Vaccination coverage of children with inflammatory bowel disease after an awareness campaign on the risk of infection

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ABSTRACT

Background: Children with inflammatory bowel disease are at risk of vaccine-preventable diseases mostly due to immunosuppressive drugs.

Aim: To evaluate coverage after an awareness campaign informing patients, their parents and general practitioner about the vaccination schedule.

Methods: Vaccination coverage was firstly evaluated and followed by an awareness campaign on the risk of infection via postal mail. The trial is a case–control study on the same patients before and after the awareness campaign. Overall, 92 children were included. A questionnaire was then completed during a routine appointment to collect data including age at diagnosis, age at data collection, treatment history, and vaccination status.

Results: Vaccination rates significantly increased for vaccines against diphtheria–tetanus–poliomyelitis (92% vs. 100%), Haemophilus influenzae (88% vs. 98%), hepatitis B (52% vs. 71%), pneumococcus (36% vs. 57%), and meningococcus C (17% vs. 41%) (p < 0.05). Children who were older at diagnosis were 1.26 times more likely to be up-to-date with a minimum vaccination schedule (diphtheria–tetanus–poliomyelitis, pertussis, H. influenzae, measles–mumps–rubella, tuberculosis) (p = 0.002).

Conclusion: Informing inflammatory bowel disease patients, their parents and general practitioner about the vaccination schedule via postal mail is easy, inexpensive, reproducible, and increases vaccination coverage. This method reinforces information on the risk of infection during routine visits.

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1. Introduction

The use of immunosuppressive therapy such as corticosteroids, antimetabolites (6-mercaptopurine [6MP], methotrexate, and azathioprine), and biologics has led to marked improvements for patients (children and adults) with inflammatory bowel disease (IBD); however, at the same time, these therapies increase the risk of opportunistic infections [1–4]. These infections can be prevented through vaccination. This is why specific recommendations have been implemented in addition to the usual recommendations. Patients must be brought up-to-date with scheduled vaccinations as soon as possible in the course of their disease (ideally from diagnosis) in order to achieve a better immune response and be able to administer live attenuated vaccines, which will be
contraindicated if immnosuppressive therapy is subsequently administered [1,4,5]. The recommended vaccines are those of the vaccination schedule (for France) plus the influenza and pneumococcal vaccines [6,7].

Several studies have shown that the level of vaccination coverage for IBD patients is insufficient [8,9]. A previous study involving 165 children with IBD, conducted between May and November 2011 at 11 hospitals in western France, showed that vaccination coverage in this population was largely insufficient [8]. The primary cause seems to be the lack of information provided to patients and to doctors responsible for vaccination. In addition to vaccine catch-up, prevention must also be implemented [8,10,11].

The aim of our study was to evaluate vaccination coverage among children with IBD following an awareness campaign about the infection risk to their family and their GP. To this aim, a letter was sent to patients of a previously evaluated cohort [8] and to their GP, in order to raise awareness about the vaccination schedule.

2. Materials and methods

The dosing schedule recommended to patients, their family, and their doctor was the one published by the French High Council for Public Health (HCSP) in February 2012 [6].

All patients with known vaccination coverage subsequent to data collection in 9 hospitals in western France [8] were included in this prospective study conducted from March 6, 2013 to January 31, 2014. The awareness-raising campaign implemented in this study consisted of providing information about the infection risk and the importance of vaccination coverage to the parents and GP of patients included in the previously evaluated cohort [8]. All families and GPs received a letter by post reminding them of the latest vaccination recommendations published in July 2012 by the HCSP [7] and encouraging them to verify the vaccination status of the patient. The recommended vaccines are the same as those for the general population: diptheria, tetanus, polio (DTP), pertussis, Haemophilus influenzae type B (Hi), hepatitis B virus (HBV), meningococcus C (conjugate, men C), and human papillomavirus (HPV). The specifically recommended vaccines are those for seasonal influenza (inactivated vaccine) and pneumococcus. The contraindicated vaccines are the live vaccines including Tuberculosis (Bacillus Calmette Guérin, BCG), yellow fever, live attenuated influenza vaccine, measles–mumps–rubella (MMR), and varicella.

Patients who had reached adulthood, and hence were no longer under the care of a paediatric gastroenterologist, and those who were lost to follow-up were excluded.

