



Clinical efficacy of seasonal influenza vaccination: characteristics of two outbreaks of influenza A(H1N1) in immunocompromised patients

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SUMMARY

Background: Influenza A(H1N1) causes serious complications in immunocompromised patients. The efficacy of seasonal vaccination in these patients has been questioned.

Aim: To describe two outbreaks of influenza A(H1N1) in immunocompromised patients.

Methods: Two outbreaks of influenza A(H1N1) occurred in our institution: on the kidney transplant ward in 2014 including patients early after kidney or simultaneous pancreas–kidney transplantation, and on the oncology ward in 2016 including patients receiving chemotherapy for malignant tumours. Factors leading to these outbreaks and the clinical efficacy of seasonal influenza vaccination were analysed.

Findings: Altogether 86 patients were exposed to influenza A(H1N1) during the outbreaks, among whom the seasonal influenza vaccination status was unknown in 10. Only three out of 38 vaccinated patients were infected with influenza A(H1N1), compared with 20 out of 38 unvaccinated patients ($P = 0.02$). The death of one out of 38 vaccinated patients was associated with influenza, compared with seven out of 38 unvaccinated patients ($P = 0.06$). Shared factors behind the two outbreaks included outdated facilities not designed for the treatment of immunosuppressed patients. Vaccination coverage among patients was low, between 40% and 70% despite vaccination being offered to all patients free of charge. Vaccination coverage of healthcare workers on the transplant ward was low (46%), but, despite high coverage on the oncology ward (92%), the outbreak occurred.

Conclusion: Seasonal influenza vaccination was clinically effective with both a reduced risk of influenza infection and a trend towards reduced mortality in these immunocompromised patients. Several possible causes were identified behind these two outbreaks, requiring continuous awareness in healthcare professionals to prevent further outbreaks.

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Introduction

Seasonal influenza vaccination has been recommended for high-risk patients for years, but since the influenza A(H1N1) pandemic in 2009, general awareness has increased, and several studies have addressed the serious consequences of

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influenza infections in immunocompromised patients, such as recipients of solid-organ transplantation [1,2]. During the 2009 pandemic, serious complications were recorded in transplant recipients infected with influenza A(H1N1), among whom pneumonia was reported in 30%, admission to intensive care unit (ICU) in 16–20%, and mortality in 4–8% of patients [2,3]. Increased rates of complications have similarly been reported in other immunocompromised patient groups, such as haematopoietic stem cell transplant recipients and patients with solid tumours, with reported mortality rates of ~6–10% [4,5]. By comparison, in healthy individuals the mortality of influenza A(H1N1) is reported as 0–2% among hospitalized patients, and the risk of ICU admission about 10–20% among hospitalized patients [6–9].

Although seasonal influenza vaccination is recommended for high-risk groups, the efficacy of vaccination has been questioned in immunocompromised patients, with seroconversion rates barely reaching 50% in several studies including solid-organ transplant recipients, patients with end-stage renal disease, or patients receiving chemotherapy [10–16].

We recently described a serious outbreak of influenza A(H1N1) in a kidney transplant unit [17]. In addition to this outbreak, another serious outbreak of influenza A(H1N1) occurred in our institution in the oncology department in 2016. Factors leading to these serious outbreaks were analysed thoroughly, and several common factors could be identified in these outbreaks despite the two somewhat different types of patient groups. The aim of this study was to describe the factors leading to these two serious influenza A(H1N1) outbreaks in a large tertiary hospital, and to describe the protective effect of vaccination observed in immunocompromised patients.

Methods

Helsinki University Hospital supplies tertiary care for a population of ~1.5 million inhabitants, and serves the whole of Finland (population ~5.5 million) for certain special treatment services, such as solid-organ transplantation. Annually ~250 kidney transplantations are performed in the transplant unit, of which 15–20 are simultaneous pancreas–kidney (SPK) transplantations.

