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Original Article

Adverse events of prophylactic anti-influenza agents in medical staffs

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ABSTRACT

Background: We undertook a survey to evaluate the compliance and the tolerability of oseltamivir and zanamivir when they were used as post-exposure prophylaxis among the medical staffs in the 2014–2015 seasons to understand a characteristic of adverse events caused by anti-influenza (flu) agents.
Materials and Methods: During the study period, 540 medical staffs received oseltamivir (75 mg twice a day for 5 days) or zanamivir (twice a day for 5 days) as post-exposure prophylaxis of influenza, respectively.
Results: Four hundred eleven medical staffs of 540 medical staffs (76.1%) provided responses to questionnaire investigations. The adverse events caused by oseltamivir were reported by 86 of 382 medical staffs (22.5%). The most frequent adverse events were gastrointestinal adverse events (13.4%), followed by systemic and local diseases (11.8%), diseases of the nervous system (7.9%) and neuropsychiatric adverse events (0.5%). On the other hand, adverse events caused by zanamivir were reported by one (3.4%) of 29 medical staffs.
Conclusion: Our survey revealed that 22.5% subjects experienced any adverse events due to oseltamivir. And the regimen showed low compliance than we expected. On the other hands, zanamivir showed high adherence with lower incidence of adverse events.

1. Introduction

Influenza is a contagious, acute febrile respiratory infection caused by the influenza virus. Influenza viruses can spread easily from person to person, and annual epidemics create serious public health problems worldwide. The World Health Organization estimates that 5–10% of adults and 20–30% of children are infected by the virus annually, resulting in approximately 3 to 5million cases of serious illness and 250,000 to 300,000 deaths [1].

The Japanese association for infectious diseases recommends conducting the post-exposure prophylaxis with anti-influenza (flu) agents, especially for medical staffs, even if people have already received vaccination. Then, oseltamivir is one of anti-flu agents recommended and emphasized for use by the World Health Organization in both treatment and prophylaxis [2,3]. Oseltamivir has been found to be generally well tolerated by patients, with frequently reported adverse effects such as nausea, vomiting, diarrhea, abdominal pain, with rarer cases of anaphylaxis central nervous system tolerability and serious skin reactions [4,5]. Shinjoh et al. reported the post-exposure prophylaxis with oseltamivir for unexpected occurrences of nosocomial influenza was safe and effective [6].

We had experienced nosocomial outbreak of influenza A (H3) in 2013. Then, a total of 97 persons were diagnosed with flu. After the incidence, we have actively recommended to take oseltamivir or zanamivir at the therapeutic dose as post-exposure prophylaxis. Until now, influenza outbreak has not occurred since 2014. Thus, the facts suggested that early case detection and the use of antiviral prophylaxis would be effective to truncate the spread of influenza during an epidemic, giving empirical support. However, there are some people who complain adverse events of anti-flu agents. Hence, we undertook a survey to evaluate the compliance and the tolerability of oseltamivir or zanamivir as post-exposure prophylaxis among the medical staffs in the 2014–2015 seasons.

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2. Materials and Methods

2.1. Study procedures

We conducted a retrospective survey of medical staffs, such as physician, nurse, pharmacist, dentist, cleaning staff, and medical student who were prescribed anti-flu agents during the 2014–2015 seasons. This survey was conducted at the Aichi Medical University Hospital (995 beds).

We prescribed anti-flu agents (oseltamivir; 75 mg twice a day for 5 days or zanamivir; 2 blisters twice a day for 5 days) for staffs who had prolonged contact with flu victim within 48 h. But, we did not prescribe anti-flu agents for medical staffs who conducted proper personal protective equipment (PPE), such as surgical mask, when they contacted flu victim. Oseltamivir and zanamivir were prescribed at the therapeutic dosage to prevent the emergence of anti-flu resistance virus by an infectious disease (ID) physician [7]. A pharmacist reviewed contraindications with the medical staff before dispensing these anti-flu agents. Almost staffs received oseltamivir, but the staffs who have allergy or had experienced any adverse events for oseltamivir, pregnant women and nursing women received zanamivir.

Our hospital infection control committee approved the post-exposure prophylaxis regimen. And written informed consent was obtained from all persons for whom ant-flu agent were prescribed for post-exposure prophylaxis.

We asked medical staff received anti-flu agents for post-exposure prophylaxis to respond to questionnaire investigations after the 2014–2015 seasons. The questionnaire included questions on year group and job category; whether they took oseltamivir or zanamivir and for what duration (adherence); and symptoms after taking oseltamivir or zanamivir (including specific gastrointestinal and neuropsychiatric symptoms). This survey study was approved by Aichi Medical University Hospital ethical committee.

