Efficacy of Influenza Vaccine among Elderly Patients by Physical Activity Status

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Abstract

Objective: Although many studies have shown the usefulness of influenza vaccine in elderly in-patients, the efficacy of vaccination with regard to the daily physical activities of patients has not been fully evaluated. To address this issue, we correlated the use of medical resources with vaccination status in patients categorized according to their daily activity levels.

Methods: The subjects comprised 237 in-patients at or above 51 years of age, who were hospitalized in the long-term care unit of a Japanese hospital between January and March, 1999. The vaccination status and medical resources use (i.e., oral antibiotics, injected antibiotics, blood cell count, chest X-ray) of each patient were recorded, and the patients were assigned to three subgroups, based on daily life activity scores.

Results: Vaccinated in-patients in the 'bed-bound' category required fewer medical resources, i.e., oral antibiotics (-2.29 days, $P<0.05$), injected antibiotics (-5.02 days, $P<0.001$), blood cell counts (-4.66 times, $P<0.001$), and chest X-rays (-4.31 times, $P<0.001$), compared with unvaccinated in-patients. There were no significant differences in treatment parameters between vaccinated and unvaccinated patients in the 'partly limited' or 'no limitation' categories.

Conclusions: It is suggested that influenza vaccination significantly reduces the need for medical treatment only among those in-patients who are the least physically active. Further studies are required to replicate these findings, and to elucidate the underlying reasons for this reduction.

Key words: influenza vaccine, daily activity, elderly, efficacy, long-term care unit

Introduction

Influenza outbreaks of variable severity are reported every winter. Baker (1) reported approximately 172,000 extra hospitalizations associated with influenza and pneumonia during influenza type-A epidemics in the USA. Although it has been recommended that persons with chronic diseases and those at increased risk of influenza complications should be vaccinated, only a small proportion of high-risk individuals actually receive vaccination. The highest priority groups for influenza vaccination are children and adults with chronic disorders of the pulmonary or cardiovascular systems requiring regular medication, and residents of nursing homes and other chronic-care facilities. The next-highest priority group includes healthy persons over the age of 65 years, and adults and children who have required regular medical follow ups or hospitalization during the preceding year (2).

Studies have shown that in some elderly patients antibody

production levels following vaccination are insufficient for protection. Gross et al. reported poor antibody responses in patients defined as 'frail elderly' according to their chronic health evaluation scores (3). Potter et al. (4) reported weak antibody responses among frail and undernourished elderly patients, classified according to the Barthel Index and the Body mass index (BMI). In addition, Webster (5) stressed the necessity for supplementary nourishment of frail elderly patients, in order to improve unsatisfactory antibody levels. On the other hand, several studies have demonstrated the effectiveness of influenza vaccination in elderly patients. These studies were generally performed in actual settings. In studies evaluating parameters of vaccine efficacy, such as morbidity (6, 7), mortality (6, 7), hospitalization rate (8–10), and side-effects (6), influenza vaccination of elderly subjects was reported to be effective (6, 7, 9–13). Furthermore, several studies showed no significant differences between healthy and frail elderly patients with respect to the induction of antibody responses following influenza vaccination (10, 12, 13). Economic impact studies also revealed that influenza vaccination was efficient in elderly patients with circulatory (2) or chronic diseases, such as asthma and diabetes mellitus (14, 15), and in-patients residing in nursing hospitals (2).

Although these findings suggest the usefulness of vaccinating

Received Dec. 11 2001/Accepted May 28 2002

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frail elderly patients against influenza, studies correlating the efficacy of vaccination with daily physical activity are lacking. Therefore, we studied the efficacy of influenza vaccination among elderly patients in a nursing hospital in Fukuoka, Japan, using criteria for activity of daily life (ADL) outlined previously (16). This study was undertaken during the period between January and March, 1999. Economic impact, measured as the frequency of testing and medication required, was used to assess the efficacy of the influenza vaccination. Thus, for patients initially categorized according to their ADL scores, efficacy was compared concerning influenza vaccination status.

Materials and Methods

Subjects and study variables

The subject groups in this study included 237 in-patients aged 51 years or above. Of the in-patients, 178 of them had received influenza vaccination within the previous year. The patients those who had been hospitalized at a long-term care unit of Hara Doi Hospital, Fukuoka City, during the study period (i.e., between January and March, 1999). Every subject had underlying conditions such as cerebral vascular accidents, rheumatism, dementia, bone fractures and other ailments. In addition, most subjects had been transferred from other hospitals for acute diseases. Hara Doi Hospital has 556 beds and three departments (internal medicine, orthopedics and psychiatry). The influenza vaccine was administered after informed consent had been obtained from the subject or authorized care-giver.

