ORIGINAL ARTICLE

Observational Study

Patients' perspectives on smoking and inflammatory bowel disease: An online survey in collaboration with European Federation of Crohn's and Ulcerative Colitis Associations

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Abstract

BACKGROUND
Smoking has detrimental effects on Crohn's disease (CD) activity while data on ulcerative colitis (UC) are conflicting. Little is known about the use and impact of alternative smoking products in inflammatory bowel diseases (IBD).

AIM
To understand the patients' perceptions of the impact of smoking on their IBD and to assess differences between CD and UC patients.

METHODS
The questionnaire was developed by Philip Morris Products SA in cooperation with European Federation of Crohn's and Ulcerative Colitis Associations. The final survey questionnaire consisted of 41 questions divided in 8 categories: (1) Subject screener; (2) Smoking history; (3) Background information; (4) IBD disease background; (5) Current disease status; (6) Current therapeutics and medications; and (7) Current nicotine/cigarettes use and awareness of the impacts of smoking on IBD. The questionnaire was submitted online from 4th November 2019 to 11th

March 2020 through the European Federation of Crohn's and Ulcerative Colitis Associations website to IBD patients who were current smokers or had a history of smoking.

RESULTS

In total 1050 IBD patients speaking nine languages participated to the survey. Among them, 807 (76.9%) patients declared to have ever smoked or consumed an alternative smoking product, with a higher proportion of current cigarette smokers among CD patients (CD: 63.1% *vs* UC: 54.1%, *P* = 0.012). About two-thirds of the participants declared to have ever stopped cigarette smoking and restarted (67.0%), with a significantly higher proportion among UC patients compared to CD patients (73.1% *vs* 62.0%, *P* = 0.001). We also found significant differences between CD and UC patients in the awareness of the health consequences of smoking in their disease and in the perceived impact of smoking on disease activity, for both cigarettes and alternative smoking products.

CONCLUSION

This survey found significant differences between CD and UC patients in both awareness and perception of the impact of smoking on their disease. Further efforts should be done to encourage smoking cessation for all IBD patients, including UC patients.

Key words: Inflammatory bowel disease; Ulcerative colitis; Crohn's disease; Cigarettes; Alternative smoking products; Tobacco; Nicotine; Marijuana

Core tip: We performed a European-wide online survey to understand the patients' perceptions on how smoking has impacted their inflammatory bowel diseases (IBD). In total 1050 IBD patients [427 with Crohn's disease (CD), 355 with ulcerative colitis (UC)] participated to the survey, with a higher proportion of cigarette smokers among CD patients. About two-thirds of the participants declared to have ever stopped cigarette smoking and restarted, with a higher proportion among UC compared to CD patients (73.1% *vs* 62.0%, *P* = 0.001). There were also differences between CD and UC patients in the awareness of the health consequences of smoking and in the perceived impact of smoking on disease activity.

INTRODUCTION

Environmental factors are probably primarily responsible for the growing incidence of inflammatory bowel diseases (IBD), encompassing Crohn's disease (CD) and ulcerative colitis (UC), around the globe over the last decades[1-3]. Accumulating evidence supports an association between IBD and several environmental factors, including smoking, diet, drugs, geographical and social status, stress, microbial agents, intestinal permeability and appendectomy[4,5]. Among these factors, smoking is the one for which the most solid evidence is currently available[5]. Smoking increases the risk of CD and worsens its clinical course[6,7], especially after digestive surgery[8], but has a protective effect in UC[6,9]. Thus, smoking habits are much more frequent in CD patients than in UC patients, except in Jewish patients in Israel in whom the stronger genetic tendency in CD may contribute to this discrepancy[10].

In CD, the odds of flare of disease activity, flare after surgery, need for first and second surgery among ex-smokers diminish upon smoking cessation and become comparable to non-smokers[11]. In UC, nicotine has been tested as a therapeutic agent in

the form of chewing gum, transdermal patches, and nicotine-based enemas[12-17], with conflicting results and variable efficacy in the induction of remission when compared to placebo and conventional treatments[18-20]. However, it is clear that the protective effect of cigarette smoking in UC is temporary, since the relative risk of developing the disease increases after smoking cessation compared with patients who have never smoked[21].

