ORIGINAL ARTICLE

Varicella Antibody in Healthy Children

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ABSTRACT Varicella is the most contagious viral exanthematous disease, which has a variable clinical course. We studied a seroepidemiological study on varicella antibody in 350 healthy children at Department of Child Health, Medical School, University of Indonesia, Dr. Cipto Mangunkusumo Hospital, Jakarta; from May to July 1998. The aim of this study was to get figures of varicella antibody in healthy children which can be used as a baseline data in the decision of recommendation in varicella vaccination. Subjects were 1-12 years old children with no history of varicella infection or immunization. The varicella antibody was determined by using Elisa assay (Enzygnost test). Among 350 healthy children, 42.9% were males; they were divided into 3 age groups: 1-3, 4-7 and 8-12 years. Fourty two children (11.1%) had seropositive varicella antibody (above protective level 0.2 mIU/ml). The prevalence of subclinical varicella significance increased with increasing age. Subjects with clinical or subclinical varicella had the same figure of age specific prevalence. The mean varicella antibody in each age group was almost similar. The minimum varicella antibody titer was quite similar between 1-3 and 4-7 age group, but not in 8-12 age group. Forty one percent had history of varicella contact, older chiildren had more history of contact. **[Paediatr Indones 1999; 39:1-7]**

Introduction

Varicella-zoster virus (VZV) belongs to the herpes virus group which causes varicella and herpes zoster. Varicella or chickenpox is the primary disease of VZV infection commonly occurs in childhood; while herpes zoster or shingles is the reactivation of latent period of VZV infection, commonly attacks adults.[1] Varicella-zoster virus infection is the most contagious viral infectious disease, which has a variable clinical course. In general the variability of clinical manifestations in viral infection is due to host-agent-environment interaction. Immuno-compromized children and newborn babies are

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prone to have severe infection. On the contrary, asymptomatic or subclinical VZV infection is possible in healthy children who live in endemic area.[2]

The age specific prevalence increases with increasing age; the highest prevalence of VZV infection in children is in school age group.[1,2] Varicella in children could manifest from a mild disease to most serious complication of VZV infection such as congenital varicella due to intrauterine transmission.[3] Some experts recommend to give varicella vaccine in children based on some reasons, such as prolonged school absence (about 5-6 days), higher medical cost, cosmetic problems due to skin scarring and to prevent the congenital varicella.[4] Every country recommends the vaccination program based on the epidemiological data of the disease, concerning reducing the sequelae and cost-benefit calculation.[5] Expanded program on immunization (EPI) created by WHO does not include varicella vaccine. The problem is that varicella vaccine is available in our country, although when the right time to give this vaccine still controversial.

The objective of this study was to get figure of varicella antibody in healthy children. The results of this study will benefit as a baseline data in making the decision for varicella vaccine recommendation in Indonesian children.

Methods

This was a sero-epidemiological survey of VZV antibody on 350 healthy children at Department of Child Health, Medical Faculty University of Indonesia, Cipto Mangunkusumo Hospital, Jakarta. The period of study was from May 3 to July 22, 1998. This study was a part of multicenter study on the evaluation of reactogenicity and safety of one dose live attenuated varicella vaccine (Oka-strain) and evaluation of immunogenicity (to be reported separately). Subjects included in the study were healthy children, 1-12 years old, who had no history of varicella infection or immunization. History of varicella infection was taken from their parents by questionnaire. They were divided into 3 age groups: 1-3, 4-7 and 8-12 years. Varicella antibody titer was examined in Prodia Laboratory, Jakarta, by using ELISA method (Enzygnost test).

Results

Among 350 healthy children enrolled in this survey, 42.9% were males and 57.1% were females. The majority (more than 80%) of the mothers graduated from high school, while the rest were equally divided into the lower and the higher education level. Forty two children (11.1%) had seropositive VZV antibody above protective level (0.2 mIU/ml). The proportion of 1-3 year age group was less than that older age groups, while 4-7 and 8-12 age group had same proportion. See Table 1.

Table 1. Serology profile of VZV antibody

Age group (years)	Seropositive		Seronegative		Total
	n	%	n	%	
1 - 3	3	2.5	113	97.5	116
4 - 7	15	11.8	112	88.2	127
8- 12	21	19.6	86	80.4	107
Total	39	11.1	312	88.9	350

The chance to have subclinical varicella infection was higher with increasing age, although the mean VZV antibody in each age group was almost similar, as shown in Table 2. The minimum level of VZV antibody titer was quite similar in 1-3 and 4-7 age group, but not in 8-12 age group. In contrast, the maximum level of VZV antibody titer in 4-7 year age group (3425 mIU/ml) and in 8-12 year age group (2994 mIU/ml) was higher than that in 1-3 year age group.

Table 2. Varicella zoster antibody

Age group (years)	Antibody titer (mIU/ml)			Total cases n=39
	mean	min	max	
1 - 3	1738	225	1995	3
4 - 7	1276	392	3425	15
8 - 12	1162	96	2994	21

Re-confirmation to history of varicella contact in seropositive antibody group was taken from their mothers. As many as forty-one percent of all subjects had a history of varicella contact. Table 3 shows that the chance to have varicella contact increased with increasing age; i.e., roughly, compared with those children of the 1-3 year age group, history of varicella contact was 5 and 10 times higher in 4-7 year group and 8-12 year group, respectively.

