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SEROPREVALENCE SURVEY OF MEASLES, MUMPS, RUBELLA, AND VARICELLA ANTIBODIES AND MEASLES VACCINATION IN JAPANESE HEALTH CARE WORKERS

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Abstract: Purpose: Vaccine-preventable viral infectious diseases have increased in adults over the past 10 years in Japan. To reduce the incidence of viral infections and determine antibody titers, a seroprevalence survey was conducted in 1560 health care workers.

Methods: Blood samples were obtained from 1560 health care workers to test antibody titers. Subjects were screened for measles, mumps, rubella and varicella immunoglobulin G (IgG) in serum samples. Measles vaccinations were offered to those with negative serologic results for antibodies against the virus.

Results: Antibody titers that meet the criteria required for HCWs were obtained from 80.7% of subjects for measles, 79.8% for rubella, 70.1% for mumps, and 98.7% for varicella. A significantly lower prevalence of the measles antibody was found in workers below 40 years of age. A significantly higher prevalence of the rubella antibody was found in female below 50 years of age. This trend was not observed in male. A lower prevalence rate of the mumps antibody was observed in all subjects compared with that of other antibody titers, while a high prevalence rate for the varicella antibody was observed in all subjects.

Conclusion: These data indicate that all health care workers should be vaccinated against (or have

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documented immunity to) these viruses.

Keywords: Vaccine-preventable viral infectious diseases; MMRV vaccination; Immunocompetence; HCWs.

1. Introduction

Measles, mumps, rubella, and varicella (MMRV) are vaccine-preventable infectious diseases common in childhood. The incidence of these viral infectious diseases has decreased in children, but has increased in the adult Japanese population. In 2009, the World Health Organization Regional Committee of the Western Pacific formally declared a regional measles elimination target date of 2012 [1].

Health care workers (HCWs) face a high risk of contracting these viral infections. The Japanese Ministry of Health and Labor is the main provider of childhood vaccinations in Japan. However, a considerable number of HCWs may not have acquired antibodies for these infectious diseases, especially young HCWs because immunizations were voluntary during their childhood and incidence of these diseases was low at that time. Therefore, few HCWs of this young generation have been vaccinated. For prevention against MMRV infection in hospitals, it is important to assess the immunity of HCWs against these viruses and to achieve immunocompetence by vaccination. The purpose of this study was to determine the need for MMRV vaccinations in HCWs in our institution by means of a seroprevalence survey for these viral infectious diseases and to recommend vaccination to those with negative antibody titers.

2. Material and methods

Subjects

Kinki University faculty of medicine and hospital has 1560 full-time employees. Serum samples for all employees in the hospital and faculty of medicine were

examined by the antibody titer test taken during annual health checkups. In total, 1560 HCWs were enrolled in this study (Table 1). Blood samples were obtained to test antibody titers. Serum was separated from other blood components and kept refrigerated at 4℃ until testing. All study procedures were approved by the Kinki University ethics committee.

Reagents, antibody assays, and criteria for the antibody titer

Antibody testing was conducted by SRL Corporation (SRL, Tokyo, Japan). Subjects were screened for measles, rubella, varicella, and mumps immunoglobulin G (IgG) in serum samples using the following methods: particle agglutination (PA, measles), hemagglutination (HI, rubella), and 2-step sandwich enzyme immunoassay (EIA, varicella and mumps). Reagents used for the antibody assays included Serodia® Measles (Fuji-rebio, Tokyo, Japan), HI reagent rubella virus (Denka-seiken, Niigata, Japan), EIA antivirus varicella IgG (Denka-seiken, Niigata, Japan), and EIA antivirus mumps IgG (Denka-seiken, Niigata, Japan). Tests were considered positive for measles if PA index values were greater than 256, for rubella if hemagglutination inhibition index values were greater than 32, and for varicella and mumps if values were above 4.0 mIU/ml. These criterion values were established by the Japan Society of Environmental Infections for HCWs [2] and are stricter than those for the general public.

Measles vaccination

Recommendation for vaccination was sent in writing to all subjects with negative antibody titers. Measles vaccination was administered to subjects who applied for vaccination. The Tanabe strain measles live-virus vaccine was used.

Statistical procedures

Statistical data analyses were conducted using SPSS® software. Continuous parameters with normal distribution were analyzed by Student’s t-test. Binary variables were analyzed by the chi-square and Fisher exact tests. A two-tailed test was

used for all statistical analyses. In all cases, $p = 0.05$ was considered as the threshold level of statistical significance.