Approximately 1000 patients are admitted to the oncology ward per year, half of whom are treated for lymphoma. The average stay is four or five days. Yearly, 25–35 autologous transplants are performed.

Primary immunosuppression after kidney or SPK transplantation is a combination of cyclosporine or tacrolimus, mycophenolate, and steroids. Patients with higher immunological risk or recipients of SPK receive induction with basiliximab or anti-thymocyte globulin. After kidney transplantation, patients remain hospitalized for about 10–21 days, after which they return for follow-up to their own district hospital. In addition to postoperative treatment early after transplantation, the kidney transplant ward also includes patients with complications after transplantation (such as acute rejection, or surgical or infectious complications). Due to ongoing renovations in the hospital facilities, the kidney transplant service was temporarily located in a ward not designed for the treatment of immunosuppressed patients. The ward had 16 patient beds: four three-bed rooms with shared sanitation, and two two-bed rooms with bathrooms, but no

single rooms. Rooms were narrow and space between beds was 60–90 cm in width. Patients shared a common dining room. In addition to inpatients on the ward, it was also used for frequent outpatient visits for patients in early stages after transplantation and for patients travelling from other parts of the country.

The oncology ward – one of the two wards in the oncology department built in the 1960s – has 18 patient beds and two beds for daycare patients. The ward specializes in treating adolescents and young adults with lymphoma, testicular cancer, osteosarcoma and Ewing sarcoma together with lymphoma patients of all ages. Patients receiving high-dose chemotherapy with autologous stem cell transplantation as a part of their treatment for lymphoma, testicular cancer and Ewing sarcoma are cared for on the ward. Patients with other cancers are mainly treated for cancer therapy-induced complications and for need of immediate palliative care. There are five single rooms with their own toilet; only one has its own bathroom. Five rooms house three beds, for which there are four toilets and three showers on the corridor. The young patients especially have been encouraged to use the dayroom to find peer support.

Influenza A was diagnosed with a qualitative real-time polymerase chain reaction from nasopharyngeal swabs, as described [18]. Seasonal influenza vaccination is recommended for all patients at risk of infection, including end-stage renal disease patients on dialysis, patients after kidney transplantation, and patients receiving treatment for cancer, and the vaccination is provided free of charge. Vaccination is also recommended for all healthcare professionals free of charge. Seasonal vaccine in the 2013–2014 campaign included three antigens: influenza A/California/7/2009 (H1N1)-like virus, influenza A/Texas/50/2012 (H3N2)-like virus, and influenza B/Massachusetts/2/2012-like virus, and was either Fluarix (GlaxoSmithKline, Brentford, UK), recommended for patients aged >65 years, or Vaxigrip (Sanofi Pasteur MSD, Brussels, Belgium) for younger patients, both inactivated trivalent vaccines without adjuvant. The seasonal vaccine in the 2015–2016 campaign was Vaxigrip (Sanofi Pasteur MSD, Brussels, Belgium), containing three antigens: A/California/7/2009 (H1N1)pdm09-like virus, A/Switzerland/9715293/2013 (H3N2)-like virus, and B/Phuket/3073/2013-like virus.

Differences in variable distributions between the two groups were analysed using the non-parametric Mann–Whitney *U*-test (continuous variables), or Fisher's exact test (categorical variables). The calculations were performed with IBM SPSS Statistics (version 20; IBM Corporation, Somers, NY, USA). Two-sided $P < 0.05$ was considered statistically significant.

Results

Description of the outbreaks

The outbreak on the kidney transplant ward has been described in detail previously [17]. Briefly, in April 2014, altogether 23 patients were treated on the ward during the outbreak (Table 1). After the first positive case, all patients were tested and seven patients were diagnosed with influenza A(H1N1). Of the 17 patients who had received adequate seasonal influenza vaccination, two out of 17 tested positive for influenza (one asymptomatic, one with mild cough). Influenza

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