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Effectiveness of vaccination and wearing masks on seasonal influenza in Matsumoto City, Japan, in the 2014/2015 season: An observational study among all elementary schoolchildren

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ABSTRACT

Measures of seasonal influenza control are generally divided into two categories: pharmaceutical and non-pharmaceutical interventions. The effectiveness of these measures remains unclear, because of insufficient study sample size and/or differences in study settings. This observational epidemiological study involved all elementary schoolchildren in Matsumoto City, Japan, with seasonal influenza during the 2014/2015 season. Questionnaires, including experiences with influenza diagnosis and socio-demographic factors, were distributed to all 29 public elementary schools, involving 13,217 children, at the end of February 2015. Data were obtained from 10,524 children and analyzed with multivariate logistic regression analysis. The result showed that vaccination (odds ratio 0.866, 95% confidence interval 0.786–0.954) and wearing masks (0.859, 0.778–0.949) had significant protective association. Hand washing (1.447, 1.274–1.644) and gargling (1.319, 1.183–1.471), however, were not associated with protection. In the natural setting, hand washing and gargling showed a negative association, which may have been due to inappropriate infection control measures or aggregating infected and non-infected children to conduct those measures. These results may indicate a pathway for influenza transmission and explain why seasonal influenza control remains difficult in school settings. The overall effectiveness of vaccination and mask wearing was 9.9% and 8.6%, respectively. After dividing children into higher (grades 4–6) and lower (grade 1–3) grade groups, the effectiveness of vaccination became greater in the lower grade group, and the effectiveness of wearing masks became greater in the higher grade group. These results may provide valuable information about designing infection control measures that allocate resources among children.

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1. Introduction

Measures of seasonal influenza control are generally divided into two categories: pharmaceutical interventions, such as vaccination, and non-pharmaceutical interventions (NPIs), not involving drugs (CDC, 2016b; WHO, 2005). Although vaccination is regarded as the most effective method of controlling the spread of influenza (CDC, 2016a; WHO, 2016), studies are needed to explore the effectiveness of vaccination and to determine the optimal type of vaccine, age at vaccination, and matching of vaccine to virus subtype (DiazGranados et al., 2012). Moreover, the effectiveness of vaccination has been found to differ among age groups (Shinjoh et al., 2015). Longitudinal epidemiological studies focused on the effectiveness of vaccines, including over several generations, are necessary.

In contrast to pharmaceutical methods, NPIs, which include wearing masks, hand washing and gargling, are designed to interfere with virus transmission (WHO, 2005). NPIs are used for infection control when pharmaceutical interventions such as vaccines are unavailable or inappropriate. Examples include the lack of vaccine to address a novel type of pandemic influenza virus or hypersensitivity to drugs. In addition, combinations of NPIs with pharmaceutical intervention may be more effective than either alone. However, studies assessing the effectiveness of NPIs have yielded inconsistent results (Aiello et al., 2010a; Smith et al., 2015), which may be caused by poor statistical power due to sample

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size or selection bias. Alternatively, randomized controlled trials may not always reflect the natural setting of an influenza epidemic.

Observational studies at the community level are required to clarify these issues. These studies should include an entire community in a natural setting, with all individuals, both those with and without influenza, evaluated to determine the effectiveness of vaccines and NPIs. This epidemiological study therefore evaluated seasonal influenza control methods in all elementary school children in Matsumoto City, Nagano Prefecture, Japan.

2. Methods

2.1. Study subjects

Before conducting the current study, a prospective first survey was performed to evaluate the dynamics of seasonal influenza during the 2014/2015 season (Uchida et al., 2016). At the end of the prospective survey period, questionnaires were administered to all subjects to obtain information about their experience with influenza infection. Briefly, the study subjects included all 13,217 schoolchildren attending all 29 public elementary schools in Matsumoto City, Nagano, Japan. Matsumoto City is a suburban area, with a population of about 240,000 individuals, located in the middle of Japan. Teachers and guardians were not included in the analysis. Questionnaires were distributed to all 13,217 schoolchildren, with answers returned by 11,390 children (response rate, 86.2%). After excluding questionnaires with missing data, 10,524 questionnaires were analyzed. To comprehensively determine the protective association and effectiveness of NPIs, all subjects were analyzed as a single group. Subjects were regarded as having seasonal influenza if they were diagnosed by physicians at medical institutions. Thus, 2149 schoolchildren (20.4%) were considered to have had influenza, a proportion similar to that in our first prospective survey in the same season (20.1%) (Uchida et al., 2016).