All of the relevant data were maintained in an administrative database at the hospital. Information collected during this study included demographic variables (i.e., age and gender of patients), vaccination status (i.e., vaccinated or unvaccinated), ADL scores, and data on healthcare resource use. Specifically, healthcare resource use represented the length of time, in days, of oral or injected antibiotic administration, or the frequency of blood cell counts and chest X-rays.

In the long-term care unit, the rules for medical testing of feverish patients have been established based on academic guidelines. According to these rules, blood-cell-count and CRP tests were performed when a patient had a temperature above 37.5°C. When a patient showed a temperature above 38.0°C, a chest X-ray was also carried out. Influenza infection was determined serologically. Cases showing a four-fold increase in HI-antibody levels were classified as having influenza infections.

Analysis

Since the purpose of this study was to correlate variation in the efficacy of influenza vaccination with ADL scores, the subjects were initially categorized into one of three groups based on their ADL scores. Subsequently, the association between vaccination status and required medical treatments was examined for each ADL subgroup. The three ADL subgroups comprised: (1) the 'no-limitation' group, defined as "although she/he has some functional disorders, she/he can do almost everything by her/himself in daily life"; (2) the 'partly limited' group, defined as "although she/he can do everything inside the house, she/he cannot go out without help"; and (3) the 'bed-bound' group, defined as "she/he is bed-bound, and needs help in using the toilet, eating, and changing clothes". The patients in each ADL subgroup were further categorized as either 'vaccinated' or 'unvaccinated'.

Finally, the mean duration in days and the frequency of medical intervention were compared for all groups.

For bivariate analyses, Student's *t* test for continuous variables was used. In order to evaluate the effects of influenza vaccination in preventing influenza infection, multiple logistic regression analysis was performed. In the model, the status of influenza infection (1: yes, 0: no) was assigned as a dependent variable, and "vaccination status" (1: yes, 0: no) and covariates were independent variables. The number of days for which 'oral antibiotics' and 'injected antibiotics' were administered and the 'blood cell count' number and 'chest X-ray' tests performed were assigned as dependent variables, and 'vaccination status', 'patient age', 'patient gender', 'physician's age', 'physician's gender' and 'physician's status' were independent variables. In these regression models, the dummy variables of 'vaccination status' (0: unvaccinated; 1: vaccinated), and 'patient gender' and 'physician's gender' (0: female; 1: male) were introduced. Since a dummy variable was introduced for 'vaccination status', the regression coefficient in this case refers to the differences between the mean values of a dependent variable in subgroups with or without the attribute shown by the dummy variable (i.e., 'vaccinated and unvaccinated groups') (17). Previous studies reported that female physicians tended to use more medical resources than male physicians (18–20), and that the quality of medical care delivered by older physicians was poorer than that of younger physicians (21, 22). In addition, full-time physicians in the hospital were in charge of patients with severe disease, while part-time physicians cared for patients with less-severe disease. Therefore, 'physician's age', 'physician's gender' and 'physician's status' were included as independent variables in the regression model. All statistical tests were performed using SPSS 9.0 with Windows software (23).

Results

Table 1 shows the subject profiles. The mean age of the 237 subjects was 80.4 (± 10.3) years. The majority of the subjects were female (74.7%). Of the 237 subjects, 176 (74.3%) were vaccinated. In terms of ADL categories, 59.0% of the subjects were 'bed-bound' and 26.2% were 'partly limited'. Of the total (237 subjects), 32 (13.5%) were judged to be infected with influenza type A (H3N2), since they showed a four-fold or higher increase in HI-antibody titers. Of the 61 unvaccinated subjects, 20 (32.8%) were judged to be infected with influenza type A (H3N2). Of the 176 vaccinated subjects, only 12 (6.8%) were infected with influenza type A (H3N2). The mean periods for which oral and injected antibiotics were administered were 2.75 and 3.83 days, respectively. In addition, blood-cell-count and chest-X-ray tests were performed at 3.11 and at 1.64 times, respectively.

Table 2 shows the odds ratios for factors related to influenza infection. Of the factors shown in Table 2, only 'vaccination status' displayed significant differences, i.e., compared with unvaccinated patients, vaccinated patients were 0.15-fold less likely to be infected with influenza during the study period.