3. Results

Among HCWs, positive antibody titers were obtained from 80.7% for measles, 79.8% for rubella, 70.1% for mumps, and 98.7% for varicella (Table 1). The prevalence rate for the measles antibody was lower in female subjects below 30 years of age (Table 2). Female subjects were divided into 2 groups: those below 30 and those above 30 years of age. A significantly lower prevalence of the measles antibody was found in female subjects in the group below 30 years of age ($p = 0.005$, Table 3). In male, the prevalence rate for measles antibody was lower below 40 years of age; however, difference was not statistically significant. Of the 301 HCWs with negative antibody titers for measles, 15 were retired, 4 were on maternity leave, and 2 were allergic to the vaccine. The remaining 280 subjects were vaccinated. In female, the prevalence rate for the rubella antibody was higher in subjects below 50 years of age (Table 2). Female subjects were divided into 2 groups: those below 50 and those above 50 years of age. A significantly higher prevalence of the rubella antibody was found in subjects below 50 years of age ($p < 0.001$, Table 4). No such trend was observed in male (Table 2). A low prevalence rate of the mumps antibody was observed in all subjects compared to that of other antibody titers (Table 1, 2). On the other hand, a high prevalence rate for the varicella antibody was observed in all subjects (Table 1, 2).

4. Discussion

Japanese vaccination schedules and recommendations differ from those in the United States, where all vaccination against (or documented immunity to) MMRV viruses is strongly recommended for all HCWs [3-4]. For American children, MMRV vaccinations are recommended at 12–15 months of age for the first dose and 4–6 years old for the second dose [5]. On the other hand, in Japan, vaccine guidelines for

HCWs were finally published in 2009 when vaccination against MMRV viruses was recommended for all HCWs [2]. For Japanese children, measles and rubella vaccinations are recommended at 12–24 months for the first dose and 5–7 years for the second dose. Mumps and varicella are optional vaccinations even today. Routine vaccinations for rubella and measles were initiated in 1977 and 1978, respectively; optional vaccinations for mumps and varicella in 1981 and 1987, respectively; and the routine measles, mumps, and rubella vaccination began in 1989. In 1994, however, the Preventive Vaccination Law was revised because of the adverse side effects associated with vaccination, after which routine group vaccinations were no longer required, although they were still strongly recommended [6]. In the United States, incidence of these 4 types of infectious diseases have declined significantly because of the routine vaccination. Vaccine-preventable infectious diseases can be reduced in Japan if a proper evaluation of the situation is performed.

The risk of acquiring measles in nonimmune HCWs is estimated to be 13 times higher than that in the general population [7]. Unfortunately, prevalence rates of the measles antibody were found to be lower in younger subjects. Incidence of measles has decreased in Japan since 1990 compared to previous years [8]. Meanwhile, measles vaccination was once until 2005. Younger subjects in this study had had less opportunity to gain natural immunity. As a consequence, Japan experienced an outbreak of measles in 2007 9 in which most patients were adolescents and young adults [9]. In 2008, 11,000 cases of measles were reported in Japan [10]. The Japanese government decided to administer measles vaccines to high school and junior high school students in that emergency situation. The National Institute of Infectious Diseases issued a guideline for dealing with measles in schools [11] and hospitals [12]. In addition, since 2008, all Japanese medical institutions are required to report all diagnosed cases of measles. As a result of these various activities, the incidence of measles has decreased.

The low prevalence of positive antibody titers for mumps indicate that herd immunity was not maintained among HCWs in our cohort. Mumps vaccination was not mandatory during the childhood of many of our subjects in Japan. However, the

incidence of mumps in Osaka Prefecture was reported to be 12,000 in 2010 [13]. HCWs face a high risk of mumps infection. Therefore, HCWs in the Japanese health care system must be vaccinated against mumps. High herd immunity for varicella, as reflected in the titers from the participants in this study, may have been maintained because of the highly contagious nature of this virus.