### 2.1. Data collection

Following the awareness-raising campaign, patient record data and vaccination data were collected successively during a routine follow-up consultation with the paediatric gastroenterologist. The patients and their families were informed about the study, and their written consent was obtained. Data were collected by questioning the patient and his/her family, as well as from the patient’s personal health records and medical records. The data collected were: age at diagnosis and at data collection, gender, type of disease (Crohn’s disease (CD), ulcerative colitis (UC), or indeterminate colitis (IC)), previous and current therapy, detailed vaccination status concerning DTP, pertussis, Hi, HBV, hepatitis A virus (HAV), pneumococcus, men C, BCG, MMR, and HPV. With regard to varicella, immunity was verified either by the fact that the child had already had the disease or that he/she had been vaccinated. We defined a minimum vaccination schedule as consisting of vaccinations against DTP, pertussis, Hi, MMR, and BCG.

### Table 1

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crohn’s disease</td>
<td>62 (67%)</td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td>22 (24%)</td>
</tr>
<tr>
<td>Indeterminate colitis</td>
<td>8 (9%)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>47 (51%)</td>
</tr>
<tr>
<td>Age at data collection</td>
<td></td>
</tr>
<tr>
<td>&lt;5 years</td>
<td>0</td>
</tr>
<tr>
<td>5–10 years</td>
<td>5 (5%)</td>
</tr>
<tr>
<td>10–15 years</td>
<td>38 (41%)</td>
</tr>
<tr>
<td>15–20 years</td>
<td>49 (53%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatments</th>
<th>Current</th>
<th>Received*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aminosalicylates</td>
<td>48 (52%)</td>
<td>53 (58%)</td>
</tr>
<tr>
<td>Corticosteroid</td>
<td>66 (72%)</td>
<td>79 (86%)</td>
</tr>
<tr>
<td>Azathioprine or 6-mercaptopurine</td>
<td>79 (86%)</td>
<td>80 (87%)</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>7 (8%)</td>
<td>7 (8%)</td>
</tr>
<tr>
<td>Anti-tumour necrosis factor α</td>
<td>47 (51%)</td>
<td>51 (55%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Current immunosuppressive therapy</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>16 (17%)</td>
</tr>
<tr>
<td>Monotherapy</td>
<td>56 (61%)</td>
</tr>
<tr>
<td>Dual therapy</td>
<td>19 (21%)</td>
</tr>
<tr>
<td>Triple therapy</td>
<td>1 (1%)</td>
</tr>
</tbody>
</table>

*“Received treatments” covers past and current treatments.

One question sought to find out the reasons for not catching up with vaccinations, and the available multiple-choice answers were: multiplicity of vaccines, non-perception of the seriousness of the disease, personal position, fear of side effects, fear of activating the disease, GP’s position, or “Other” (with space provided to specify reason).

The study was approved by the Ethics Committee of the Rennes University Hospital.

2.2. Expression of results, statistics

Results are expressed as whole-number percentages (%), as well as medians, highest values, lowest values, and means to one decimal point.

The McNemar’s test was used for the before vs. after comparison among the 92 patients included in the study. A Chi-square test with Yates correction for counts below 5 was used to compare catch-up rates between patients with Crohn’s disease and the rest, and between patients on anti-TNF therapy and the rest.

Univariate analyses for being up-to-date with the minimum vaccination schedule (DTP, pertussis, Hi, MMR, and BCG) were performed for gender, type of disease, age at diagnosis, age at data collection, duration of disease on the campaign date, treatments received, and other vaccines. Qualitative variables were evaluated using a two-tailed Fisher’s test and quantitative variables using a two-tailed Student’s t-test (equal variances) or Welch’s t-test (unequal variances).

A difference was considered significant when p < 0.05.

3. Results

The campaign letters were sent out to 105 includable patients and their GPs. Among these, 2 refused to participate in the study and 11 were not subsequently seen. Hence, 92 patients were included, giving a response rate of 88%.
### 3.1. Population characteristics

Patient characteristics are provided in Table 1. Overall 62 patients with CD (67%), 22 with UC (24%), and 8 with IC (9%) were enrolled. Forty-seven patients were males (51.1%), median age was 15.4 years (range, 7.5–18.6 years), and median age at diagnosis was 10.7 years (range: 6 months to 16.3 years). The duration of follow-up at the campaign date ranged from 1.3 to 14.8 years, with a median of 3.6 years. The length of time from the campaign date to data collection ranged from 0.1 to 11.6 months, with a median of 5 months. Among the 92 patients, 76 had at least one current immunosuppressive therapy: 61% as monotherapy, 21% as dual therapy, and 1% as triple therapy. Only five patients had never had any immunosuppressive therapy. With regard to the current and past use of immunosuppressive therapy, the rates were, respectively, 72% and 86% for corticosteroids, 86% and 87% for azathioprine or 6-mercaptopurine, 8% and 8% for methotrexate, and 51% and 55% for anti-TNFs.