Until now, there has been little patient-centered research aiming at assessing the perceived impact of smoking or nicotine use on IBD symptoms by patients who are current adult smokers and/or nicotine-containing products users. Few studies demonstrated that a high proportion of patients with IBD are unaware of the effects of tobacco on their disease, but these limited available data are solely based on small-scale studies[22-26]. Yet, making patients aware of the impact of nicotine use on the course of their IBD is essential to expect smoking cessation and improve the management of their disease.

Thus, the objectives of this European-wide online survey developed in collaboration with European Federation of Crohn's and Ulcerative Colitis Association (EFCCA) were to understand the patients' perceptions on the impact of smoking on their IBD and to assess differences of these perceptions between CD and UC patients. The results of this study will be shared with the IBD community through EFCCA in order to facilitate the management of smoking cessation among patients.

MATERIALS AND METHODS

Questionnaire development
The questionnaire was developed by Philip Morris Products SA in cooperation with EFCCA and reviewed prior to use by health informaticians. Le Berre C and Loy L also participated in the design of the questionnaire. The final survey questionnaire consisted of 41 questions divided in 8 categories: (1) Subject screener; (2) Smoking history; (3) Background information; (4) IBD disease background; (5) current disease status; (6) current therapeutics and medications; and (7) Current nicotine/cigarettes use and awareness of the impacts of smoking on IBD (Supplemental document).

In most questions, participants were allowed to tick one applicable option. In some questions, such as those concerning the type of alternative smoking products that were used, several options could be chosen. In others, such as questions concerning the duration of use of nicotine products, therapy change due to smoking habits or use of alternative smoking products, or the perceived impact of nicotine use on disease activity, participants were given multiple categorical options.

The survey was made available in English, French, German, Spanish, Portuguese, Italian, Greek, Finnish and Slovenian. Translations were made by translators that EFCCA has previously worked with. They were proofread by native speakers from EFCCA's member associations and revised, if necessary. Philip Morris International did final checks and revisions on the translations in order to have a double validation before the survey was launched.

Questionnaire administration
The questionnaire was submitted through EFCCA to IBD patients who were current smokers or had a history of smoking. Patients were not pre-screened and were eligible for inclusion if they were aged over 18 years and had a confirmed diagnosis of IBD, including CD or UC. Patients gave their consent and were not paid for participating.

The online survey was open from 4th November 2019 to 11th March 2020 on the EFCCA website. National associations were encouraged to promote the survey online by providing their members with an online link on their website. Information on this survey was also displayed in posters and flyers at the clinic of each participating investigator. The survey was closed after having enrolled more than 1000 participants, whatever their characteristics in terms of gender or nationality.

As this was a non-interventional survey, ethics committee approval was not required. Data was collected anonymously online, and participation was entirely optional. Since it was an anonymous survey, there was no data or user tracking. EFCCA strictly follows the General Data Protection Regulation and does not own the data that was transferred in a secured way to the biostatistician.

Statistical analysis
Descriptive statistics included means with standard deviations and medians with interquartile ranges (IQR) for continuous variables, and frequency analyses

(percentages) for categorical variables. The association between categorical variables was investigated with the Fisher's exact test. Stata 15.0 software was used for all the analyses (Stata Corp, College Station, TX, United States). *P* values less than 0.05 were considered statistically significant. All statistical tests were two-sided.

RESULTS

This survey enrolled 1180 IBD patients speaking nine different languages. However, 130 patients only selected their language and did not answer the first question (*i.e.*, if they have ever smoked or consumed an alternative smoking product). This group of patients was excluded, and we considered 1050 patients as participants. The most represented countries were Italy (20.3%), Finland (13.9%) and Portugal (13.9%). Among them, 807 (76.9%) patients declared to have ever smoked or consumed an alternative smoking product and proceeded to complete the rest of the questionnaire.

Baseline characteristics and treatmen

Participants were mainly females (65.4%) with a median age of 40 (IQR: 32-51) years old. Most patients were diagnosed with CD (53.5%) with a disease duration of 11 (IQR: 5-20) years. Patients diagnosed with UC (44.5%) had a shorter median disease duration (4 years; IQR: 1-8). About one quarter of the participants perceived their disease as severe (26.2%) and 28.8% had undergone surgery. The most common type of surgery was ileocaecal resection (11.8%). The most common drug treatment regimens were oral aminosalicylates (39.8%), anti-TNF agents (28.2%) and immunomodulators (26.7%). Baseline characteristics reported by the patients are detailed in (Table 1 and Supplemental Table 1) compares these baseline characteristics by type of IBD diagnosis.

