



Active surveillance and early intervention with oseltamivir for controlling influenza outbreaks in aged care facilities

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Introduction

Despite annual immunisation of older people against influenza, seasonal influenza outbreaks in aged-care facilities (ACFs) remain a significant public health problem and cause significant morbidity and mortality. Outbreaks are often not reported or diagnosed until they are full-blown, and a high attack rate in both residents and staff can ensue. [1-4]

A cluster-randomised controlled study to compare the impact of using oseltamivir for treating patients with influenza to using oseltamivir for both treatment and post-exposure prophylaxis of residents and staff is currently underway in the Sydney-Newcastle region of Australia. In this study context, mechanisms for active surveillance of respiratory illness in ACFs and rapid diagnosis of influenza were established in the participating facilities.

Aim

To assess the feasibility and impact of implementing

- active surveillance for influenza-like illness,
- rapid diagnosis of respiratory viruses including influenza in ACFs, and
- antiviral treatment for controlling influenza outbreaks in ACFs.

Method

Active surveillance & outbreak identification

Active surveillance was established for influenza-like illness in staff and residents of 16 participating ACFs in Sydney-Newcastle region of Australia during the 2006 influenza season (June to November 2006). ACFs were contacted at least three times a week to determine if clinical influenza-like illness (ILI) occurred in any of their residents or staff.

Clinical ILI was defined as acute onset of fever with temperature $\geq 38^\circ\text{C}$ associated with newly-acquired cough or another respiratory symptom or sign (e.g. sore throat, shortness of breath, tachypnoea), irrespective of presence of any other systemic symptoms in a person. A respiratory illness outbreak was defined by occurrence of 2 persons with clinical ILI within a 3-day period, or 3 persons meeting these criteria within 7 days.

Timely microbiological diagnosis

At the first suspicion of a respiratory outbreak through surveillance as per definition, a point-of-care (POC) influenza antigen test for the influenza A and B virus (QuickVue Influenza A+B test, Quidel Corp., San Diego, U.S.A.), which had high specificity though limited sensitivity, was performed on a nose swab obtained from every symptomatic subject on-site in the ACF initially if possible. The test result was read within 10 minutes.

Throat and nose swabs were also obtained from all symptomatic subjects, and from any new symptomatic subjects within 24 hours of the time of symptom onset during the outbreak period. The swab specimens were tested by direct immunofluorescence (DIF) techniques for some common respiratory viruses: influenza A and B, respiratory syncytial virus (RSV), parainfluenzaviruses 1–3, and adenoviruses. Results were available within 24 hours. Nucleic acid tests by polymerase chain reaction (PCR) technique for influenza A and B were also used if DIF tests did not provide any positive identification. Results were available later, but within a week.

All subjects who received oseltamivir treatment or prophylaxis were tested for seroconversion against influenza A and B (4-fold increase in titre 4 to 6 weeks after the initial or pre-prophylaxis sample). All subjects who received prophylaxis also had a set of pre-prophylaxis nose and throat swabs taken, and tested for respiratory viruses if he/she became symptomatic during the outbreak.

Outbreak management including antiviral use

For all facilities with respiratory illness outbreaks, enhanced infection control measures were implemented immediately after an outbreak was identified. In the ACFs with influenza outbreaks, participants (residents or staff) with clinical ILI symptoms received oseltamivir treatment if they were identified within 48 hours of symptom onset. Other participants who were exposed received oseltamivir prophylaxis during the influenza outbreak period (as per randomisation according to the main study protocol).

Method (continued)

Detailed epidemiological investigations

Epidemiological information, including onset of any fever or any respiratory symptoms in any residents or staff reported one week before and during the outbreak period was sought and reviewed. Consequently some cases were identified retrospectively after an outbreak was identified. A subject was regarded as a suspect case if he/she developed a fever or a respiratory symptom or sign during an outbreak, and would be considered a confirmed case of influenza if the full clinical definition of ILI was met and at least one laboratory test results was positive for influenza.

The duration of each outbreak, the illness attack rates in residents and staff, and timeliness of diagnosis and management response to outbreaks were also measured.

