Immunization Rates and Vaccine Beliefs Among Patients with Inflammatory Bowel Disease: An Opportunity for Improvement

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Background: Immunosuppressive agents used to treat inflammatory bowel disease (IBD) can increase the risk for infections, several of which are preventable through vaccination. Our study aimed to describe vaccine utilization by immunosuppression status, examine reasons for vaccine refusal, and identify characteristics associated with lack of influenza vaccination in patients with IBD.

Methods: We administered an online survey between February 2012 and April 2012 to an internet-based cohort of patients with IBD in the Crohn's and Colitis Foundation of America Partners program.

Results: During this time, 958 individuals completed the survey. The median age was 45, 72.8% were female, and 62.0% had Crohn's disease. Self-reported vaccination rates were low. Those on immunosuppression (n = 514) were more likely to be counseled to avoid live vaccines ($P < 0.01$). However, counseling rates were low (3.5%–19.1% for various live vaccines). Among the 776 individuals who received the influenza vaccine, maintaining health (74.1%), importance of prevention (66.1%), and provider recommendation (38%) were the most frequently cited motivations. Factors associated with lack of influenza vaccine included lower education level ($P = 0.01$), younger age ($P = 0.02$), and no chronic immunosuppression use ($P < 0.01$). Five hundred seventy (59.5%) individuals thought that patients were responsible for keeping track of their vaccines, whereas 428 (44.7%) placed responsibility on their gastroenterologist and 595 (62.1%) on their primary care physician.

Conclusions: Vaccine utilization remains suboptimal in patients with IBD. Educational interventions may increase vaccination rates by clarifying misconceptions. Gastroenterologists can play a more active role in health care maintenance in patients with IBD by counseling patients on which vaccines to receive or avoid.

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Key Words: vaccine beliefs, immunization rates

Current therapy for patients with inflammatory bowel disease (IBD) often involves agents that suppress the immune system. These treatments put patients at an increased risk for developing infections, of which several are potentially preventable through timely vaccination. Previous work has shown a significantly increased risk of pneumonia among patients with IBD, highlighting the importance of primary prevention through vaccination.[1] Unfortunately, despite guidelines specifying appropriate vaccination strategies in immunosuppressed patients,[2,3] many patients with IBD are not being vaccinated appropriately. For example, in one tertiary care center study of vaccination efforts in patients with IBD, only 28% received annual influenza vaccine and only 9% received pneumococcal vaccine.[4] Reported barriers to vaccination include a lack of awareness and concern for side effects by patients, suggesting that providers may not appropriately educate patients as to the importance of these vaccines.

Similarly, gastroenterologist (GI) knowledge of the appropriate immunizations for the patients with IBD is poor.[5,6] A recent survey demonstrated that nearly one-third of GIs would mistakenly recommend live vaccines to their immunosuppressed patients with IBD.[5] Up to one-half of the GIs in this survey would incorrectly withhold inactivated vaccines to their immunocompromised patients. Additionally, nearly one-third of GIs would avoid live vaccinations in their immunocompetent patients, despite guideline recommendations that they can be safely administered, placing this patient group at a particularly high risk given the potential need for immunosuppression to treat their IBD at a later date. Given that physician knowledge is poor, it should therefore come as no surprise that patients are not being adequately immunized. Previous studies have emphasized the importance of provider recommendations in patient decisions to receive vaccines.[7,8] However, if providers lack knowledge about and confidence in which vaccinations to recommend, patients will then be less likely to receive the appropriate vaccines.

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Although smaller surveys of patients have been done[3] to date, there have been no large studies examining vaccination perceptions among a diverse IBD population in the United States. Furthermore, little is known about the reasons behind suboptimal rates of vaccination in patients with IBD and whether patient preferences, patient-provider interactions, or systems issues (e.g., access to care, insurance, cost) are the main driving force. The aims of our study were to: (1) describe vaccine utilization in individuals with IBD and whether this differs by immunosuppression status; (2) examine both the motivation and rationale for vaccine acceptance and refusal among individuals with IBD; and (3) identify characteristics associated with lack of influenza vaccination.