Smoking habits and use of alternative smoking products

Among patients declaring themselves as having ever smoked cigarettes or having ever used an alternative smoking product, more than half were current cigarette smokers (59.0%). This proportion was significantly higher in CD than in UC patients (63.1% *vs* 54.1%, *P* = 0.012) (Table 2). Most ever smokers smoked cigarettes for more than 10 years (63.4%) and declared to have consumed on average more than 10 cigarettes per day (50.6%). The extent of cigarette smoking was significantly higher in CD than in UC patients (*P* < 0.001). The most commonly used products were cigarettes (91.6%), followed by e-cigarettes (19.2%) and marijuana (17.0%). There were no significant differences in the use of any nicotine-containing product between CD and UC patients.

The vast majority of patients declared to be aware of the adverse health consequences of smoking (97.0%) and started cigarette smoking before IBD diagnosis (88.7%). This proportion was significantly higher in CD than in UC patients (92.0% *vs* 84.6%, *P* = 0.001). About two-thirds of the participants declared to have ever stopped cigarette smoking and restarted (67.0%), with a significantly higher proportion among UC patients compared to CD patients (73.1% *vs* 62.0%, *P* = 0.001). Most UC patients stopped cigarette smoking before diagnosis (59.1%), while this was true for only about one-third of CD patients (34.0%).

Among patients declaring to have ever smoked cigarettes or used an alternative smoking product, 20.0% were current users of an alternative smoking product. Differently from cigarette smokers, most users of these products declared a duration of use of less than one year (56.1%). Most users of alternative smoking products started using them (57.0%) or switched from cigarettes to these products after IBD diagnosis (59.6%).

Impact of cigarette smoking or use of alternative smoking products on IBD

Most cigarette smoking patients perceived that smoking significantly or moderately worsened disease activity (60.9%), while a lower proportion of patients using alternative smoking products had the same impression (15.3%). A much lower proportion of patients believed their habit had no impact on disease activity among cigarette smokers (8.3%) than among users of alternative smoking products (66.4%).

Most patients did not have any therapy change due to smoking habits or use of alternative smoking products (66.7% after starting smoking, 79.2% after restarting smoking, 75.2% after stopping smoking, 90.1% after switching to alternative smoking products and 89.7% after starting to use an alternative smoking product).

The perception of the impact of cigarette smoking significantly differed between CD and UC patients (*P* < 0.001) (Table 3). More than three-quarters (79.2%) of CD patients

Table 1 Baseline characteristics reported by the participants (*n* = 1050)

Questionnaire items	mean ± SD; median (IQR) or *n*(%)
Demographic characteristics	
Age (*n* = 796)	41.9 ± 12.4; 40.0 (32.0–51.0)
Gender	
Female	522/798 (65.4)
Male	276/798 (34.6)
Language	
Italian	213 (20.3)
Finnish	146 (13.9)
Portuguese	146 (13.9)
Slovenian	128 (12.2)
Spanish	120 (11.4)
Greek	102 (9.7)
English	83 (7.9)
German	57 (5.4)
French	55 (5.3)
IBD characteristics and treatments	
Diagnosis	
Crohn's disease	427/798 (53.5)
Ulcerative colitis	355/798 (44.5)
No gastrointestinal condition	5/798 (0.6)
Other gastrointestinal condition	11/798 (1.4)
Crohn's disease duration (yr)	13.6 ± 10.6; 11 (5–20)
Ulcerative colitis duration (yr)	7.52 ± 9.12; 4 (1–8)
Self-perceived disease activity	
Inactive	155/770 (20.1)
Mildly active	261/770 (33.9)
Moderately active	251/770 (32.6)
Severely active	76/770 (9.9)
Not sure	27/770 (3.5)
Self-perceived disease severity since diagnosis	
Mild	173/768 (22.5)
Moderate	360/768 (46.9)
Severe	201/768 (26.2)
Not sure	34/768 (4.4)
Intestinal surgery	230/798 (28.8)
Type of surgery	
Partial colectomy	41/798 (5.1)
Full colectomy	29/798 (3.6)
Small-bowel resection	48/798 (6.0)
Ileocaecal resection	94/798 (11.8)
Other	79/798 (9.9)