Table 3 shows the odds ratios for factors related to influenza infection by three ADL categories. Of the factors shown in the table, 'vaccination status' displayed significant differences only among the partly limited and bed-bound categories. Specifically, among the partly limited category, vaccinated patients were 0.19-fold less likely to be infected with influenza during the study

period ($P<0.05$), and among the bed-bound category, vaccinated patients were 0.09-fold less likely to be infected with influenza ($P<0.001$).

Table 4 shows the mean duration or frequency of medical treatment in relation to vaccination status. The mean values of days during which oral and injected antibiotics were administered to vaccinated patients were 2.32 and 2.55 days, respectively, while in unvaccinated patients the corresponding values were 3.98 and 7.52 days, respectively. The mean numbers of days during which

injected antibiotics were used were significantly lower for the vaccinated than for the unvaccinated patients ($P<0.001$). The mean frequencies of blood cell counts and chest X-rays were 2.62 and 1.31 times for vaccinated patients, respectively, and were 4.49 and 2.61 times for unvaccinated patients, respectively. The mean frequency of blood cell counts and chest X-rays were significantly lower for the vaccinated than for the unvaccinated patients ($P<0.001$ and $P<0.008$, respectively).

The subjects in each ADL group were subsequently divided into two subgroups based upon vaccination status (i.e., 'vaccinated' or 'unvaccinated'). We compared the duration (in days) and the frequency of medical intervention between groups (Table 5). In the 'bed-bound' group, with respect to the number of days or occasions for all medical testing or medication, there was a significant difference between subgroups with and without vaccination (see Table 5). Generally, the mean values for the duration or frequency of treatment were lower for vaccinated than for unvaccinated subjects. However, in the 'partly limited' or 'no limitation' groups, the mean values for treatment duration and frequency were not significantly different between the vaccinated and unvaccinated groups.

Table 6 shows the beta coefficients of the 'vaccination status' parameter, calculated by multiple regression analyses for the three ADL categories. In the 'bed-bound' category, with respect to oral antibiotics the beta value for 'vaccination status' was -2.29 ($P<0.05$). This implies that, after controlling for patient's age,

Table 1 Profile of study subjects

Characteristics	Number (%) / mean
Age (mean years $\pm$ SD; range)	80.4 $\pm$ 10.3 (51–101)
Gender	
Male	60 (25.3%)
Female	177 (74.7%)
Vaccination status	
Vaccinated	176 (74.3%)
Unvaccinated	61 (25.7%)
ADL category	
No limitations	35 (14.8%)
Partly limited	62 (26.2%)
Bed-bound	140 (59.0%)
Influenza infection	
Total infected subjects	32 (32/237, 13.5%)
Vaccinated subjects	12 (12/176, 6.8%)
Unvaccinated subjects	20 (20/61, 32.8%)
Oral antibiotics (mean days $\pm$ SD; range)	2.75 $\pm$ 5.47 (0–39)
Injected antibiotics (mean days $\pm$ SD; range)	3.83 $\pm$ 7.71 (0–41)
Blood cell counts (mean frequency $\pm$ SD; range)	3.11 $\pm$ 2.63 (0–14)
Chest X-rays (mean frequency $\pm$ SD; range)	1.64 $\pm$ 2.58 (0–17)

Table 2 Odds ratio of factors relating to influenza infection

Variable	Case number	OR	95% CI	P
Gender male ^a	60	1.00		
female	177	0.51	0.19–1.26	0.15
Age ^b		1.04	0.99–1.08	0.12
Vaccination status				
unvaccinated ^a	61	1.00		
vaccinated	176	0.15	0.06–0.34	0.00
ADL categories				
no limitations ^a	35	1.00		
partly limited	62	0.69	0.20–2.20	0.55
bed-bound	140	0.44	0.26–1.65	0.15

a: Reference

b: Age was entered into the model as a continuous variable.

Table 3 Odds ratio of influenza infection factors among subjects grouped by ADL categories

Variable	OR	95% CI	P
ADL categories: no limitation			
Gender male ^a	1.00		
female	1.59	0.12–21.8	0.73
Age ^b	1.09	0.96–1.23	0.21
Vaccination status unvaccinated ^a	1.00		
vaccinated	0.19	0.02–2.00	0.17
ADL categories: partly limited			
Gender male ^a	1.00		
female	0.49	0.08–2.82	0.42
Age ^b	1.09	0.99–1.19	0.08
Vaccination status unvaccinated ^a	1.00		
vaccinated	0.19	0.05–0.84	0.03
ADL categories: bed-bound			
Gender male ^a	1.00		
female	0.37	0.10–1.36	0.13
Age ^b	1.00	0.94–1.05	0.86
Vaccination status unvaccinated ^a	1.00		
vaccinated	0.09	0.02–0.30	0.00

a: Reference

b: Age was entered into the model as a continuous variable.

