

Systematic Intervention by Prophylactic Use of Anti-Influenza Agents Reduced Influenza Outbreaks in a Tertiary Hospital in Japan

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Abstract

We regularly experienced influenza outbreaks in a tertiary-care university hospital in Japan from 2011 to 2014. Prophylactic anti-influenza agents were arbitrarily administered in each ward during each hospital-acquired influenza outbreak until 2014, although routine vaccination programs were implemented for both patients and hospital personnel. After 2015, use of prophylactic anti-influenza agents was controlled by infectious diseases (ID) physicians, and both the number of outbreaks and costs of prophylactic drugs were subsequently reduced. Starting in 2016, laninamivir use increased while oseltamivir use decreased, especially in hospital personnel. Prophylactic use of anti-influenza agents in patients was effective and should be systematically managed by ID specialists.

Keywords: Influenza; Outbreak; Oseltamivir; Laninamivir; Prophylaxis; Cost

Introduction

Influenza virus infection is a major respiratory infectious disease that generally induces bronchitis and pneumonia [1]. The virus causes an acute febrile illness with malaise, and complication with bacterial pneumonia can become fatal in the elderly [2,3]. An influenza outbreak is a regular occurrence during the annual influenza season, despite high rates of influenza vaccination, and is also common in medical facilities with attack rates varying from 25% to 70% [4,5].

The main strategy for influenza outbreak prevention might be annual influenza vaccination. However, anti-influenza agents as prophylaxis for healthcare workers and patients are also recommended to inhibit viral transmission. Some clinical studies have shown the effectiveness of neuraminidase inhibitors, such as oseltamivir and zanamivir, when used as primary or post-exposure prophylaxis in healthy adults [6-8]. Another neuraminidase inhibitor, laninamivir, which is a one-dose and inhaled treatment, is now prophylactically administered in Japan [9].

The regularly experienced influenza outbreaks in a tertiary-care university hospital in Japan. Several cases of influenza virus infection were transmitted from patients to healthcare workers and other patients, although vaccination was routinely performed until 2014. After 2015, our infectious disease (ID) physicians started to integrate not only vaccination programs but also the prophylactic use of anti-influenza agents because they were arbitrarily used in each case and ward and not systemically managed.

In this study, aimed to analyze the relation between the occurrence of influenza outbreaks and the effective use of anti-influenza agents.

Materials and Methods

Patients and outbreak

This analysis was retrospectively performed at the Tohoku Medical and Pharmaceutical University Hospital (557 beds) from the 2014 to 2017 season. After 2015, ID physicians assigned and started to integrate management of influenza as next seasons. Influenza virus infection was confirmed by examination of nasopharyngeal swab samples using a rapid antigen detection kit (ESPLINE Influenza A and B-N; Fujirebio, Tokyo, Japan). Influenza-infected patients were isolated in our hospital or discharged on home leave to prevent transmission. Contact tracing was performed to identify individuals with close contact with influenza patients.

Influenza outbreaks were defined as: More than 3-10 patients and personnel infected in each ward (40-50 beds) and, the time period when new patients were not admitted because of a significant decrease in ward functions.

Prophylactic use of anti-influenza drugs

Anti-influenza agents were used for non-influenza patients who were hospitalized in the same rooms and/or wards as influenza patients.

Until 2014, anti-influenza agents were used for not only non-influenza patients who were hospitalized with influenza patients but also personnel who had contact with influenza patients. The costs for these anti-influenza agents were covered by the hospital as public expenses and administered at the discretion of each physician and nurse.

However, after 2015, the use of anti-influenza agents for personnel was generally prohibited, and administration for the prophylactic use of anti-influenza agents for non-influenza patients was systemically determined by ID physicians and specialists.

Oseltamivir and laninamivir

Prophylaxis with oseltamivir (75 mg once a day for 10 days) or laninamivir (2 blisters for one dose was administered after close contact with influenza patients. Laninamivir was used for very close contact cases, such as an individual sharing a bed next to an influenza patient in a room without curtains. Written informed consent was obtained from all individuals prescribed the prophylaxis agents.

Statistical analysis

Differences between groups were determined using analysis of variance, with Fisher's exact test employed for multiple comparisons. A p-value less than 0.05 denoted a statistically significant difference. All analyses were carried out using StatView software (Abacus Concepts, Cary, NC, USA).

Result

Outbreaks, costs of prophylaxis agents, and anti-influenza agents used by season

Four influenza outbreaks occurred in 2014 (Figure 1) and four to seven outbreaks annually occurred until 2014 (data not shown). However, the number of outbreaks decreased after 2015 when ID physicians were employed by the hospital.