Current IBD-related medications	
Antibiotics	41/798 (5.1)
Oral aminosalicylate	318/798 (39.8)
Topical aminosalicylate	91/798 (11.4)
Topical steroid	47/798 (5.9)
Systemic steroid	78/798 (9.8)
Budesonide	28/798 (3.5)
Immunomodulator	213/798 (26.7)
Anti-TNF	225/798 (28.2)
Combination of anti-TNF and immunomodulator	69/798 (8.6)
Anti-integrin	51/798 (6.4)
Tofacitinib	6/798 (0.8)
Ustekinumab	28/798 (3.5)
None	76/798 (9.5)
Other	135/798 (16.9)
Duration of current medical therapy (yr)	
< 1	240/765 (31.4)
1-5	262/765 (34.2)
> 5	263/765 (34.4)
Concomitant non-IBD drug treatment	
Yes	282/767 (63.2)
No	485/767 (36.8)

The survey had a hierarchical structure, meaning that only patients who answered to certain items could answer to other following questions. For this reason, the denominator for several questions is different. In some cases, the patient did not answer and this can result in a missing value. We have transparently declared in our tables the denominator we have used to calculate the proportion of patients giving certain answers. IBD: Inflammatory bowel diseases; IQR: Interquartile ranges.

perceived that smoking significantly or moderately worsened disease activity versus 34.0% of UC patients. Similarly, the perceived impact of using alternative smoking products on disease activity significantly differed between CD and UC patients (*P* = 0.004), even though the magnitude of the effect was less strong (Table 3).

Discussion with own physician about the effect of smoking on IBD
Among patients having ever smoked cigarettes, 31.7% did not receive any information from their physician on the effect of smoking on disease activity, while 45.4% of them received the information that smoking is detrimental to disease activity. These proportions were significantly different in CD than in UC patients (not discussed: 21.6% *vs* 44.6%; detrimental: 69.4% *vs* 14.6%; *P* < 0.001) (Table 4).

Among patients having ever used alternative smoking products, 56.8% did not discuss the effect of these products on disease activity, and 25.2% of them received the information that using them is detrimental to disease activity. These proportions were significantly different in CD than in UC patients (not discussed: 51.8% *vs* 62.5%; detrimental: 37.4% *vs* 11.1%; *P* < 0.001) (Table 4).

DISCUSSION

Our first objective was to assess patients' perceptions about the impact of smoking on their disease, and next to assess differences of these perceptions between CD and UC patients, with the aim to understand how different smoker profiles perceived the impact of smoking on their IBD.

Most patients were aware of the adverse health consequences of smoking and

Table 2 Smoking habits and use of alternative smoking products based on type of diagnosis