METHODS

Crohn's and Colitis Foundation of America Partners

We used an internet-based cohort, the Crohn's and Colitis Foundation of America (CCFA) Partners, to investigate vaccine beliefs in individuals with self-reported IBD. CCFA Partners follows individuals with self-reported IBD who were recruited from CCFA e-mail lists and other social media outlets. Participants complete baseline and semiannual follow-up surveys regarding demographics, disease location and activity, medication use, prevention activities (such as screenings or vaccines), and quality of life measurements. Further details of the cohort and baseline characteristics of the population are described elsewhere.[9]

Vaccine Beliefs Survey

We developed a 7 question close-ended survey instrument about vaccine utilization and beliefs, including motivating factors and concerns (Appendix, Supplemental Digital Content 1, http://links.lww.com/IBD/A385). The survey was developed based on a previous survey study used to describe GIs behavior in prescribing vaccines[5] and was piloted in 5 patients with IBD seen in our gastroenterology office at Boston Medical Center. The vaccine beliefs survey module was then administered in all online follow-up surveys to the CCFA Partners cohort that were completed between February 16, 2012 and April 24, 2012 until a total of at least 950 responses were obtained. This number was based on a power calculation to estimate the number of individuals required to be able to detect a 10% difference in influenza receipt among those on immunosuppresssion as compared with those not on immunosuppression.

Data Collection and Management

The data were collected entirely in a Web-based format, which allowed for real-time implementation of range and consistency checks. Therefore, missing data were minimized at point of entry. The data management system has previously been described.[9] The Web forms were accessible from any computer running a modern Internet browser with an active connection to the Internet; no special software was required. Data on demographics, disease type, medications, and vaccination status were extracted from CCFA Partners core data for survey respondents.

Statistical Analysis

All outcomes and characteristics were stratified by the primary categories of interest: use of immunosuppression and influenza vaccination within the previous 12 months. Descriptive statistics were used to characterize the population including proportions, means, and SD for normally distributed variables and medians and interquartile ranges for nonparametic data. Chi-square, Fisher's exact, Wilcoxon's rank sum, Student's *t*-test and one way analysis of variance were used to compare characteristics and beliefs by use of immunosuppression and by influenza vaccination. STATA version 10.0 (College Station, TX) was used for all analyses and $P < 0.05$ were considered statistically significant. The study protocol was approved by the Institutional Review Board at the University of North Carolina at Chapel Hill.

RESULTS

A total of 958 persons completed the vaccine survey. Those persons (n = 33) who did not provide information on whether they had received vaccinations were excluded from the study. The median age of the surveyed group was 45 (interquartile range, 31–57), 72.8% were female and 62% had Crohn's disease (CD). Table 1 summarizes the characteristics of the study population. No differences in age, sex, race, ethnicity, education, IBD type, and rating of general health were detected between vaccine survey participants compared with those participants in the CCFA cohort who were not given the vaccine survey.

Overall, self-reported vaccination rates were low (Fig. 1). As noted in the vaccine module (Appendix, Supplemental Digital Content 1, http://links.lww.com/IBD/A385), we used terminology that patients would understand and thus did not ask about specific brands or subtypes of vaccines, such as differentiating between the pneumococcal conjugate vaccine (PCV13) and the pneumococcal 23-valent polysaccharide vaccine (PPVSV23). Of the inactivated vaccines, the influenza vaccine (received in 2011, just before the survey) was most commonly received (81.5% of the population). Only 47.7% reported receiving the hepatitis B vaccine, 42.6% the pneumococcal vaccine, and 34.1% the hepatitis A vaccine. Among women under age 27, 50% reported that they had received the human papilloma virus vaccine (vaccine only approved in women at the time of the survey). Of the live vaccines, 33.3% of those older than 60 years recalled receiving the herpes zoster vaccine.