### 3.2. Rate of vaccination coverage

The rates of vaccination coverage pre and post-campaign are summarised in Table 2: 9 patients out of 92 (10%) were up-to-date for DTP, pertussis, Hi, HBV, men C, pneumococcus, MMR, and BCG.

The rates of complete vaccination coverage with regard to the minimum vaccination schedule were 77% before the campaign and 83% at the time of data collection.

The vaccination rates pre and post-campaign by individual vaccine were, respectively, 92% and 100% for DTP, 88% and 98% for Hi, 96% and 100% for pertussis, 52% and 71% for HBV, 90% and 91% for BCG, and 91% and 91% for MMR. HPV vaccination concerned 31 girls; the vaccination rate was 23% before the campaign and 58% at the time of data collection. The post-campaign increase in the vaccination rate was significant for vaccines against DTP, HI, HBV, pneumococcus, and men C (p < 0.05). By contrast, this rate was non-significant for pertussis, HAV, BCG, and MMR. Among patients who received catch-up vaccinations post-campaign, a higher catch-up was observed among patients with CD than among patients with UC or IC for men C (OR = 4.2 [1.1–25.3]; p = 0.03) and pneumococcus (OR = 4.7 [1.1–29.3]; p = 0.02). No difference in post-campaign catch-up vaccination was found between patients on anti-TNF therapy and the rest.

With regard to varicella, 86 patients had had the disease, 3 had been vaccinated, and for the 3 remaining patients, 2 had an unknown status and serology was ongoing for the other.

### 3.3. Reasons for not performing vaccine catch-up

The reasons for not performing vaccine catch-up included the multiplicity of vaccines (21%), the fear of side effects (21%, including 6 patients who were “afraid” of the HBV vaccine, 2 of the influenza vaccine, and 1 of the men C vaccine), the patient’s or the family’s personal position (13%), the non-perception of the seriousness of the infectious disease (3%), the fear of activating IBD (3%), and the GP’s personal position (3%). Other causes of delay were given as free text comments, including the doctor not offering the vaccine, which was cited 7 times for the HAV vaccine and 6 times for the men C vaccine.

Among the children who were not vaccinated against HBV, 3 had a family history of multiple sclerosis. For some patients, vaccinations were planned but had not yet been administered: 9 for the men C vaccine, 4 for the HBV vaccine, and 3 for the HPV vaccine. One patient could not have a catch-up MMR vaccination because he was on immunosuppressive therapy. Two others could not catch up because of repeated infections and macrophage activation syndrome.

### 3.4. Univariate analyses for the minimum vaccination schedule

After the campaign, 76 patients (83%) were up-to-date with the minimum vaccination schedule. Children who were older at the time of diagnosis were 1.26 times [1.08–1.48] more likely to be up-to-date (p = 0.002) than younger children. Children with longer disease duration at the campaign date were 1.28 times [1.09–1.56] less likely to be up-to-date with the minimum vaccination schedule (p = 0.02) than those with shorter disease duration. Gender, type of disease, and whether or not the patient was receiving immunosuppressive therapy, were not shown to be significant factors for being up-to-date with the minimum vaccination schedule.

### 4. Discussion

Clear recommendations exist for evaluating IBD patients before initiating treatment, especially with anti-TNF agents, and bringing them up-to-date with vaccinations [1,6,7,12,13]. Although such patients, who are currently immunosuppressed or likely to be immunosuppressed in the future, are at a higher risk of infection, particularly opportunistic infections [1–4], several studies have shown that doctors and patients are not provided information [8,9] about the importance of vaccination in IBD. Some studies have shown a lack of knowledge and interest among gastroenterologists towards the immune status of their IBD patients [11,14,15]. It is therefore necessary to raise awareness as early as possible among patients, their families and their doctor, so that they do not accumulate delays with regard to the vaccination schedule and that catch-up vaccinations can be administered before any immunosuppressive therapy is started [1,5]. Various ways of raising awareness among doctors and patients have already been tested: a study by Parker et al. [16] showed that the vaccination rate could be significantly increased following application of a PLAN-DO-STUDY-ACT method that involved providing patients with the due vaccine(s).

