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Original article

The uptake of influenza and pneumococcal vaccination among immunocompromised patients attending rheumatology outpatient clinics

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ABSTRACT

Purpose and objectives: The patients using immunosuppressive agents are considered at high risk for acquiring different infections. Accordingly, international guidelines recommend vaccinating such patients against influenza and pneumococcal organisms. The aims of this study were two-fold: (1) to assess the influenza and pneumococcal vaccination uptake among our rheumatology outpatients who are immunosuppressed; (2) to identify the factors influencing immunisation uptake among our sample of patients.

Methods: This was a questionnaire-based study. Patients were eligible to partake in this study if they were using immunosuppressive drugs. During the study period (4 weeks), 337 patients were screened, and 110 patients fulfilled the criteria for inclusion.

Results: Positive vaccination uptake of our cohort was as follows: common influenza alone (34%, 37 out of 110), pneumonia alone (11%, 12 out of 110), and both pneumococcal and influenza vaccination (11%). The status of influenza A (H1N1) vaccination was not recorded as a part of this audit. The two most common reasons cited by patients for non-uptake of vaccinations were: 'not offered' and 'thought it was unnecessary'. Of 37 patients who had influenza vaccination, 33 patients (89%) had additional risk factors, and there were only four patients who had influenza vaccine solely because they were taking immunosuppressive drugs. All pneumococcal vaccinated patients ($n = 12$) were noted to have additional risk factors.

Conclusion: There is suboptimal uptake of influenza and pneumococcal vaccinations among immunosuppressed patients attending rheumatology outpatient clinics. These results are a cause of concern given the morbidity and mortality of associated infections.

Patients with rheumatoid arthritis, systemic lupus erythematosus, vasculitis, and other chronic inflammatory rheumatic diseases are at increased risk of infection compared with the general population [1–3], and concomitant medication use (immunosuppressive agents) may increase this risk further [4]. This is associated with significant morbidity and mortality. Not all antirheumatic drugs are same as regards their immunosuppressive effect. Methotrexate, leflunomide, prednisolone, cyclophosphamide, cyclosporine, mycophenolate mofetil and biologic agents are generally considered as major immunosuppressives. Among them, anti-TNF agents carry a significant risk given the commonness of their use, and being used as a maintenance therapy; moreover, such agents are combined with other DMARDs, which possibly worsen the immunosuppression status of patients. However, hydroxychloroquine, and sulphasalazine are considered to cause either no immunosuppression or minor immunosuppression [5,6].

The two vaccines that are routinely recommended to adults using immunosuppressives are: firstly, the influenza vaccination, given that such patients are at the heightened risk of complications of influenza infection; secondly, the pneumococcal vaccine, as pneumonia is one of the most common and life-threatening infections requiring hospitalization. Accordingly, international guidelines recommend that such patients should have influenza and pneumococcal vaccinations [5]. Moreover, such vaccinations have also been recommended for a number of other high risk groups, such as individuals over the age of 65 years, and the patients with chronic renal failure, chronic heart failure, chronic liver failure, chronic lung disease, and hyposplenism [7]. During the autumn 2009, Government bodies in Ireland instigated a mass vaccination programme against H1N1 infection, and these vaccines were provided free of cost through our primary care physicians. Similarly, Irish Society of Rheumatology published its recommendations

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regarding the implications of swine flu risk for immunosuppressed infections [8]. These recommendations were published in autumn 2009, and it was suggested that all patients with inflammatory rheumatic diseases should be offered both the seasonal flu vaccine and the swine flu vaccine; these information were sent to general physicians and patients on their request.

The aims of this study were two-fold: (1) to assess the influenza and pneumococcal vaccination uptake among immunosuppressed patients attending rheumatology outpatient clinics; (2) to identify the factors influencing immunisation uptake among our sample of patients.

1. Methods

This study was carried out in the setting of a tertiary university hospital in Ireland. The study participants were all consecutive patients attending our rheumatology outpatient departments, and this audit was carried out over a period of 4 weeks (September 2009). Patients were eligible to partake in this study if they were using immunosuppressive drugs–methotrexate, leflunomide, biologic agents, azathioprine, mycophenolate mofetil, cyclosporine, cyclophosphamide, systemic corticosteroids (over 20 mg per day for at least 1 month in the last 12 months). This was a questionnaire-based study. The patients were interviewed and their medical records were reviewed for their demographic details, rheumatologic diagnosis, comorbid conditions, medications used, uptake of dual vaccination (influenza vaccination during the previous one year and pneumococcal vaccination during the previous 5 years), and the reasons if not being vaccinated. This audit was undertaken before the Irish Society of Rheumatology published its recommendations in October 2009; hence, the status of influenza A (H1N1) vaccination was not recorded as a part of this audit. The information about patient's immunisation status was based on patient's self report. No particular exclusion criteria were specified. All participants were briefed regarding the purpose of survey and verbal consent was obtained before their participation. The response rate in this questionnaire-based study was 100%. The statistical analysis was performed using SPSS version 17. Univariate and multivariate regression models were used to test the predictive value of different variables.

