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CLINICAL TRIAL OF THE OKA STRAIN OF LIVE ATTENUATED VARICELLA VACCINE ON HEALTHY CHILDREN

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Clinical and serological follow-up studies were made on 257 healthy children who had received live varicella vaccine (strain Oka) in Showa Hospital. Good antibody responses were shown with a seroconversion rate of 98.4% (253/257) by the immune adherence hemagglutination test. Mild adverse reactions were observed in 11 of the vaccinated children. During observation periods of 6 months to 4 years, 6 of the 253 children who were successfully vaccinated contracted mild varicella, while all 4 vaccinees who showed no primary immune response contracted mild to moderate clinical varicella. It is concluded that this vaccine is highly immunogenic and causes few clinical reactions in normal children.

INTRODUCTION

Recently, attenuated strains of varicella-zoster virus (VZV) have been developed and tested for possible use as vaccines in humans (Takahashi et al., 1975; Neff et al., 1981). We previously reported the use of a live varicella vaccine (Oka strain) for children with underlying diseases such as leukemia and the nephrotic syndrome (Asano et al., 1977; Ozaki et al., 1978). Recently, the morbidity and mortality of varicella in normal individuals were found to be higher than thought previously (Preblud, 1981; Fleisher et al., 1981), and from our clinical experience we have the impression that the need for vaccination of guardians of children is gradually increasing. Since 1979, we started clinical trials of vaccination on healthy children with live varicella vaccine (Oka strain) at the vaccine clinic of Showa Hospital in Aich, Japan. This paper reports the results of studies with the Oka strain of varicella vaccine in Showa Hospital.

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VACCINE AND VACCINATION

The vaccine used was derived from the Oka strain of VZV (Takahashi et al., 1975). The immunizing dose was 250 plaque forming units (PFU) (Lot No. 7905) or 500 PFU (Lot No. 7912–7914) per child given subcutaneously. At the time of vaccination, the children ranged from 1 to 15 (3.8±2.7) years old, most being under 7 years old. They were in good health and had no underlying disease. All had a negative history of varicella and herpes-zoster. Informed consent was obtained from the parents of vaccinees before immunization.

SEROLOGIC RESPONSES AFTER VACCINATION

Two hundred and fifty-seven seronegative healthy children were immunized in the hospital during a 4-year period. Blood samples for serological study were taken before and 4 weeks after the vaccination. Antibodies were measured by a immune adherence hemagglutination (IAHA) method as described by Gershon et al. (1976). The results are summarized in Table 1, and the overall seroconversion rate was 98.4% with a geometric mean titer (GMT) (log 2) of 4.02±1.32.

CLINICAL REACTIONS AFTER VACCINATION

Clinical observations were made daily by the mothers for 20 days after vaccination. Peak increases in body temperature during this observation period, which could not be explained by another illness, were thought to be vaccine-related. Temperatures of 37.8 C to 39.7 C were seen in 11 of 257 (4.3%) vaccinees (Table 2); fever developed 8 to 19 (13.9±5.0) days after vaccination, and lasted less than 3 days. None of the 11 children had an eruptive episode.

CLINICAL FOLLOW-UP OF THE VACCINEES

For evaluation of the protective efficacy of the

TABLE 1. *Serologic responses after immunization with varicella vaccine (strain Oka) measured by the IAHA test*

Vaccine lot No.	No. of vaccinees	Seroconversion rate	GMT±SD (log 2)
7905	46	45/46 (97.8%)	4.11±1.97
7912	75	74/75 (98.7%)	3.62±0.91
7913	82	80/82 (97.6%)	3.9 ±1.37
7914	54	54/54 (100%)	4.69±1.54
Total	257	253/257 (98.4%)	4.02±1.32

TABLE 2. *Clinical reactions of 11 febrile cases after vaccination*

Case	Age	Sex	Onset of fever (Days after vaccination)	Duration of fever (Maximum temp. C)	Eruption	IAHA antibody titer Pre/Post (4 wk)
1	2	F	19	2 days (38.6 C)	(−)	<2/16
2	1	F	17	1 day (38.5 C)	(−)	<2/16
3	2	M	9	1 day (38.1 C)	(−)	<2/8
4	6	M	19	2 days (37.8 C)	(−)	<2/8
5	2	M	16	3 days (38.8 C)	(−)	<2/8
6	4	M	9	2 days (39.7 C)	(−)	<2/8
7	2	M	13	3 days (38.0 C)	(−)	<2/16
8	8	M	16	1 day (37.8 C)	(−)	<2/256
9	2	M	8	2 days (38.4 C)	(−)	<2/128
10	3	M	15	1 day (38.5 C)	(−)	<2/8
11	2	F	12	1 day (39.3 C)	(−)	<2/16

TABLE 3. *Contraction of natural disease after contact with varicella patients*

Type of exposure	No. of vaccinees	No. of children who contracted varicella	Attack rate (%)
Family	11	2	18.2
Indoor[a]	72	4(1)[c]	5.6
Outdoor[b]	32	0	0
Unknown	115	4(3)	3.5
Total	230	10(4)	4.3

[a] Children were exposed to VZV in their own class in kindergarten or primary school, or in their playmate's house.

[b] Contact with varicella patients outside the playmate's house or school.

[c] Numbers in parentheses indicate numbers of children in whom primary vaccination was unsuccessful.

varicella vaccine, a questionnaire survey was made on 230 of 257 vaccinees who had been inoculated with the vaccine 0.5 to 4.0 (2.2 ± 1.2) years earlier. The results of the follow-up study are shown in Table 3. In all, 10 children developed varicella during this observation period, and data on them are shown in Table 4. The 4 vaccinees who showed no primary response to the vaccine all developed varicella within 1 year after vaccination (cases Nos. 7 to 10 in Table 4). After close contact with varicella patients in the family, 2 of 11 children showed mild clinical features of varicella (cases Nos. 4 and 5 in Table 4). In addition, 3 children developed the disease after indoor contact with varicella patients, and 1 after contact of unknown type (Table 4). Thus only 6 vaccinees who showed antibody responses after vaccination contracted varicella (cases Nos. 1 to 6 in Table 4), and their clinical symtoms were mild.

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TABLE 4. *Summary of 10 cases of varicella infection after vaccination*

Case	Age at vaccination (years)	Sex	Interval between vaccination and onset of varicella	Clinical course	Primary antibody response	Type of contact with varicella patient
1	5	M	6 mo	Mild	+	Unknown
2	2	M	10 mo	Mild	+	Indoor
3	3	M	13 mo	Mild	+	Indoor
4	1	M	14 mo	Mild	+	Family
5	7	F	35 mo	Mild	+	Family
6	1	M	7 mo	Mild	+	Indoor
7	4	F	10 mo	Moderate	−	Unknown
8	5	F	6 mo	Mild	−	Indoor
9	2	F	3 mo	Mild	−	Unknown
10	5	F	6 mo	Mild	−	Unknown

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