When asked who shared responsibility for vaccination efforts, 570 (59.5%) subjects thought that they (patients) were responsible for keeping track of their vaccines, whereas 428 (44.7%) placed the responsibility on their GI and 595 (62.1%) on their primary care provider. Only 430 subjects (44.9%) recalled that their GIs had previously taken a vaccination history. Those patients on immunosuppression were significantly more likely to be counseled on avoidance of live vaccines ($P < 0.01$). However, counseling rates as a whole were low, ranging from 3.5% to

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TABLE 1. Characteristics of the Population of Patients with IBD in the CCFA Partners Cohort Who Reported Information on Vaccine Utilization and Beliefs

Characteristic	N = 958	
IBD type		
Crohn's disease	594	62.0
Ulcerative colitis	364	38.0
Age, median (IQR)	957	45 (31–57)
Sex (female), %	697	72.8
Primary care physician (yes), %	858	89.6
Education level		
<12th grade	10	1.1
High-school graduate	67	7.3
Some college	169	18.4
College graduate	382	41.7
Graduate school	289	31.5
Current smoker	40	4.2
Current medications (yes), %		
Antibiotics[a]	49	5.1
5-ASA, oral	542	56.8
5-ASA, rectal	91	9.5
Biologic[b]	337	35.2
Thiopurine[c]	248	26.0
Methotrexate	33	3.5
Calcineurin inhibitor[d]	3	0.3
Corticosteroid, oral	101	10.6
Corticosteroid, rectal	43	4.5
Budesonide (oral)	40	4.2
Clinical trial medication	4	0.4
Any chronic immunosuppression[e] (% yes)	514	53.7

5-ASA, 5-aminosalicylic acid. Values are expressed as percentage or median (interquartile range).
[a]Ciprofloxacin or metronidazole.
[b]Defined as infliximab, adalimumab, certolizumab pegol, or natalizumab.
[c]6-mercaptopurine or azathioprine.
[d]Cyclosporine or tacrolimus.
[e]Chronic immunosuppression defined as current use of biologic or immunomodulator (thiopurine, methotrexate, and calcineurin inhibitor).

19.1% for the various live vaccines (Table 2). There were no differences noted in the concerns about the vaccines effectiveness or the possible side effects of the vaccines by immunosuppression status.

Among the 776 individuals who received the influenza vaccine, maintaining health (74.1%), importance of prevention (66.1%), and provider recommendation (38%) were the most frequently cited motivations. Patients receiving the influenza vaccine were more likely to have a primary care provider than those who did not receive the vaccine (91.2% versus 81.8%, $P < 0.01$). There was also a higher rate of immunosupression use among those receiving the influenza vaccine when compared with

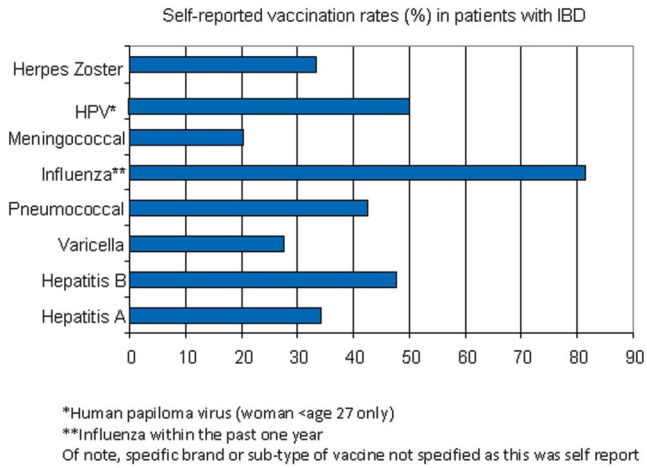

FIGURE 1. Self-reported vaccination rates (%) in patients with IBD. *Human papilloma virus (woman younger than 27 years only) **Influenza within the past 1 year Of note, specific brand or subtype of vaccine not specified as this was a self report.

those who did not receive the vaccine (55.8% versus 44.9%, $P < 0.01$). Age, gender, and smoking status did not differ by vaccination status.