Questionnaire items	Crohn's disease	Ulcerative colitis	P value[1]
Smoking habits and use of an alternative smoking product			
Current cigarettes smoker			
Yes	268/425 (63.1)	187/346 (54.1)	0.012
No	157/425 (36.9)	159/346 (45.9)	
Duration of cigarette smoking (yr)			
< 1	22/410 (5.4)	26/317 (8.2)	0.13
1-5	46/410 (11.2)	47/317 (14.8)	
6-10	69/410 (16.8)	56/317 (17.7)	
> 10	273/410 (66.6)	188/317 (59.3)	
Extent of cigarette smoking (cigarettes per day)			
< 1	12/425 (2.8)	22/341 (6.5)	< 0.001
1-5	51/425 (12.0)	67/341 (19.6)	
6-10	120/425 (28.3)	106/341 (31.1)	
11-20	179/425 (42.1)	113/341 (33.1)	
> 20	63/425 (14.8)	33/341 (9.7)	
Current use of an alternative smoking product			
Yes	343/427 (80.3)	282/355 (79.4)	0.79
No	84/427 (19.7)	73/355 (20.6)	
Type of smoking/nicotine product ever used			
Cigarettes	409/427 (95.8)	330/355 (93.0)	0.11
E-cigarettes	84/427 (19.7)	71/355 (20.0)	0.93
Heat not burn tobacco product	19/427 (4.5)	25/355 (7.0)	0.12
Nicotine gum	37/427 (8.7)	36/355 (10.1)	0.54
Nicotine patches	21/427 (4.9)	23/355 (6.5)	0.35
Chewing tobacco/snus/snuff	10/427 (2.3)	15/355 (4.2)	0.16
Cigars	44/427 (10.3)	31/355 (8.7)	0.47
Pipes	13/427 (3.0)	8/355 (2.3)	0.66
Marijuana	81/427 (19.0)	56/355 (15.8)	0.26
Any other combustion/smoking product	11/427 (2.6)	5/355 (1.4)	0.31
None of the above	2/427 (0.5)	7/355 (2.0)	0.09
Ever stopped cigarette smoking and restarted			
Yes	264/426 (62.0)	253/346 (73.1)	0.001
No	162/426 (38.0)	93/346 (26.9)	
Ever user of an alternative smoking product			
Yes	215/427 (50.4)	196/354 (55.4)	0.17
No	212/427 (49.6)	158/354 (44.6)	
Current use of an alternative smoking product			
Yes	84/427 (19.7)	73/355 (20.6)	0.79
No	343/427 (80.3)	282/355 (79.4)	
Duration of use of alternative smoking products			

< 1	44/76 (55.3)	46/81 (56.7)	0.33
1-5	23/76 (30.3)	16/81 (19.8)	
6-10	10/76 (13.1)	16/81 (19.8)	
> 10	1/76 (1.3)	3/81 (3.7)	
Started cigarette smoking			
Before IBD diagnosis	392/426 (92.0)	290/343 (84.6)	0.001
After IBD diagnosis	34/426 (8.0)	53/343 (15.4)	
Stopped cigarette smoking			
Before IBD diagnosis	85/250 (34.0)	146/247 (59.1)	< 0.001
After IBD diagnosis	165/250 (66.0)	101/247 (40.9)	
Restarted cigarette smoking			
Before IBD diagnosis	89/260 (34.2)	66/243 (27.2)	0.10
After IBD diagnosis	171/260 (65.8)	177/243 (72.8)	
Started using an alternative smoking product			
Before IBD diagnosis	85/210 (40.5)	85/185 (46.0)	0.31
After IBD diagnosis	125/210 (59.5)	100/185 (54.0)	
Switched from cigarette smoking to using an alternative smoking product			
Before IBD diagnosis	77/207 (37.2)	81/184 (44.0)	0.18
After IBD diagnosis	130/207 (62.8)	103/184 (56.0)	

The survey had a hierarchical structure, meaning that only patients who answered to certain items could answer to other following questions. For this reason, the denominator for several questions is different. In some cases, the patient did not answer and this can result in a missing value. We have transparently declared in our tables the denominator we have used to calculate the proportion of patients giving certain answers.

[1]Fisher's exact test. IBD: Inflammatory bowel diseases.

started cigarette smoking before IBD diagnosis. However, CD and UC patients showed different awareness about the impact of smoking cigarettes on their disease activity. Indeed, most CD patients were aware of a detrimental effect of smoking, and a large proportion of UC patients was aware of possible beneficial impact of smoking on their disease activity. Interestingly, most UC patients did not discuss this topic with their own physician. This is in line with previous studies conducted on this issue[25,26]. Both Wahed *et al*[25] and Ducharme-Bénard *et al*[26] reported informed rates of 52% and 57.7% in patients with CD, whilst this was the case in only 21% and 13% of patients with UC Saadoune *et al*[27] Reported about two-thirds of smoking CD patients were aware of the harmful effects on the course of disease, whereas all UC patients were aware of its protective role[27]. The detrimental effects of smoking on CD are well-established in the literature. On the contrary, health professionals might be reticent to explain the apparent and less-proven benefit of smoking to UC patients, by fear of discouraging them to stop[28-30].