Table 3. History of varicella contact

Varicella contact	Age group (years)			Total	
	1-3	4-7	8-12	n	%
Yes	1	5	10	16	41.0
No	2	10	11	23	59.0
Total	3	15	21	39	100

Discussion

Age specific prevalence

The varicella prevalence in Indonesia at present time is almost similar to the situation in England or USA 10-20 years ago. The age specific prevalence in 0-4 year age group reported from United States,[2] England,[1] and Singapore[6] was 18%, 15%, and 4%, respectively. The question is whether the age prevalence of varicella infection in tropical countries younger than that in subtropical countries.

Graham[7] in a sero-epidemiology study in Yogyakarta reported that in 4 and 9 year old group had 30% and 48% positive varicella antibody, respectively. Data of varicella cases recorded at the Outpatient Clinic of Department of Child Health Cipto Mangunkusumo Hospital, Jakarta[8] showed that the proportion of varicella in infants was 17.9%, increased twice in 1-4 year age group, while in 5-14 year age group the proportion was and almost half of all cases (Table 4). Similar increase of proportion of varicella patients with increasing age was also reported from several hospitals in Indonesia (Table 5).[9]

Subclinical varicella infection

After the maternal antibody disappears in around one year of life, children one year and older are prone to have varicella infection. Our data showed that the chance to have varicella infection in 1-3 age group was less than that older age groups (Table 1). Among 116 cases of 1-3 age group, 2.5% had subclinical varicella infection with high antibody titer. The prevalence of subclinical varicella increased significantly in older age groups. It was shown that either clinical or subclinical varicella had the same figure of age specific prevalence.

Table 4. Distribution of varicella patients by age, Outpatient Clinic, Department of Child Health, Cipto Mangunkusumo Hospital, Jakarta, 1990-1995

Period of time	Age group (years)			
	< 1	1-4	5-14	Total
1990	28	55	62	145
1991	9	24	49	82
1992	11	24	34	69
1993	11	27	30	68
1994	23	32	55	110
1995	12	21	17	50
Total	94 (17.9%)	183 (34.9%)	247 (47.2%)	524

Table 5. Distribution of varicella patients by age, Dermatology Out Patient Clinic in several hospital in Indonesia, 1994-1995

Hospital	Age group (year)						Total
	<1	1-4	5-14	15-24	25-44	45-64	
Surakarta	0	2	5	3	9	0	19
Jogyakarta	1	6	6	45	45	0	103
Surabaya	2	15	65	41	69	4	196
Semarang	8	16	30	46	44	1	145
Palembang	2	11	22	16	15	8	74
Jakarta	0	6	15	28	20	1	70
Total	13 (2.1%)	56 (9.2%)	144 (23.5%)	179 (29.4%)	202 (33.1%)	14 (2.1%)	607

Varicella contact

Varicella is the most contagious exanthematous disease. The transmission of this disease is especially via droplets or direct contact with active varicella cases. The incubation period of VZV infection is 11-20 days, including the time for multiplication of virus

in the nasopharyngeal lymph nodes, primary and secondary viremia, and manifestations of specific skin lesion. The infectious period of VZV starts at 24 hours before and during skin lesion appears (approximately 7-8 days). Infection by less virulence VZV to healthy host will give subclinical manifestations.[1,2]

Among 501 healthy children in this study, 11.1% had high varicella antibody titer; the mothers never noticed that their children had had varicella infection before. It means that they had subclinical varicella infection. Children who had positive varicella antibody, 41% were reported to have contact to varicella cases. History of varicella contact was significantly found in older children; this was natural, as they have more chance to be infected by their friends than in younger children. These results supported to Lieu's[10] study that among children whose parents were uncertain about their varicella history, almost one-half (48%) were seropositive. Twenty-five percent of children whose parents said that they definitely had no contact to varicella patients were seropositive; the figure was 32% in children whose parents said that they probably had no varicella contact.

VZV antibody titer

Our data show that subclinical varicella cases showed a high varicella antibody titer (above 1000 mIU/ml, cut off point is 0.2 mIU/ml) in all age groups, including the 1-3 year of age group. Since maternal antibody in the infants disappears by one year of life, the child was able to produce the immune respons to varicella properly. The minimal level of varicella antibody in older age group was 96 mIU/ml lower than younger age group; this suggested that they had varicella infection in the very young age and the titer decreased after several years. These findings are important as a justification on approximate age of varicella vaccine using.

In summary, our study on the varicella antibody in 350 healthy children aged 1 to 12 years who had no history of varicella infection or vaccination showed that 11% of the children had seropositive varicella antibody. The prevalence of subclinical varicella significantly increased with increasing age. Subjects with clinical or subclinical varicella had the same figure of age specific prevalence. The mean varicella antibody in each age group was almost similar. The minimum varicella antibody titer was quite similar between 1-3 and 4-7 age group, but not in 8-12 age group. Forty one percent had history of varicella contact. These results may be used as an addition data in deciding for varicella immunization. In practice, many other factors than epidemiological data should be considered to decide the policy for varicella vaccination. This should including the presence recommendation of Indonesian Society of Pediatricians[11] as well as prractice in USA based on the recommendation of Committee on Infectious Diseases American Academy of Pediatrics, that varicella vaccine should be given between 12 months and 13th birthday.[12]

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