An audit of influenza vaccination status in adults with inflammatory bowel disease

Neeraj Narula MD, Amit S Dhillon MBBS, Usha Chauhan RN MN, John K Marshall MD MSc FRCP AGAF

BACKGROUND: Several guidelines recommend influenza vaccination for high-risk patients, including those on immune-suppressing medications (IS).

OBJECTIVE: To assess the vaccination status and immunization history of an outpatient inflammatory bowel disease (IBD) population for H1N1 and seasonal influenza.

RESULTS: Among 250 patients, 104 (41.6%) had been immunized against H1N1 and 62 (24.8%) against seasonal influenza, and 158 (63.2%) were taking IS (azathioprine, 6-mercaptopurine, infliximab, adalimumab, methotrexate, cyclosporine or prednisone). Among subjects on IS, the presence of comorbidities warranting vaccination was associated with higher likelihood of H1N1 immunization (62.5% versus 35.8%; P=0.022) but not of seasonal influenza vaccination (25.0% versus 17.2%; P=0.392). Among patients without comorbidities warranting vaccination, IS was associated with a decreased likelihood of vaccination against seasonal influenza (17.2% versus 30.7%; P=0.036) but not H1N1 (35.8% versus 41.3%; P=0.46). The frequency of H1N1 vaccination was significantly higher among patients who visited a general practitioner at least once yearly (45.7% versus 20%; P=0.0027), with a similar trend for seasonal influenza vaccination (27.1% versus 12.5%; P=0.073). Among 91 patients on IS who declined vaccination, 39.6% reported fear of immediate side effects, 29.7% reported concerns about developing serious medical complications, 15.4% reported concerns about activating IBD and 15.4% were not aware that vaccination was indicated.

CONCLUSIONS: Current strategies for vaccinating IBD patients on IS are inadequate. Primary care provider education, incentive programs and regular primary care contact may improve immunization uptake.

Key Words: Crohn disease; Immunization; Influenza; Inflammatory bowel disease; Ulcerative colitis; Vaccination

Influenza infection is responsible for significant morbidity and mortality in epidemic years (1). Patients undergoing immunosuppressive therapies are considered to be more susceptible to influenza infection and its complications (2). Although most individuals recover from influenza infection, adults and children with chronic illnesses, such as inflammatory bowel disease (IBD), are at greater risk for poor outcomes such as pneumonia and death (3). Infections, including influenza, may also exacerbate IBD (4).

Influenza is one of many vaccine-preventable illnesses in adults and children (5). Annual vaccination of immune-suppressed patients has been recommended by several agencies including the Public Health Agency of Canada (2,5-7). Furthermore, recent guidelines from the European Crohn’s and Colitis Organization recommend routine influenza vaccination of all IBD patients, irrespective of therapy (8). Influenza vaccination is safe and immunogenic in patients with IBD using immune-suppressing medications (IS) (9). Despite this, influenza vaccination uptake has previously been noted to be as low as 24% among IBD patients, the majority of whom reported current or previous use of IS (10). To explore influencing factors, an audit of immunization status for both H1N1 and seasonal influenza was undertaken among IBD patients attending outpatient gastroenterology clinic at a Canadian university hospital.

METHODS

A total of 250 consecutive adult patients (≥17 years of age) with IBD attending the McMaster University Medical Centre Digestive Disease Clinic (Hamilton, Ontario) were enrolled between May and August 2010. No exclusion criteria were specified. A two-page questionnaire was used to gather information regarding age, sex, diagnosis, comorbidities, current treatment, vaccination status (including receipt of H1N1 influenza and/or seasonal influenza in the preceding 12 months), sources of counsel regarding vaccination and underlying motive for vaccine refusal, if applicable. No patient refused to participate. The research was approved by the McMaster University/Hamilton Health Sciences Research Ethics Board.

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Statistical analysis

Frequencies were compared using Fisher’s exact test. To assess the strength of the associations while controlling for possible confounding variables, a Cox proportional hazards regression model was used. All baseline variables suspected to impact vaccination status (age >65 years, IS use, other indications for vaccination, sex and regular follow-up with a primary care physician) were entered into the model. Results of the analysis are presented as ORs with 95% CIs. Statistical analysis was performed using GraphPad Prism version 5.03 (GraphPad, USA).