We also can presume that a different perception of smoking on IBD activity between CD and UC patients could influence the need to be informed about risks and benefits of smoking habits. In our cohort, the large majority of CD patients perceived their disease activity significantly or moderately worsened by cigarette smoking, while 59.7% of UC patients perceived a positive effect of cigarette smoking on their disease activity. Patients' perceptions in our cohort thus confirm previous results in literature on this topic[11,18-21]. It was not surprising to find different smoking profiles between CD an UC patients based on timing of IBD diagnosis. Most CD patients stopped cigarette smoking after IBD diagnosis, whereas most UC patients stopped cigarettes before IBD diagnosis. Among participants declaring to have ever stopped cigarette smoking and restarted, we expected to find a large majority of UC patients restarting smoking after IBD diagnosis. Quite surprisingly, the same result was observed in the CD group of patients while smoking is known to worsen the course of CD. In a study conducted by the Nancy group, similar results were reported, with about one-third of IBD patients who had already stopped smoking to prevent flares with a significant difference

Table 3 Perceived effect of smoking on inflammatory bowel diseases based on type of diagnosis

Questionnaire items	Crohn's disease	Ulcerative colitis	P value[1]
Perceived impact of cigarette smoking on disease activity			
Significantly worsened	12/279 (4.3)	2/191 (1.0)	< 0.001
Moderately worsened	209/279 (74.9)	63/191 (33.0)	
No impact	27/279 (9.7)	12/191 (6.3)	
Moderately improved	25/279 (9.0)	58/191 (30.4)	
Significantly improved	6/279 (2.2)	56/191 (29.3)	
Perceived impact of using alternative smoking products on disease activity			
Significantly worsened	4/211 (1.9)	12/187 (6.4)	0.004
Moderately worsened	31/211 (14.7)	14/187 (7.5)	
No impact	146/211 (69.2)	118/187 (63.1)	
Moderately improved	23/211 (10.9)	28/187 (15.0)	
Significantly improved	7/211 (3.3)	15/187 (8.0)	

The survey had a hierarchical structure, meaning that only patients who answered to certain items could answer to other following questions. For this reason, the denominator for several questions is different. In some cases, the patient did not answer and this can result in a missing value. We have transparently declared in our tables the denominator we have used to calculate the proportion of patients giving certain answers.
[1]Fisher's exact test.

Table 4 Extent of discussing with own physician the effect of smoking on inflammatory bowel diseases based on type of diagnosis

Questionnaire items	Crohn's disease	Ulcerative colitis	P value[1]
Cigarette smoking			
Not discussed	89/412 (21.6)	143/321 (44.6)	< 0.001
Detrimental	286/412 (69.4)	47/321 (14.6)	
Possibly beneficial	37/412 (9.0)	131/321 (40.8)	
Use of alternative smoking products			
Not discussed	43/83 (51.8)	45/72 (62.5)	< 0.001
Detrimental	31/83 (37.4)	8/72 (11.1)	
Possibly beneficial	9/83 (10.8)	19/72 (26.4)	

The survey had a hierarchical structure, meaning that only patients who answered to certain items could answer to other following questions. For this reason, the denominator for several questions is different. In some cases, the patient did not answer and this can result in a missing value. We have transparently declared in our tables the denominator we have used to calculate the proportion of patients giving certain answers.
[1]Fisher's exact test.

between CD and UC patients[27], whereas we did not observe any significant difference among CD and UC patients restarting smoking to prevent flares.

Evidence from literature underlines the importance of informing patients with CD about the negative influence of smoking on their disease, as this will directly influence their intent to quit smoking and positively impact clinical outcomes if they succeed[26,31,32]. Education on smoking is probably insufficiently considered for the management of our patients, particularly in CD. Hilsden *et al*[33] suggested that patients with CD are not more refractory to smoking cessation compared to the general population of active smokers and factors unrelated to CD may be more important in their decision to smoke than CD-related factors[33].

Furthermore, recent data from the Epi-IBD cohort also highlights the economic impact of smoking on IBD, especially in CD, where smoking cessation has medical and economic benefits[34].

To our knowledge, the present study represents the most complete survey

evaluating the consumption of any type of nicotine-containing products in IBD patients. The available literature previously addressed the topic of smoking habits focusing on cigarettes, which are the most commonly used nicotine-containing products[7,9,11,20]. Our survey represents a further effort to fill the gap about former or present use in IBD patients also considering alternative smoking products, like e-cigarettes.