Table 4 Frequency of testing or medication according to 'vaccination status' in 237 subjects

Medical resources	mean $\pm$ SD		<i>P</i> ^a
	Vaccinated (n=176)	Unvaccinated (n=61)	
Oral antibiotic (days)	2.32 $\pm$ 4.60	3.98 $\pm$ 7.35	0.10
Injected antibiotic (days)	2.55 $\pm$ 5.55	7.52 $\pm$ 11.2	<0.001
Blood cell counts (times)	2.62 $\pm$ 2.22	4.49 $\pm$ 3.19	<0.001
Chest X-rays (times)	1.31 $\pm$ 2.08	2.61 $\pm$ 3.50	0.008

a: Student's *t* test

Table 5 Frequency of testing and medication according to vaccination status among three ADL categories

		ADL category		
		Bed-bound	Partly limited	No limitation
Oral antibiotic (days)	vaccinated	2.58±4.92 (n=108)	1.88±3.98 (n=40)	1.93±4.21 (n=28)
	unvaccinated	6.03±9.28 (n=32)	1.63±3.57 (n=22)	2.00±2.00 (n=7)
Injection antibiotic (days)	vaccinated	3.63±6.62 (n=108)	0.88±2.76 (n=40)	0.75±1.71 (n=28)
	unvaccinated	12.10±13.30 (n=32)	3.05±5.40 (n=22)	0.86±2.27 (n=7)
Blood cell count (times)	vaccinated	2.94±2.41 (n=108)	2.47±2.10 (n=40)	1.64±1.06 (n=28)
	unvaccinated	5.47±3.74 (n=32)	3.59±2.21 (n=22)	2.86±1.07 (n=7)
Chest X-ray (times)	vaccinated	1.49±1.96 (n=108)	1.25±2.83 (n=40)	0.71±0.81 (n=28)
	unvaccinated	3.53±3.91 (n=32)	1.55±2.70 (n=22)	1.71±2.87 (n=7)

Student's *t* test

* $p<0.05$, ** $p<0.01$, *** $p<0.001$

Table 6 Beta value and SE of 'vaccination status' with respect to each medication or testing among the three ADL groups

		ADL category		
Medical resources		Bed-bound	Partly limited	No limitation
Oral antibiotics		-2.29 (1.30)*	0.36 (1.06)	1.00 (1.93)
	$R^2=0.13$		$R^2=0.05$	$R^2=0.34$
	$F=3.20$ ($P=0.006$)		$F=0.50$ ($P=0.805$)	$F=1.82$ ($P=0.137$)
Injected antibiotics		-5.02 (1.79)***	-1.94 (1.12)	-0.17 (0.96)
	$R^2=0.23$		$R^2=0.08$	$R^2=0.22$
	$F=6.33$ ($P=0.000$)		$F=0.80$ ($P=0.574$)	$F=1.19$ ($P=0.346$)
Blood-cell count		-4.66 (0.59)***	-2.28 (0.56)	-2.52 (0.59)
	$R^2=0.19$		$R^2=0.21$	$R^2=0.27$
	$F=4.99$ ($P=0.000$)		$F=2.31$ ($P=0.051$)	$F=1.51$ ($P=0.217$)
Chest X-ray		-4.31 (0.53)***	-0.67 (0.76)	-1.55 (0.72)
	$R^2=0.19$		$R^2=0.11$	$R^2=0.28$
	$F=4.86$ ($P=0.000$)		$F=1.10$ ($P=0.375$)	$F=1.60$ ($P=0.188$)

Note: Beta-coefficient values of the 'vaccination status' parameter (0: unvaccinated; 1: vaccinated) in a regression model [$Y=a \times (\text{Vaccination status}) + b \times \text{Age} + c \times (\text{Patient gender}) + d \times (\text{Physician's age}) + e \times (\text{Physician's gender}) + f \times (\text{Physician's status}) + \alpha$]. The dependent variable is each medication or testing item.

* $p<0.05$ ** $p<0.01$ *** $p<0.001$

patient's gender, physician's age, physician's gender, and physician's status, the vaccinated patients required oral antibiotic treatment for 2.29 days less on average than the unvaccinated subjects. With regard to injected antibiotics, the beta value of 'vaccination status' was -5.02 ($P<0.001$), implying that, after controlling for the covariates, vaccinated subjects required injected antibiotic treatment for a shorter period by 5.02 days on average than unvaccinated subjects. With respect to blood cell counts, the beta value of the 'vaccination status' term was -4.66 ($P<0.001$), and the corresponding value for chest X-rays was -4.31 ($P<0.001$). These findings suggest that, after controlling for the effects of the covariates, vaccinated subjects required blood cell counts 4.66 times fewer on average and chest X-rays performance 4.31 times fewer than unvaccinated subjects; these difference is significant.