RESULTS

Characteristics of the 250 subjects are summarized in Table 1. The age range was 17 to 86 years, with a mean age of 38.6 years. Most participants were female and 70.8% had Crohn disease. Of the 250 subjects, 104 (41.6%) had been immunized against H1N1 and 62 (24.8%) against seasonal influenza. Use of IS was reported by 158 subjects (63.2%). The most common IS was azathioprine (83 subjects). In total, 41 subjects (16.4%) had additional indications for vaccination (chronic cardiac, pulmonary or renal disease, diabetes mellitus, cancer, pregnancy or age >65 years), of whom 24 were also on IS. Age was the most common additional indication, with 18 subjects >65 years of age.

The frequency of vaccination among immune-suppressed and non-immune-suppressed patients with and without additional indications for vaccination are shown in Table 2. Among 209 patients without additional comorbidities warranting vaccination, IS was associated with decreased uptake of vaccination against seasonal influenza (17.2% versus 30.7%; P=0.036) but not H1N1 (35.8% versus 41.3%; P=0.46). Among 158 subjects on IS, the presence of comorbidities warranting vaccination was associated with higher likelihood of H1N1 immunization (62.5% versus 35.8%; P=0.022) but not seasonal influenza vaccination (25.0% versus 17.2%; P=0.392). The frequency of H1N1 vaccination was significantly higher among patients who visited a general practitioner at least once yearly (45.7% versus 20%; P=0.0027), with a similar trend for seasonal influenza vaccination (27.1% versus 12.5%; P=0.073) compared with patients who visited a general practitioner less frequently or not at all.

Influenza vaccination had been declined by 91 patients on IS (Figure 1). Of these, 36 (39.6%) reported fear of immediate side effects and 27 (29.7%) reported concerns about medical complications of vaccination. A smaller number of patients (15.4%) reported concerns about vaccination leading to relapse of IBD. Importantly, four subjects (4.4%) were advised against vaccination by a health practitioner.

Figure 2 reports the sources of counsel for patients who received vaccination against H1N1, seasonal influenza or both. GI Gastrointestinal

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Characteristics of the sample population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
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<tr>
<td>Patients, n</td>
<td>250</td>
</tr>
<tr>
<td>Age range, years (median)</td>
<td>17–86 (36)</td>
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<tr>
<td>Female sex</td>
<td>153 (61.2)</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
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<tr>
<td>Crohn disease</td>
<td>177 (70.8)</td>
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<tr>
<td>Ulcerative colitis</td>
<td>70 (28.0)</td>
</tr>
<tr>
<td>Indeterminate colitis</td>
<td>3 (1.2)</td>
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<tr>
<td>Immunosuppressive therapy</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>158 (63.2)</td>
</tr>
<tr>
<td>No</td>
<td>92 (36.8)</td>
</tr>
</tbody>
</table>

Data presented as n (%) unless otherwise indicated

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>H1N1 and seasonal influenza vaccination profile of sample population</th>
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<tbody>
<tr>
<td>n</td>
<td>H1N1</td>
</tr>
<tr>
<td>Patients on immunosuppression</td>
<td></td>
</tr>
<tr>
<td>No other risk factor + IS</td>
<td>134</td>
</tr>
<tr>
<td>Risk factor + IS</td>
<td>24</td>
</tr>
<tr>
<td>P=0.022</td>
<td>P=0.392</td>
</tr>
<tr>
<td>Patients without comorbidities meriting vaccination</td>
<td></td>
</tr>
<tr>
<td>No other risk factor + IS</td>
<td>134</td>
</tr>
<tr>
<td>No other risk factor + no IS</td>
<td>75</td>
</tr>
<tr>
<td>P=0.46</td>
<td>P=0.036</td>
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<tr>
<td>Patients with primary care follow-up</td>
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<tr>
<td>≥1 visit(s) per year</td>
<td>210</td>
</tr>
<tr>
<td>&lt;1 visits per year or no PCP</td>
<td>40</td>
</tr>
<tr>
<td>P=0.0027</td>
<td>P=0.071</td>
</tr>
</tbody>
</table>

