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Vaccination of chemotherapy patients—effect of guideline implementation

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Abstract

Purpose: Despite substantial morbidity and mortality of influenza and pneumococcal infections in cancer patients treated with chemotherapy, vaccination against both illnesses is infrequent. We evaluated the impact of implementation of clinical guidelines on vaccination of chemotherapy patients treated in our institute.

Methods: Prospective audit before (2012) and after (2013–2014) the introduction of immunisation guidelines for chemotherapy patients in a UK tertiary cancer centre.

Results: Guideline implementation was associated with a significant increase in the rate of pneumococcal vaccination compared to the 2012 baseline (47% vs. 25%, $P=0.0018$), though this was not sustained the following year (34%, $P=0.13$ vs. baseline). Influenza vaccine coverage was high (~70%) throughout. There was a marked disparity between patients aged ≤ 65 and those >65 years in the rate of pneumococcal vaccination in both 2013 and 2014 (38% vs. 68% and 17 vs. 53%, respectively, both $P<0.001$), and, to a lesser extent, in the rate of influenza vaccination in the same period (64 vs. 82%, $P<0.1$, and 63% vs. 85%, $P=0.009$ respectively).

Conclusions: The implementation of clinical vaccine guidelines was associated with a significant increase in pneumococcal vaccination, though continued effort appears required to deliver persistent improvement. Initiatives to increase vaccination uptake in patients aged ≤ 65 are merited.

Keywords

Influenza; *Streptococcus pneumoniae*; vaccination; immunisation; chemotherapy; cancer.

Introduction

Cancer patients treated with chemotherapy are at increased risk of developing complications from influenza and *Streptococcus pneumoniae* (pneumococci), with mortality approaching 9% in some subgroups [1]. These illnesses may also compromise cancer treatment by delaying chemotherapy, and result in substantial costs to healthcare providers [2]. Although concerns have been raised regarding the efficacy of vaccination in patients with malignant disease, studies demonstrate that patients with cancer—including those treated with chemotherapy—remain able to respond to vaccination and that influenza immunisation in this group reduces mortality [3, 4]. Side-effects of both influenza and pneumococcal vaccines are mild, and similar to those experienced by the general population [3, 5-7]. Consequently, the UK Department of Health (DH) and the US Center for Disease Control (CDC) recommend that in the absence of contraindications, patients planned for cytotoxic therapy should be vaccinated against both *S.pneumoniae* and influenza [8, 9].

In the UK, influenza and pneumococcal vaccines are also recommended for adults in clinical risk groups, including (but not limited to) chronic respiratory, cardiac, or kidney disease, diabetes, immunosuppression and asplenia, and for all adults aged over 65 irrespective of risk factors in the absence of contraindications [8]. The US CDC recommends that all adults receive annual influenza vaccination regardless of age, and that pneumococcal vaccination is given as a one-off (one or two doses depending on vaccine type) to adults under 65 with a wider range of risk factors than those used in the UK (also including alcoholism and smoking), and those 65 and over irrespective of risk. The pneumococcal vaccine strategy in the US includes both PCV13 and PPV23 while in the UK only adults with substantial immunosuppression as a risk factor receive PCV13 in addition to PPV23 [9].

Previous studies have demonstrated that vaccination uptake in cancer patients is generally poor [10-16] (Table 1), and initiatives to improve this are therefore potentially of substantial clinical benefit. We noted that vaccination advice to patients from oncologists in our centre was variable, and frequently inconsistent with UK DH recommendations. We performed a prospective audit to examine this, developed clinical guidelines with intention of improving vaccination uptake, and repeated the audit following their implementation.

Materials and Methods

We asked patients attending the Chemotherapy Day Unit in the Oxford Cancer Centre in January 2012 to complete an anonymous questionnaire regarding vaccination status and prior advice on immunisation from oncologists / specialist nurses (Supplementary data 1). We developed vaccination guidelines, and publicised these to hospital practitioners by email and internal presentation, and to local primary care physicians by email. The guidelines were implemented in September 2012 and included a detailed version on the hospital intranet, a summary poster in clinic rooms, and a letter for patients to take to primary care physicians. To assess their impact, we repeated the audit in January 2013, and April 2014. We used Fisher's exact test to compare categorical data between audits. All *P* values were two-sided, and significance was accepted at $P < 0.05$. Ethical approval was not required for this clinical audit, the protocol for which is provided in the Supplementary information accompanying this report (Supplementary data 2).