Results

Seven respiratory outbreaks were identified through the surveillance system. The causes of four of these outbreaks were identified: two were influenza A, one was parainfluenzavirus-1, and the other respiratory syncytial virus (RSV). (Table 1)

Table 1 – Summary of respiratory illness outbreaks in participating ACFs in 2006

Outbreak identifier	Aetiology	Number of residents in facility	Total number of cases (suspect + confirmed)	Number of cases in residents	Number of cases in staff	Attack rate in residents	Number hospitalised	Number of death	Duration of outbreak (days) ^A	Time from first case ^{AA} to first POC test	Time from first case ^{AA} to an outbreak being identified
A	Not identified – not influenza	78	19	18	1	23%	0	0	17	11 days	11 days
B	Not identified – not influenza	160	10	10	0	6%	0	0	20*	4 days	4 days
C	Not identified – not influenza	130	28	28	0	22%	0	0	19	4 days	4 days
D	Parainfluenza 1	80	12	11	1	14%	0	1	10	2 days	4 days
E	RSV	147	16	13	3	9%	1	2	18	11 days	11 days
F	Influenza A	92	17	13	4	14%	2	0	19	2 days	6 days
G	Influenza A	160	9	0	9	0%	0	0	7	3 days	5 days

^A from symptom onset time of the first case to that of the last case

^{AA} the first case was identified retrospectively from epidemiologic information, and might not be the first reported case in the outbreak

* outbreak occurred in 2 phases at different geographical sections within the ACF

The median time from symptom onset of the first actual case to the time that the first diagnostic test of an outbreak was carried out was 4 days (range 2–11 days). The median time taken for respiratory illness outbreaks to be identified and acted upon was 5 days (range 4–11 days).

For the two influenza outbreaks (F & G), outbreak management measures were instigated as soon as the outbreak was defined on the basis of cluster occurrence of clinical ILI cases with one of the case subjects having a positive POC test result. The outbreaks would have been identified to be caused by the influenza A virus 4 days and 1 days later respectively if the POC test was unavailable and that the diagnosis was based on the earliest positive DIF or PCR tests.

Antiviral treatment and prophylaxis were initiated 0–1 days after diagnosis of the outbreak. In both outbreaks <12 cases of probable or confirmed influenza accrued with no associated deaths. In the more severe influenza outbreak (F), 13 (14%) residents and 4 (5%) members of staff had possible or proven infection. Although all residents and staff without clinical ILI in this outbreak were offered oseltamivir prophylaxis, only a proportion accepted the antiviral. (Table 2)

Table 2 – Attack rates and use of oseltamivir in the two influenza outbreaks in ACFs

	Outbreak F			Outbreak G		
	Residents	Staff	Overall	Residents	Staff	Overall
Total number	92	79 (39#)	171	160	150 (76#)	310
Proportion who have received influenza vaccination 2006	76.40%	Insufficient data	-	81.20%	Insufficient data	-
Total number of cases (suspect + confirmed)	13	4	17	0	9	9
Attack rate	14%	5%	10%	0%	6%	3%
Use of Oseltamivir (commenced 1 day after outbreak identified)	(commenced on the day of outbreak)			(commenced on the day of outbreak)		
Number of subjects who received oseltamivir treatment	3	1	4	0	8	8
Number of subjects who received oseltamivir prophylaxis (% of total)	49 (53%)	14 (18%)	63 (37%)	6 (4%)	25 (17%)	31 (10%)

average number of staff per day being on-duty during the outbreak period

Discussion

Despite limitations in prospective case identification and timely reporting, active surveillance for influenza-like illness in ACFs facilitated early detection of respiratory illness outbreaks.

On identification of a respiratory outbreak, early microbial diagnosis enabled early institution of antivirals when influenza was the proven pathogen. In the two influenza outbreaks, the availability of positive POC antigen test results allowed prompt specific control measures, in particular timely use of antiviral treatment and prophylaxis, to be implemented 1 to 4 days before laboratory results confirming influenza was available. This time gain might be crucial to more effective outbreak control, especially since therapeutic benefits of oseltamivir would become insignificant if it was commenced more than 48 hours from symptom onset.

Instead of targeted use of oseltamivir when influenza was diagnosed, an alternative outbreak control policy could possibly be the use of oseltamivir based on clinical definition before microbiological diagnosis. However, this study showed that only a small proportion of respiratory outbreaks were in fact caused by influenza. Emergent oseltamivir-resistance in influenza viruses resulting from widespread use is a potential concern.

Although only a proportion of staff and residents received oseltamivir as antiviral treatment or prophylaxis, the outcomes of these 2 influenza outbreaks compared very favourably with outbreaks reported in recent years in comparable settings in Australia, in which the attack rates were in the range of around 40% despite the use of neuraminidase inhibitors. [1-4]

Conclusion

- Active surveillance for influenza-like illness in ACFs facilitates early detection and intervention for respiratory outbreaks.
- Early laboratory diagnosis, supplemented by POC tests, enables early institution of antivirals when influenza is the proven pathogen.
- Timely confirmation of influenza allows targeted rather than indiscriminate use of antivirals and early effective outbreak control.

References

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