The percentage of HCWs with positive antibody titers for rubella was low in comparison with the percentage with positive titers for varicella. Gender differences were also revealed in rubella antibody titers, especially in subjects above 50 years of age. This result may reflect the efficacy of the vaccine program conducted among female junior high school students between 1970 and 1979 to reduce the incidence of congenital rubella. Rubella vaccination for male students was voluntary during this period. The vaccination programs for the other 3 viruses also underwent policy changes during this time, which explains why many participants in this study were uncertain about their immunization coverage. Because of the adverse publicity regarding the side effects of vaccinations, the 1994 Preventive Vaccinations Law was introduced to change requirements for these vaccines from “mandatory” to “strongly recommended” [3]. At that time, health professionals expressed concerns about how this legislation would affect vaccination rates [14-15]. Concerted efforts are needed to educate the public about the benefits of vaccination.

The design of the present study provided several advantages over previous Japanese studies [16]. Data were collected from a larger representative sample of Japanese HCWs. In our medical faculty and associated hospital, 100% of HCWs were examined by means of a seroprevalence survey. However, the study’s limitations must not be overlooked. First, previous vaccination history for many subjects was unknown. Second, most subjects were young (below 40 years of age) in our study; therefore, data for older HCWs in this study was insufficient to draw definitive conclusions. Third, in our program, vaccination for all viral infectious diseases examined in this study except measles is voluntary. Thus, seroconversion has been left to the will of the individual HCW.

5. Conclusions

This seroprevalence survey provides information that may improve vaccine-preventable infection rates, decrease number of work days lost, and result in fewer HCWs requiring hospitalization for these viral infections. Therefore, it is strongly recommended that all HCWs should be vaccinated against (or have documented immunity to) these viruses in Japan, as is the case in the United States. The seroprevalence survey and vaccination program described here was successful in improving vaccine-preventable infection rates among the cohort of employees in our institution. Reduced risk of secondary transmission to compromised hosts in our tertiary care hospital was an extremely important outcome of this study.

6. Conflict of Interest

No conflict of interest associated with this work.

7. Contribution of Authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors.

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Table 1: Basic characteristics and percentage of antibody-positive in all subjects

	Female (n = 1052)	Male (n = 508)
Age** (mean ± SD)	40.6 ± 11.0	43.4 ± 10.7
Height** (mean ± SD)	158.3 ± 5.4	171.4 ± 6.0
Weight** (mean ± SD)	53.5 ± 9.7	69.6 ± 10.7
BMI** (mean ± SD)	21.3 ± 3.7	23.7 ± 3.3
Subjects with positive measles antibody titer, n (%)	851 (80.9)	408 (80.3)
Subjects with positive rubella antibody titer*, n (%)	859 (81.7)	386 (76.0)
Subjects with positive mumps antibody titer, n (%)	753 (71.6)	340 (66.9)
Subjects with positive varicella antibody titer, n (%)	1037 (98.6)	502 (98.8)

**; Significant differences between sex groups, P < 0.001.

*; Significant differences between sex groups, P < 0.01.

Table 2: Percentage of health care workers with positive titers by age and sex

Sex	female					male				
Age	n	Measles	Rubella	Mumps	Varicella	n	Measles	Rubella	Mumps	Varicella
20～	215	74.0	81.9	67.0	98.1	50	74.0	70.0	60.0	98.0
30～	311	82.3	83.9	73.6	98.7	167	76.6	74.3	66.5	97.6
40～	282	85.1	86.2	72.0	98.6	120	84.2	75.0	60.8	99.2
50～	180	83.9	74.4	70.6	98.9	136	83.1	79.4	74.3	100.0
60～	64	70.3	70.3	78.1	98.4	35	82.9	82.9	71.4	100.0
Chi-square value		16.026	16.655	4.347	0.468		4.613	3.101	6.742	4.565
P value		0.003	0.002	0.361	0.977		0.329	0.541	0.150	0.335

Table 3: Measles antibody prevalence rate in female health care workers

Age group		Measles titers		
		Positive	Negative	Total
Under 30	n	159	56	215
	%	74.0	26.0	100.0
Over 30	n	692	145	837
	%	82.7	17.3	100.0
Total	n	851	201	1052
	%	80.9	19.1	100.0

Chi-square value = 8.421, P = 0.005

Table 4: Rubella antibody prevalence rate in female health care workers

Age group		Rubella titers		Total
		Positive	Negative	
Under 50	n	680	128	808
	%	84.2	15.8	100.0
Over 50	n	179	65	244
	%	73.4	26.6	100.0
Total	n	859	193	1052
	%	81.7	18.3	100.0

Chi-square value = 14.586, $P < 0.001$