Results

Patient age, tumour type and influenza / pneumococcal vaccination coverage are shown in Table 2. Of 72 patients who completed the questionnaire at baseline, 49 (68.1%) reported prior influenza vaccination, and 18 (25%) reported previous pneumococcal vaccination. 18 (25%) respondents recalled specific discussion with their oncologist / specialist nurse regarding immunisation (Table 2). In 2013 following guideline implementation there was a significant increase in the frequency of pneumococcal vaccination (47.7%, $P = 0.002$), and in the proportion of patients who recalled advice regarding immunisation from their oncologist / specialist nurse (45.5%, $P = 0.02$), though the rate of influenza vaccination was similar to baseline (71.6%, $P = 0.73$) (Table 2). However, in 2014 the increase in pneumococcal vaccination and recollection of oncology guidance was more modest and not significantly greater than baseline (33.6%, $P = 0.13$; and 36.7%, $P = 0.14$, respectively). The rate of influenza vaccination (72.7%) was similar to the two previous years (Table 2).

We found a substantial and highly significant disparity in the frequency of pneumococcal vaccination between patients ≤ 65 and those > 65 years in both 2013 (37.5% vs. 67.5%, $P = 0.0004$) and 2014 (17.4% vs. 53.4%, $P < 0.0001$). Though less marked, there was also discordance in the rates of influenza vaccination according to

age in the same periods (64.0% vs. 81.6%, $P=0.09$ and 62.9% vs. 84.5%, $P=0.009$ respectively). In 2013 and 2014, patients aged <65 years more commonly cited chemotherapy as the reason for influenza vaccination than older patients (68.8% vs. 16.1%, and 56.8% vs. 14.3%, respectively; $P<0.0001$ for both comparisons). Similar discordance between age groups was evident in the proportion that reported that pneumococcal vaccination was given due to planned systemic anti-cancer therapy (40.0% vs. 18.5%, $P=0.16$ and 75.0% vs. 16.1%, $P=0.0005$ respectively). Unfortunately, lack of collection of data on patient age in the 2012 audit precluded comparison of guideline impact between age strata.

Discussion

We have shown that implementation of a vaccination guideline in our centre was associated with a significant improvement in the rate of pneumococcal immunisation, and an apparent increase in the proportion of physicians/specialist nurses offering advice on vaccination. However, the intervention was not associated with an increase in the rate of influenza vaccination from a high baseline. The improvement in pneumococcal vaccination and proportion recalling vaccination advice was less marked two seasons following guideline introduction, suggesting that continued emphasis may be required to maintain physician / specialist nurse awareness.

The low coverage of pneumococcal vaccination at baseline in our study (25%), is comparable to that previously reported (4-16%) [10-16] (Table 1). Similarly, the rate of influenza immunisation in 2011/12 is consistent with the UK national average of 74% achieved in 'high risk' patients (>65 or 'at risk') in those years [17], and higher than most previous reports (Table 1), due at least in part to the excellent coverage in patients aged >65. The failure of our intervention to increase uptake from this high baseline is likely to reflect the challenge of improving on what is an already an effective primary care-based vaccination strategy in the UK. An important finding of our study is the poor vaccination coverage in patients aged 65 or under in contrast to high coverage in those aged over 65 where these vaccines form part of a universal national programme. This is concordant with previous reports [11, 14, 15], and may result from less effective invitation of patients for targeted immunisation by primary care physicians than the more systematic invitation of patients that occurs after their 65th birthday. Improving awareness of the importance of vaccination of such patients among general practitioners is likely to be as important as educating hospital practitioners in reducing this disparity.

Our study has limitations. The use of questionnaires to obtain vaccination histories relies on patient recollection, with its attendant risk of bias. However we note that for each year in our series all patients recalled their history of influenza vaccination, while >80% were able to recall pneumococcal immunisation status. Another limitation is the absence of data regarding patient age at baseline, which meant we were unable to examine the effect of our guidelines on patients stratified by age. As our results highlight that age ≤ 65 is strongly associated with lack of influenza and pneumococcal vaccination in cancer patients, it is important that further studies focus on the effect of vaccination initiatives in this patient cohort.