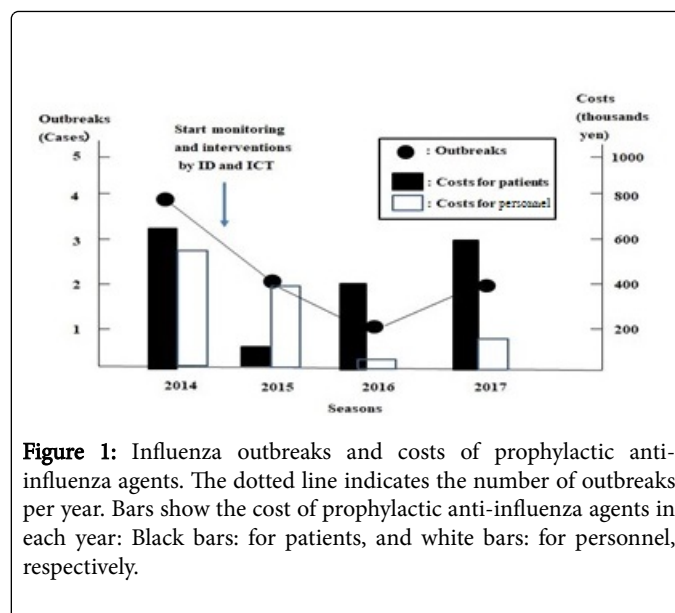


Figure 1: Influenza outbreaks and costs of prophylactic anti-influenza agents. The dotted line indicates the number of outbreaks per year. Bars show the cost of prophylactic anti-influenza agents in each year: Black bars: for patients, and white bars: for personnel, respectively.

Seasons	Osertamivir			Laninamivir			Total
	Patients	Personnel	Total	Patients	Personnel	Total	
2014	191	166	357	0	0	0	357
2015	42	134	176	2	0	2	178
2016	88	0	88	38 [#]	0	38 [#]	126
2017	101	59	160	71 [#]	4	75 [#]	235
Total	422	359	781	111	4	115	896

Note: [#]p<0.01, increase of laninamivir, compared with 2014 and 2015 season, respectively.

Table 1: Items of prophylactic anti-influenza agents.

Although the vaccinations programs were not changed, pre-and post-exposure management of anti-influenza agents was integrated by ID physicians starting in 2015. Costs of prophylactic anti-influenza agents were reduced from total 1,190,000 yen (patients: 569,000 yen, personnel: 621,000 yen) in 2014 to total 503,000 yen (patients: 379,000 yen, personnel: 124,000 yen). A 58% reduction in costs overall and 50% reduction in a number of outbreaks (4 in 2014 to 2 in 2015) were observed.

The costs for prophylactic use of anti-influenza agents were further reduced to overall 449,000 yen (patients: 437,000, personnel: 12,000 yen) in 2016. A 63% reduction in costs overall for prophylactic use of anti-influenza agents and 75% reduction in a number of outbreaks (4 in 2014 to 1 in 2016) were achieved.

Unfortunately, two outbreaks occurred in 2017 and the costs for patients (609,000 yen) to prevent transmission of influenza infections increased in 2017. However, the cost of anti-influenza agents for personnel was low at 180,000 yen.

Furthermore, we analyzed anti-influenza drugs administered as prophylactic agents in our hospital by season (Table 1). Only oseltamivir was used as a prophylactic agent in 2014, and laninamivir use was introduced in 2015. In 2016, laninamivir use was significantly increased (2 patients in 2015 compared with 38 patients in 2016) and remained increased in 2017.

DISCUSSION

The prophylactic effects of anti-influenza agents have been reported, however, the preventive effects of anti-influenza agents against outbreaks administered under integrated management by ID physicians and specialists remain unclear.

In this study, we analyzed the occurrence of influenza outbreaks before (2014) and after (2015-2017) prophylactic intervention in a tertiary-care university hospital in Japan. We found the number of outbreaks subsequently decreased, and costs were also reduced after assignment of ID physicians. Excessive prescription of anti-influenza

agents might be not effective to prevent influenza outbreaks and may be more costly than controlled use of these drugs.

Several studies have examined both the clinical and economic benefits of prophylaxis with anti-influenza agents [10-12]. Among them, Hagihara et al., [12] experienced a large influenza outbreak in Japan, and their interventions finally inhibited influenza virus transmission: the reproductive value was reduced from 1.89 to 0.65. However, over 3,000 people including patients, personnel, students, and attendants received neuraminidase inhibitors. Therefore, the total cost was estimated at >10,000,000 yen. Furthermore, lost hospital revenue's sum was 91,080,000 yen (mean: 6,505,714 yen/day). Ward closure due to influenza outbreaks has significant and direct effects on hospital management. In our hospital, total 50,000,000 yen were estimated as the lost revenue when the cardiology ward was closed in March 2017 (data not shown). Therefore, intervention by ID physicians was crucial. Similarly, we found reductions of 75% for a number of outbreaks and 68% for anti-influenza agent use.

In addition, laninamivir was more often prescribed after our interventions and might have recently become preferred over oseltamivir in Japan. Nakano et al., [9] reported that laninamivir is superior to oseltamivir at inhibiting secondary influenza transmission in family members [9]. Because laninamivir is a one-dose inhaled treatment, patient compliance was also improved compared with oseltamivir, which is administered at 2 doses/day for 5 days. Further examination of the preventive effects of laninamivir in hospitals, nursing homes, and long-term care facilities is needed.

Conclusion

The reduced the number of influenza outbreaks in a tertiary-care university hospital by using integrated management of anti-influenza agents after 2015. Increased laninamivir use focused on post-exposure patients might be effective, although excessive use of oseltamivir for personnel was decreased. Prophylactic use of anti-influenza agents should be systematically controlled by ID physicians/specialists.

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