Another study [10] by Walsh et al. showed that using a pro forma screening tool to raise awareness among gastroenterologists of screening and vaccination against opportunistic infections led to a change in their behaviour, namely a significant increase in screening for vaccination status and vaccination recommendations to patients (from 47 to 97%, p < 0.001). However, patient compliance with these recommendations was not optimal and suggested the need to educate them too.
Our study shows that raising awareness via posted letters, a simple and reproducible method, is an effective approach for significantly increasing the vaccination rate against certain infections such as diphtheria, tetanus, poliomyelitis, Hi, HBV, pneumococcus, and men C. Although the difference did not reach significance for other vaccines, the absolute number of vaccinations increased in all cases. Some patients who were not up-to-date with their vaccinations at the time of data collection had consultations scheduled during which catch-up vaccines were to be administered, hence the period of time between the campaign date and data collection was not long enough to give the truest picture of vaccination rates.

With regard to varicella, even though the diagnosis is clinical, we feel it could be useful to perform varicella serology testing to confirm the immune status of patients before initiating immunosuppressive therapy. The difference in vaccination coverage among patients at the first data collection may be attributed to the child’s year of birth and the evolution of vaccination recommendations in recent years. For example, BCG has not been routinely recommended since 2007. Conversely, HPV vaccination, which was recommended from the age of 14 between 2007 and 2013, is now recommended from the age of 11.

Post-campaign, the vaccination coverage rate of our patients seemed better than that of the overall French paediatric population, particularly for DTP, Hi, pertussis, HBV, measles, and BCG (Table 3) [17].

Vaccination catch-up was better among CD patients than among patients with UC or IC. This may reflect a higher level of concern about the infection risk among these patients. The univariate analysis showed that being younger at the time of diagnosis decreased the probability of being up-to-date with the minimum vaccination schedule; conversely, in 2013, the French Institute for Public Health Surveillance (InVS) reported an increase in vaccination coverage among the general population [18]. The main reasons provided for not performing catch-up vaccination despite the campaign letter were fear of side effects, the multiplicity of vaccines, and the personal position of parents. Notably, these same reasons were given by parents who refused to vaccinate their children in the study by Harmsen et al. [19]. Other reasons reported in this study were: the perception of the child’s body and the immune system, the level of knowledge concerning the risks of the disease, the efficacy of vaccines and their side effects, a previous negative experience, and the impression that there are advantages to immunisation acquired by contracting the disease “naturally”.

The GP’s position can influence vaccination status. Maayan-Metzger et al. [20] showed that paediatricians had to reconcile two conflicting ideas: the importance of immunisation vs. the right of parents to make decisions concerning their child. Practitioners could receive communications training so that they could convince parents of the benefits of vaccination.

Data collection for the present study was conducted in spring, thus vaccination against influenza was not studied in our population. A study conducted in Poland [21] by Banaszkiewicz et al. showed that only 7–8% of 242 children with IBD were vaccinated against influenza vs. 18.3% of 142 children in the control group (p = 0.001), regardless of the diagnosis, disease activity, and current treatments. Awareness-raising actions are useful but do not lead to complete vaccination coverage among children with IBD. The consequences of this lack of protection could be highlighted in a study looking at the prevalence of vaccine-preventable infections among these at-risk patients. In 2010, Chevaux et al. [22] showed that the prevalence of HBV and hepatitis C in patients with IBD (only half of whom were vaccinated against HBV) was identical to those in the general population.

Given the increased use of immunosuppressive therapy, doctors responsible for the care of children with IBD must periodically evaluate the vaccination status of their patients and update it whenever necessary. A previous study [8] demonstrated that these children were not up-to-date with their scheduled vaccinations due to a lack of information provision to patients, their family and their doctor. Sending out a letter to the various people involved is a straightforward, inexpensive method for achieving higher vaccination coverage. This method of information provision should be expanded to include all children with IBD from the diagnosis of their disease, during follow-up consultations, and in individual or group education/therapy sessions.

### Conflict of interest
None declared.

### References