While cancer patients treated with chemotherapy may be less likely to benefit from influenza and pneumococcal vaccination than the healthy population (in whom the protection is estimated at 50-80% [18], and $\sim 50\%$ [19] respectively), the available evidence suggests that the proportion of patients who mount an adequate serological response is sufficient to justify immunisation. While this is reflected in current DH and CDC recommendation [8,9], as noted previously vaccination coverage in this patient group is unsatisfactory [10-13]. While demonstrating that implementation of immunization guidelines may help to improve coverage, our study highlights that there remains scope for improvement, particularly in the ≤ 65 group.

Conclusions

In our study, a simple intervention of guidelines, clinician education and a letter for general practitioners was associated with a significant improvement in pneumococcal vaccination coverage in chemotherapy patients. However, the increase was no longer significant two years after baseline, suggesting that continued emphasis on the importance of vaccination is required to deliver sustained improvement.

Vaccination of patients aged ≤ 65 , who are not routinely invited for immunisation by general practitioners, is poor – particular effort appears merited to improve uptake in this population.

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Conflict of Interests

The authors declare no conflicts of interest.

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Ethical Approval

Not required

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Table 1. Uptake of influenza and pneumococcal vaccination in cancer patients

	Patient cohort	n	Date	Country	Rate of vaccination	Reference
Influenza vaccination	Solid tumours	110	2003	UK	36%	Ring et al [12]
	Solid tumours	1225	2003	USA	26.7% in 1993 - 43% in 1998	Earle et al [13]
	Solid tumours	112	2008	France	30%	Loulergue et al [11]
	Haematological malignancies	200	2010	France	25.5%	Lachenal et al [16]
	Solid tumours and haematological malignancies	100	2011	Iran	9%	Meidani et al [10]
		129	2011	Canada	57.0%	Chin-Yee et al [15]
	Solid tumours I	359	2013	Turkey	17%	Urun et al [14]
Pneumococcal vaccination	Solid tumours	359	2013	Turkey	4.2%	Urun et al [14]
	Solid tumours	96	2014	Sweden	15.6%	Berglund et al [23]

Table 2. Frequency of influenza and pneumococcal vaccination in chemotherapy patients prior and subsequent to guideline implementation

		Jan 2012 (n=72)		Jan 2013 (n=88)		April 2014 (n=128)		<i>P</i>	
		n	%	n	%	n	%	2013 vs. baseline	2014 vs. baseline
Age									
	Median (range)	–		63.5 (21-83)		62.0 (21-103)		–	–
	<65	–	–	50	56.8	70	54.7	–	–
	>65	–	–	38	43.2	58	45.3	–	–
Influenza vaccination*									
	Yes	49	68.1	63	71.6	93	72.7	0.73	0.52
	No	23	31.9	25	28.4	35	27.3		
	Unsure	0	0	0	0	0	0		
Pneumococcal vaccination**									
	Yes	18	25.0	42	47.7	43	33.6	0.002	0.13
	No	43	59.7	32	36.4	59	46.1		
	Unsure	11	15.3	13	14.8	26	20.3		
Received vaccination advice***									
	Yes	18	25.0	40	45.5	47	36.7	0.02	0.14
	No	45	62.5	41	46.6	70	54.7		
	Unsure	8	11.1	7	8.0	9	7.0		

Cancer types by audit period:

– 2012: breast 16.7%; colorectal 15.3%; gynaecological 16.7%; lung 9.7%; urological 8.3%; other 30.6%; unknown 2.8%.

– 2013: breast 6.8%; colorectal 15.9%; gynaecological 8.0%; lung 13.6%; urological 8.0%; haematological 34.1%, other 11.4%, unknown 2.3%.

– 2014: breast 16.4%; colorectal 14.8%; gynaecological 11.7%; lung 6.3%; urological 7.0%; haematological 15.6%; other 27.3%; unknown 0.8%.

* influenza vaccination during current influenza season. **any prior pneumococcal vaccination. *** received vaccination advice from treating oncologist / specialist nurse prior to chemotherapy. – Data not available.