Those not receiving the influenza vaccine (n = 176) were significantly more concerned about side effects, effectiveness, and the worsening of their IBD by vaccines than those who received the influenza vaccine ($P < 0.01$). Other factors associated with not receiving the influenza vaccine included lower education level ($P = 0.01$), younger age ($P = 0.02$), and absence of chronic immunosuppression use ($P < 0.01$).

DISCUSSION

Appropriate immunizations are an important component of routine preventive services in patients with IBD. Immunosuppressive therapy puts patients at increased risk of developing infections, which account for significant morbidity and mortality in patients with IBD.[10,11] Active CD has also been shown to increase the risk for serious infections,[10] further supporting the crucial need for appropriate immunization to avoid potentially preventable infections. A recent study demonstrated that patients with IBD are at increased risk for pneumonia, particularly among patients on corticosteroids and narcotics.[1] Varicella infection[12] and herpes zoster[13] infection have also been found to be increased in immunosuppressed patients with IBD, particularly in those on corticosteroids, thiopurines, anti-TNF agents, or combination immunosuppression. As demonstrated in this large, cross-sectional survey of IBD patients, however, vaccination rates for these preventable diseases remain suboptimal, despite over a decade of data confirming that patients with IBD are at an increased risk of vaccine preventable diseases. Patients who were most likely to receive the influenza vaccine were most concerned about maintaining their health, preventing disease, and followed their provider's recommendations. In contrast, patients who did not receive the vaccine had misconceptions about possible

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TABLE 2. Individual Vaccines Patient Were Told to Avoid by Use of Chronic Immunosuppression[a]

Vaccine, yes (%)	Chronic Immunosuppression[a] (n = 514) n (%)	No Chronic Immunosuppression (n = 444) n (%)	*P*
Hepatitis	8 (1.6)	2 (0.5)	0.09
Influenza mist	98 (19.1)	20 (4.5)	<0.01
Influenza injection	13 (2.5)	7 (1.6)	0.30
Pneumonia[b]	8 (1.6)	2 (0.5)	0.09
Herpes zoster	30 (5.8)	4 (0.9)	<0.01
Varicella	23 (4.5)	3 (0.7)	<0.01
MMR	18 (3.5)	2 (0.5)	<0.01

MMR, Measles, mumps, rubella.
[a]Chronic immunosuppression defined as current use of biologic or immunomodulator (thiopurine, calcineurin inhibitor, methotrexate).
[b]Self-reported receipt of pneumonia vaccine (no data on whether 23-valent or 13-valent vaccine administered).

side effects of the vaccine or worsening of their IBD after vaccination. "Provider recommendation" was one of the most frequently cited motivations for receiving the influenza vaccine, the most commonly received vaccine in this study. Yet, only half of the patients recalled being asked by their GI about their vaccination history.

Several previous studies have demonstrated that provider recommendations are a strong predictor for receipt of preventative health services including vaccination and cancer screening.[14–16] Unfortunately, primary care clinicians are uncomfortable managing routine health maintenance issues in their patients with IBD. For example, only 30% of family medicine doctors felt comfortable coordinating vaccinations for the immunosuppressed patients with IBD.[17] Because primary care physicians may not adequately prescribe vaccines for immunosuppressed patients with IBD, GIs should obtain a vaccine history and should accept the responsibility of either offering vaccinations in their office or providing recommendations to the primary care clinician for the appropriate vaccines to be adminsitered.[18,19] Immunization status should be detailed during the first office visit, and the required vaccines, especially the live attenuated vaccines, should be administered during the period before immunosuppressive medication is started. In one study, the influenza vaccine was offered and administered to eligible immunosuppressed patients with IBD during their IBD office visit. Vaccination rates for influenza increased in this group from 54% to 81% suggesting that easy access to vaccines can also improve uptake.[20] In our study, rates of influenza vaccine were 81.5%, which is higher than that reported in previous studies. This suggests that awareness for vaccinations in patients with IBD has improved over time, possibly because of increased media focus, interventions in GI offices, and reminders for all patients regardless of IBD status.