2. Results

During the study period, 337 patients were screened and 110 patients fulfilled the criteria for inclusion. The mean age of patients was 55 years with a standard deviation of 13.49, and 63% ($n = 69$) of the cohort was female. We found that only 11% (12 out of 110) of patients had received both influenza and pneumococcal vaccination, 34% (37 out of 110) of the cohort had the influenza vaccine during the previous 12 months, and only 11% ($n = 12$) could recall having a pneumococcal vaccine. Sixty-six percent ($n = 73$) of patients had received neither of these vaccines, and none of the patients received pneumococcal vaccine alone.

Seventy-two percent (79 out of 110) of the cohort had rheumatoid arthritis (RA), and seronegative peripheral arthropathy was a diagnosis in 14% ($n = 15$) of the patients. Disease-modifying antirheumatic drugs (DMARDs) usage among our cohort was as follows: 63% of patients were taking methotrexate, 17% (19 out of 110) of patients were using TNF blockers, and 24.5% (27 out of 110) of patients were using prednisolone. Of these 27 patients using prednisolone, 21 patients were on concomitant DMARDs (Table 1). Moreover, there were nine patients using maintenance low-dose steroids (≤ 7.5 mg a day), and they did not require greater or equal to 20 mg of corticosteroids for one month in the last 12 months. These patients were excluded from the analysis; however, all such patients ($n = 9$) were using concomitant DMARDs/TNF blockers and they were already included for the assessment of vaccination status. The main reasons given for not being vaccinated were as follows: "not offered" ($n = 88$, 80% of patients), "thought it was unnecessary" ($n = 9$, 12%) (Table 2).

Table 1
Demographic characteristics and the immunosuppressive drugs used.

Demographics	Number (%)
Total number of patients screened	337
Number of patients fulfilling the inclusion criteria	110
Response rate	100%
Female patients	69 (66%)
Mean age of patients	55 years (±13.49)
Immunosuppressive drugs used	
Methotrexate	69 (63%)
Leflunomide	4 (3.6%)
Azathioprin	7 (6%)
Etanercept	12 (11%)
Adalimumab	7 (6%)
Cyclosporin	1 (0.90%)
Mycophenolate mofetil	5 (4.5%)
Prednisolone	27 (24.5%)
Prednisolone + DMARDs	21 (19%)
Combination DMARDs	6 (5.45%)

We also documented the presence of additional risk factors (besides being on immunosuppressives) for which influenza and pneumococcal vaccination are also recommended (such as individuals over the age of 65 years, and the patients with chronic renal failure, chronic heart failure, chronic liver failure, chronic lung disease, and hyposplenism), and this has been summarised in the Table 2. In total, there were 45 patients (45 out of 110) who had additional risk factors, and the most common among them was the age above 65 years (33 out of 45). Of 37 patients who had influenza vaccination, 33 patients (89%) had additional risk factors, and there were only four patients who had influenza vaccine solely because they were taking immunosuppressive drugs. All pneumococcal vaccinated patients ($n = 12$) were noted to have additional risk factors.

The presence of additional risk factor was found to be a significant factor for influenza vaccine uptake (OR 23.97, 95% CI 7.96–72.16, $P < 0.0001$), and pneumococcal vaccination (OR 7.42, 95% CI 1.51–36.22, $P = 0.013$) (Table 3). It was also noted that the

Table 2
Demographic characteristics and the brief summary of results.

Diagnoses	
RA	79 (72%)
Psoriatic and seronegative spondylarthropathies	15 (14%)
Ankylosing spondylitis	6 (5.45%)
SLE	6 (5.45%)
Scleroderma	2 (1.8%)
Beçhet's disease	1 (0.90%)
Additional risk factors	
Age > 65 years	33 (30%)
Chronic kidney disease	7 (6%)
Ischemic heart disease	8 (7%)
Chronic lung disease	13 (12%)
Diabetes mellitus	6 (5.45%)
Splenectomy	2 (1.8%)
Positive vaccination uptake	
Influenza	37 (34%)
Pneumonia	12 (11%)
Both vaccinations	12 (11%)
Reasons given for non-vaccination	
Not offered	88 (80%)
Thought it was unnecessary	9 (12%)
Not that old	6 (8%)
No reason	5 (4.5%)
Fear of vaccination	2 (1.8%)