IS Immune-suppressive medications; PCP Primary care physician

68.8% Family physician
28.6% Family or friends
19.6% GI physician
8.9% Primary care nurse
2.7% Hospital physician

Figure 1) Motive for vaccination refusal by patients using immune-suppressing therapies. IBD Inflammatory bowel disease

Figure 2) Primary counsel for those vaccinated against H1N1, seasonal influenza or both. GI Gastrointestinal
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Several larger studies involving other autoimmune conditions have described exacerbation of IBD after vaccination (17,18). However, three studies have shown no increase of disease activity in pediatric and adult IBD patients following the administration of H1N1 and/or seasonal influenza at the same frequency as immunocompetent individuals. Guillain-Barré Syndrome (GBS) is a rare neurological syndrome that was associated with the 1976 swine influenza vaccine at a rate of one per 100,000 persons vaccinated (13). However, subsequent influenza vaccines have not been found to be associated with GBS, and the Advisory Committee on Immunization Practices has stated that the potential benefits of influenza vaccination in preventing serious illness, hospitalization and death outweigh the possible risk of vaccine-associated GBS (2). However, influenza vaccine should not be given to people with acute febrile illnesses, an anaphylactic reaction to a previous dose or with known immunoglobulin E-mediated hypersensitivity to eggs (7). Apart from these scenarios, the safety of vaccination in immune-suppressed patients is good and the risk-benefit ratio is favourable.

Both health care providers and patients may also have concerns regarding immune reactivity, and 15.4% of our subjects on IS who declined vaccination reported concern about triggering a relapse of IBD. Physicians have reported similar concerns about vaccination of patients with other autoimmune conditions (16). Two case reports have described exacerbation of IBD after vaccination (17,18). However, three studies have shown no increase of disease activity in pediatric and adult IBD patients following the administration of inactivated H1N1 and/or trivalent influenza vaccine (15,19,20). Several larger studies involving other autoimmune conditions have reported adequate humoral responses to vaccination without clinical or biochemical disease reactivation (21-23). Many transplant recipients are not adequately immunized due to concerns about an allograft rejection, even though most studies have failed to demonstrate an association between influenza vaccination and graft rejection (24-26). Patients who express concern about disease reactivation should be counselled about the rarity of such events and the clear health benefits of vaccination.

The majority of patients who received vaccination were counselled to do so by their family physician. In the case of H1N1 influenza vaccination, follow-up with a family physician at least once yearly (OR 2.94 [95% CI 1.26 to 6.83]) was a significant predictor for vaccination. Increasing patients’ contact with their family physicians is one way to increase influenza vaccination uptake. All patients, including those without adequate primary care, should also be counselled about vaccination by their gastroenterologist. Gastroenterologists should also collaborate with primary health care providers before each immunization campaign to ensure vaccination of patients on IS. In the present cohort, there was a trend toward higher uptake of seasonal influenza vaccination among individuals ≥65 years of age. This may reflect reimbursement plans in Ontario that reward family health teams for comprehensive vaccination of senior citizens (27). Similar incentives for vaccination of patients using IS should be considered.

Limitations of our study include its moderate sample size and use of a single centre to recruit patients. The results obtained reflect the vaccination status of a referral population, which may not reflect the true immunization state among IBD patients using IS who are followed by a primary care physician. In addition, vaccination status was obtained by self-report, which is subject to recall bias and may not be as accurate as the use of serum titres.

CONCLUSIONS

Patients with IBD using immune-suppressing therapies are not adequately vaccinated against influenza virus. Poor awareness and uncertainties regarding vaccine safety are two factors responsible for this failure. This may have significant consequences for patients using IS who are vulnerable to serious complications from infection. Raising patient awareness is not sufficient to ensure optimal immunization. Collaboration among primary care providers, gastroenterologists and health care policy makers is needed to improve vaccination uptake.

REFERENCES