In the 'partly limited' category, the beta value of 'vaccination status' was not significant with respect to any medical test or treatment, implying that, whether the subjects were vaccinated or not, the mean duration and frequency of treatments did not differ after controlling for covariates. In the 'no limitation' category, with respect to blood cell counts, the beta value of 'vaccination status'

was -2.52 ($P<0.01$). However, this model was not effective ($F=1.51$, $P=0.22$).

Discussion

We examined the relation between the efficacy of influenza vaccination in elderly patients in a long-term care unit and their physical activity levels over a three-month period. Vaccinated patients were significantly less likely to be infected with influenza (Table 2). This finding corroborates the results of previous studies (6, 8, 10–12, 24). Since the effect of influenza vaccination on infection was evaluated after controlling for the effects of variables such as patient age, gender, and ADL category, the net impact of vaccination was highly positive.

The efficacy of influenza vaccination in elderly in-patients was previously reported (13, 25). Since previous studies reported that antibody production levels were high among healthy subjects (3, 4), the efficacy of vaccination was expected to be greatest in patients in the 'no limitations' group. However, the opposite was found in the present study: Influenza vaccination was found to be

effective in reducing the frequency of medical interventions only among bed-bound patients (Table 6). The following explanations are suggested for this observation. Firstly, patients with few limitations on their physical activities (i.e., those in the 'partly limited' and 'no limitations' groups) were more likely to move around the hospital, and thus may have been at higher risk of becoming infected. However, the results of the logistic regression analysis do not appear to support this possibility, although the findings are not conclusive (Table 2).

Secondly, according to previous studies, it is widely recognized that, once infection with influenza has been established, serious complications are often observed among high-risk patients, such as those with chronic diseases, elderly patients, and children (3, 4, 14, 16, 26). In line with these findings, we found significant differences in the frequencies of medical testing and treatment between vaccinated and unvaccinated groups only among bed-bound in-patients, and demonstrated that bed-bound patients were at the highest risk for co-morbidity.

Based on the findings of previous studies, it is inferred that influenza vaccination appears to be also effective among elderly patients with higher daily activity level because the vaccination works well in preventing the influenza infection getting worse (4, 5, 25). In short, the finding of the present study appears to be useful in setting a priority of influenza vaccination among the elderly patents.

Use of the influenza vaccine lowers the economic cost of treating influenza (27, 28). Therefore, influenza vaccination of the elderly and children is recommended by health professionals. However, there has been worldwide under-application of the influenza vaccine (19, 29). In Japan, one of the primary reasons for under-usage is that the economic impact of influenza vaccination has not been fully evaluated. In a series of studies evaluating the economic efficacy of influenza vaccination of elderly in-patients

in Japanese nursing hospitals, we reported that the health insurance fees of individual patients ranged from 7,000 to 90,000 yen (30). This wide variation was suggested to reflect the use of multiple drugs with the same efficacy, but with different prices. These factors make studies of vaccination efficacy based on hospitalization fees extremely difficult. Furthermore, since each country has its own healthcare delivery system, simple comparisons of the costs associated with influenza treatment might not be appropriate. In the present study, to overcome some of these problems and to elucidate the economic aspects of influenza vaccination, we used the duration and frequency of testing and medical treatment as the measures of vaccine efficacy. We demonstrated that influenza vaccination significantly reduced medical resource use only among the least physically active inpatients (Table 6). Studies using these parameters would allow international comparisons of medical resource use, and further studies in different settings would lead to a better understanding of the efficacy of influenza vaccination. Although the international comparisons are limited to those countries whose health care delivery systems are similar to Japan, it is suggested that non-monetary indices, such as the frequencies or duration of medical resource usage, are somewhat better than monetary indices because these non-monetary indices can avoid biases due to the health care system of each country.

One limitation of the present study is that it is based upon cross-sectional data. Thus, we cannot conclude a causal relation. This will be the topic of a future study. In conclusion, we examined how the efficacy of influenza vaccination varied with the level of physical activity among elderly in-patients. It was revealed that influenza vaccination significantly reduced medical resource use only among in-patients with little physical activity. Further studies will be needed to clarify the reasons behind this finding.

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