2.2. Ethics statement

The study was reviewed and approved by the Medical Ethics Board of Shinshu University School of Medicine (approval number 2715). Because this study was performed anonymously and questionnaires were returned voluntarily, informed consent was not obtained from study subjects.

2.3. Questionnaire and data sampling

Before the survey, study aims were explained to administrators of the board of education, the medical associations, public health centers and each school in Matsumoto City, with all providing approval. At the end of February 2015, questionnaires were distributed to school nurses. The nurses distributed questionnaires to class teachers, who, in turn, handed them to the guardians of all schoolchildren and requested their return within 1 week. Guardians were asked to answer questionnaires by themselves anonymously. Class teachers subsequently collected the questionnaires and gave them to the school nurses.

The questionnaire included questions about children's experiences with seasonal influenza during the 2014/2015 season (yes/no); if yes, the date of onset (calendar month), and diagnosis by a medical institution (yes/no). Because self-reported diagnosis at a medical institution is generally accepted criteria for infectious disease statistics at schools, we relied on and used this information. Sociodemographic factors for each child included sex (male/female), grade in school (description), and class (description). In Japan, as elementary school grades 1–6 correspond to ages 7–12 years old, their grade was used as the factor for age in this study. Questions also asked about any underlying disease associated with influenza-related complications (CDC, 2015) including cardiovascular disease, pulmonary disease, kidney disease, liver disease, nerve disease, muscle disease, blood disease and diabetes (description). To determine associations with household-related infections, questions were asked about family members in the household (e.g. father, mother, grandfather, grandmother, brother, sister, others) and number of siblings (description). To assess the possibility of transmission among children, the questionnaire asked about places the child regularly goes at least once per week (description). Questions about interventions included vaccination during that influenza season (yes/no), and if yes, the date of vaccination (calendar month). To analyze individual infection control measures, questions asked about each child's use of NPIs at any place or time, including wearing a mask, hand washing, or gargling with water (yes/no). To determine prior experience with influenza, questions included whether the child had been diagnosed with seasonal influenza (yes/no) or vaccinated against influenza (yes/no) during the previous influenza season. All the questions included in this study were based on our previous survey (Uchida et al., 2016).

Guardians who had already filled out questionnaires in our first prospective study were specifically asked to fill out this questionnaire also. Data were input to a database by researchers or trained operators using standardized sorting methods.

2.4. Statistical analysis

Categorical data were compared by Chi-square tests. To determine the associations of infection control measures for individuals, the associations were evaluated by multiple logistic regression analysis and expressed as odds ratios (ORs) and 95% confidence intervals (95% CIs). In this multivariate analysis, explanatory variables were adjusted for each other and subjects with or without diagnosis were regarded as objective variables. To avoid multi-collinearity, Spearman's correlation analysis was used for the correlation matrix. If multi-collinearity was found, insignificant variables were not included in further analysis.

The simultaneous effects of infection control measures were not determined in this study. All analyses were performed with SPSS ver.22 (Chicago, IL, USA) and $P < 0.05$ was regarded as statistically significant.

This study gathered vaccination and diagnosis information about all subjects. In general, to assess the effect of infection control measures at the group level, the effectiveness of vaccination was calculated as follows:

1 – RR (Relative Risk).

In this study, this formula was modified appropriately and expressed as follows:

1 – (the number of vaccinated children with influenza/the number of non-vaccinated children with influenza).

In addition, information was obtained about mask wearing at any place or time by all subjects. Because the equation was utilized to assess the effectiveness of NPIs (Aiello et al., 2008), it was applied to assess the effectiveness of wearing a mask:

1 – (the number of children with influenza who wore a mask/the number of children with influenza who did not wear a mask).

Furthermore, to evaluate whether effectiveness differed by age groups, elementary school children were subdivided into those in higher (grades 4–6) and lower (grades 1–3) grades. The above equations applied to each subgroup.

3. Results

Of the 10,524 children included in this survey, 2149 (20.4%) were diagnosed with influenza. None died of influenza. Almost all children were diagnosed using rapid diagnosis kits (96.4%), and the remainder were diagnosed based on symptoms of influenza-like illness as reported in a previous report (Uchida et al., 2016). There were no laboratory confirmed cases. During this influenza season, there were no major outbreaks in schools requiring school closure, but classes in 26 schools were temporarily closed. These closures may affect the study result, however, the closure effect was not evaluated in this study because data was limited and could not be linked with study subjects.

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