against poliomyelitis in Iran was started in 1967. At the beginning the vaccine was only administered to children who were referred to the treatment and health centers, and vaccine coverage was not remarkable. Nationwide vaccination against the disease started in 1985, using OPV containing all three types of attenuated virus, and since then it has been regularly done under expanded program on immunization (EPI). Iranian ministry of health, treatment, and medical education recommends that primary immunization of infants begin at birth. The second, third, and fourth doses should be given at 1½ month intervals thereafter, and a fifth dose at 1¼ years of age which is followed by sixth dose given at 6 years of age, just before entering the primary school. The above immunization strategy had resulted in more than 85% coverage of children under 6 years of age, with remarkable reduction in rate of incidence of poliomyelitis.

Iran adopted mass immunization campaigns called national immunization days (NIDs) in 1994, for which 500,000 members of the Islamic youth movement took OPV to every house in the country, in on order to stop wild poliovirus transmission. From 1994 through 1997 four rounds of supplemental vaccination of all Iranian children <5 years were done. Besides the above mentioned campaigns a sensitive surveillance system capable of identifying cases of polio has been done in the country. Data obtained from this surveillance system showed that there was only one case identified in 1995. In 1996 and 1997 there were a few and two cases,

respectively. Epidemiological study indicated that none of the cases originated from Iran.

Iran is determined to interrupt the circulation of wild polioviruses. This goal can be achieved successfully if regular vaccination covering all children >5 years of age is done. On the other hand it must be shown that the vaccination campaigns result in production of solid immunity against all three types of the poliovirus.

This study was done to measure the level of poliovirus neutralizing antibodies in pregnant women, in order to see what the amount of passive immunity transferred to infants is. We were also going to evaluate the results of NIDs of 1994 and 1996. As shown in the results, 82.26%, 80.84%, and 68.7% of the women had neutralizing antibodies in their sera at dilution of >1/8 against types 1, 2 and 3 of the virus, respectively. According to the information we must consider the probability of neutralization of the viruses present in the OPV given at birth and thereafter, by the maternal immunity transferred by milk (Hinman 1987). It is clear that repetition of vaccination at regular intervals will greatly reduce this probability.

In our study, seroprevalences and neutralizing antibody titers among the first group of immunized children under study, who had received two supplemental doses of OPV during 1994 mass vaccination campaigns were higher for all three poliovirus types, particularly type 3, that the levels among those before receiving the supplemental doses. It was also shown that seroprevalence and NAs against all poliovirus types were high among the second group of children.

Our findings and those from studies conducted in Jordan and Morocco (Hull *et al* 1994, Hull *et al* 1997) support current WHO recommendations that mass vaccination campaigns with OPV should be implemented biannually in all remaining polio-endemic countries. There has been a rapid acceleration in the number of countries with endemic polio that have conducted NIDs. Mauritania and Algeria successfully implemented NIDs in1995. Seven African countries (with mature immunization programs) planned to conduct NIDs in 1996 (Melnick 1996). The remaining countries have started implementing NIDs in 1997 (Melnick 1996). According to countrywide activities conducted in the Americas (Okwo *et al* 1997, Richardson *et al* 1995, Reichler 1997, WHO/EPI/GEN 1995) and what is being done in many other

countries in the world, poliomyelitis can be eradicated using a series of well-defined and effective strategies.

References

Centers for Disease Control and Prevention. (1994). Progress toward global eradication of poliomyelitis, 1988-1993. *Morbidity and Mortality Weekly Report* 43:499-503.

de Quadros, C.A., Andrus, J.K., Olive, J.M., de Macedo, C.G. and Henderson, D.A..(1992). Polio iradication from the Western Hemisphere. *Annual Review of Public Health* 13:239-252.

Hinman, A.R. (1987). The case for global eradication of poliomyelitis. *Bulletin of World Health Organization* 65:835-840.

Hull, H.F., Ward, N.A. and Hull, B.P. (1994). Paralytic poliomyelitis: seasonal strategies, disappearing disease. *Lancet* 343:1331-1337.

Hull, H.F., Birmingham, M.E., Melgaard, B. and Lee, J.W. (1997). Progress toward global polio eradication. *Journal of Infectious Diseases* 175(Supp. 1):4-9.

Melnick, J.L. (1996). Enteroviruses. In:B.N.Fields *et al* (Eds.). *Fields Virology* vol.2. (3rd edn). Lippincott-Raven Publishers, Philadelphia.

Okwo-Bele, J.M., Lobanov, A. (1997). Overview of poliomyelitis in the African region and current regional plan of action. *Journal of Infectious Diseases* 175(Suppl.):10-15.

Richardson, G., Linkins, R. and Eames, M. (1995). Immunogenisity of oral poliovirus vaccine adminsistered in mass campaigns versus routine immunization programs. *Bulletin of World Health Organization* 73:769-777.

Reichler, M.R. (1997). Increased immunogenicity of oral poliovirus vaccine administered in mass vaccination campaign compared with the routine vaccination program in Jordan. *Journal of Infectious Diseases* 175(Suppl.):198-204.

World Health Organization, Field Guide. Background. WHO/EPI/GEN/95.1, 1995.