Patients on immunosuppressive medications were more likely to be counseled to avoid live vaccines, but counseling rates overall were low, again suggesting that physicians are missing the opportunity to prevent potential infectious complications in their patients. Because provider recommendation was found to be an important reason why patients chose to receive a vaccine, spending time educating patients on the importance of vaccines during an office visit either through a face-to-face discussion with a member of the GI team or through a handout may be beneficial. Side effects, effectiveness, and worsening of their IBD by vaccines were cited as the biggest concerns among the 176 patients who did not receive the influenza vaccine. Although immunologic response to vaccination seems to be decreased in immunosuppressed patients, there is no convincing evidence to suggest that immunization will lead to an exacerbation of IBD activity.[2] These concerns emphasize the importance of intensive educational efforts, for both provider and patient, to ensure that misconceptions are clarified and that patients receive the appropriate vaccinations. It is important to remember that based on our results, in those patients who are younger or less educated, additional time discussing these misconceptions might increase vaccination rates.

The strengths of this study include the large number of surveyed participants who were geographically diverse and represent many different clinical practices. Additionally, we were able to obtain detailed information on demographics, disease status, and medication use. The anonymous nature of the survey may have allowed participants to honestly provide their views on recommended routine vaccinations.

The main limitation of this cross-sectional study was in its design as a self-administered electronic survey. Methods of recruitment included an interest in participating, requirement for the English language, and the technology to join the cohort. The sample therefore may not necessarily represent the U.S. IBD population as a whole. In addition, all of the data collected were based on participant's self-reporting rather than on audit of medical records. Reassuringly, a previous validation study has been completed on a subset of the study cohort. Within this group on whom physicians confirmed diagnoses through medical record

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review, 94% of patients have a diagnosis of IBD Additionally, other previously established associations were confirmed within this cohort, supporting the validity of this patient reported data. Vaccine utilization was also obtained through self-report, which may be subject to under or over reporting. Because billing records would not contain information on vaccination through employers or at local pharmacies where no insurance billing occurs, self-report may actually be the best means at obtaining vaccine utilization information. Other studies of self-report of vaccine utilization have shown a high concordance between the medical records and patients' self-reported vaccine exposure to influenza, pneumococcal, and human papilloma virus vaccines.[21,22] However, because vaccines were self-reported, no distinction was made about which particular vaccine the patients had received. Another limitation of our study is that it did not include a pediatric/adolescent IBD subset, who have also been shown to have suboptimal immunization rates.[23] We did find that the younger patients in this cohort were less likely to have received the influenza vaccine suggesting that we do need to improve our vaccination rates in our younger patients as well. Lastly, we could not control for other potential confounders in vaccination utilization such as other comorbidites (e.g., asthma) or occupation because we did not have this information.

In summary, our study confirms previous reports that patients with IBD are not receiving counseling regarding appropriate vaccinations and are inadequately vaccinated. Importantly, we were also able to determine patient perceptions and rationales for avoiding vaccination to target future educational efforts. The findings of this study thus serve as an important reminder that we need to continue to improve the education of this high-risk population of patients and their primary health care providers regarding the safety of administering vaccinations while remembering to address possible misconceptions are paramount in increasing vaccine rates. Because physician's recommendation for vaccinations is a primary motivation among patients with IBD, future efforts should focus on education and systems-based practices to improve vaccination efforts. As a community of GIs, we should play a more active role in the health care maintenance in our patients with IBD.

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