2.2. Statistical analysis

The categorical data were analyzed using the chi-squared test between two groups in the percentage of patients. Statistical analysis was performed with JMP, version 10.0 (SAS, Tokyo, Japan). A p value of <0.05 was required to achieve statistical significant.

3. Result

3.1. Subjects

In the 2014–2015 seasons, 540 medical staffs received oseltamivir or zanamivir for prophylaxis. Four hundred eleven of 540 medical staffs (76.1%) responded to our questionnaire investigations. In total, 540 medical staffs had some possibilities to contact with influenza patients, received oseltamivir (n = 382) or zanamivir (n = 29) as post-exposure prophylaxis from November 2014 to March 2015(the 2014–2015 seasons).

The major population who took part in this study was nurses (n = 198, 48.2%; oseltamivir: n = 179, 46.9%; zanamivir: n = 19, 65.5%), followed by doctors (n = 71, 17.3%; oseltamivir: n = 70, 18.3%; zanamivir: n = 1, 3.4%), co-medical (n = 61, 14.8%; oseltamivir: n = 58, 15.2%; zanamivir: n = 3, 10.3%), office worker (n = 27, 6.6%; oseltamivir: n = 27, 7.1%; zanamivir: n = 0, 0%), hospital officials (n = 36, 8.8%; oseltamivir: n = 32, 8.4%; zanamivir: n = 4, 13.8%) and unknown (n = 18, 4.4%; oseltamivir: n = 16, 4.2%; zanamivir: n = 2, 6.9%).

The higher rate of ages in medical staffs who took oseltamivir or zanamivir was 20's (~25; 18.8%, ~30; 19.3%) or early 30's (34.5%). The distribution of ages in medical staffs who reported the incidences of adverse events were shown in Fig. 1 and showed large percentage of late 20's and early 30's (~30; 28.8%, ~35; 30.0%).

3.2. Compliance

The duration of administration for oseltamivir was 1–3 days (n = 114, 29.8%) and 4–5 days (n = 268, 70.2%). On the other hand, everyone took zanamivir for 4–5 days (n = 29, 100.0%).

3.3. Incidence of adverse events

In this survey, adverse events caused by oseltamivir were reported by 86 of 382 medical staffs (22.5%). The most frequent adverse events were gastrointestinal (in 51 of 130; 39.2%), followed by systemic and local disease, especially fatigue.

Table 1 showed major adverse events answered. Eighty six medical staffs (22.5%) experienced more than one symptom. Gastrointestinal adverse events (defined as one or more of the

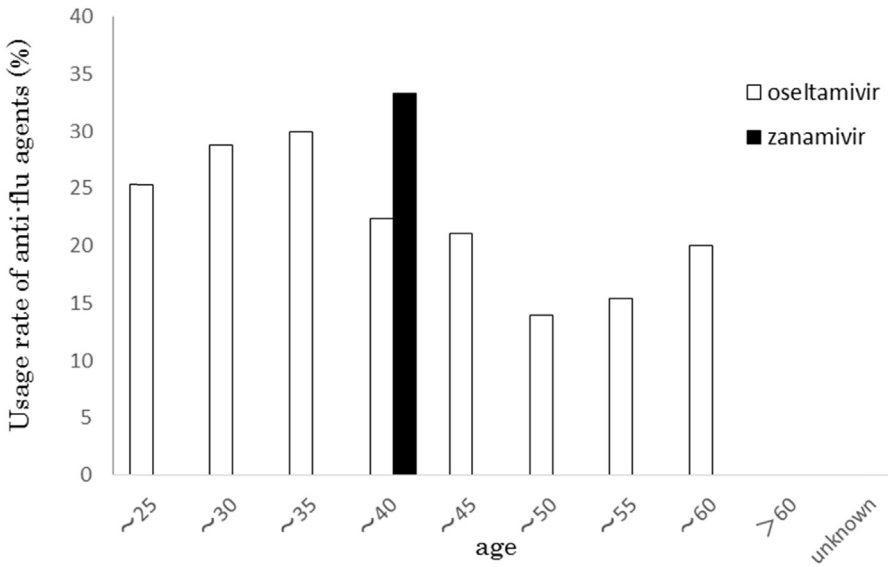

Fig. 1. Usage rate of anti-flu agents separated by ages in medical staffs who reported any adverse events.

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