Despite the absence of any significant differences in the use of any nicotine-containing product between CD and UC patients, the two groups had a different perception about the impact of using alternative smoking products on their disease activity, with a trend in favor of worsening in CD patients and a trend in favor of improvement in UC patients; however, in both groups most patients perceived no change in their disease activity. Additionally, a higher proportion of CD patients discussed with their physician about a detrimental effect of these products, while a higher proportion of UC patients never discussed about this subject.

Despite the study design did not allow to stratify our data for the specific type of nicotine-alternative products used, it is interesting to appreciate a growing interest regarding the consumption of electronic cigarettes and its possible impact in IBD populations. A recently published study conducted in United Kingdom showed the proportion of e-cigarette users among IBD patients was marginally lower than in the general population, with no significant difference between CD and UC patients. However, due to the small number of cases, the authors failed to demonstrate a significant different rate of disease-related complications in e-cigarettes users (higher in UC, lower in CD) compared with cigarette users[35].

Regarding e-cigarettes, that deliver nicotine *via* aerosol formed through the heating of a mixture of liquid usually made up of nicotine, propylene glycol or glycerol (glycerine) and flavouring chemicals, their use among European population has been growing steadily since they entered the European market in 2006[36]. The impact of e-cigarettes remains unknown. The lack of evidence about safety requires to remain vigilant over potential adverse effects; however, current available research also suggests the potential benefits of e-cigarettes as a harm reduction model for those who use combustible cigarettes, and e-cigarettes may have an important role to play in preventing death and disability from tobacco use[37,38]. Those devices may theoretically have less impact on the course of IBD because of lower nicotine concentrations, but the latter vary considerably. Despite that, the safety of e-cigarettes in diseases such as IBD remains unknown. Thus, further research is warranted to assess whether e-cigarettes could be an effective smoking cessation tool, and to evaluate both short- and long-term health effects of e-cigarettes.

In this large, European, multicenter survey of over 1000 IBD patients, we assessed the level of knowledge of patients with IBD regarding the impact of any type of nicotine-containing products in both CD and UC. We found significant differences between CD and UC patients in both awareness and perception of the impact of smoking on their disease. Furthermore, despite most CD patients were aware of a detrimental effect of smoking, and a large part of UC patients was aware of possible beneficial impact of smoking in their disease, further efforts should be done to encourage smoking cessation for all IBD patients, including UC patients, because of the well-established beneficial effects of smoking cessation on general health. In light of the increasing use of alternative nicotine-containing products, like e-cigarettes, further studies are mandatory to explore the safety and impact of these products in patients with IBD.

ARTICLE HIGHLIGHTS

Research background
Environmental factors are probably primarily responsible for the growing incidence of inflammatory bowel diseases (IBD), encompassing Crohn's disease (CD) and ulcerative colitis (UC), around the globe over the last decades. Among these factors, smoking is the one for which the most solid evidence is currently available. Smoking increases the risk of CD and worsens its clinical course but has a protective effect in UC.

Research motivation
Until now, there has been little patient-centered research aiming at assessing the perceived impact of smoking or nicotine use on IBD symptoms by patients who are

current adult smokers and/or nicotine-containing products users. Few studies demonstrated that a high proportion of patients with IBD are unaware of the effects of tobacco on their disease, but these limited available data are solely based on small-scale studies. Yet, making patients aware of the impact of nicotine use on the course of their IBD is essential to expect smoking cessation and improve the management of their disease.

Research objectives

To understand the patients' perceptions on the impact of smoking on their IBD and to assess differences of these perceptions between CD and UC patients.

Research methods

This was a European-wide online survey developed by Philip Morris Products SA in collaboration with European Federation of Crohn's and Ulcerative Colitis Association. The final survey questionnaire consisted of 41 questions divided in 8 categories: (1) Subject screener; (2) Smoking history; (3) Background information; (4) IBD disease background; (5) Current disease status; (6) Current therapeutics and medications; and (7) Current nicotine/cigarettes use, and awareness of the impacts of smoking on IBD. The survey was made available in English, French, German, Spanish, Portuguese, Italian, Greek, Finnish and Slovenian. The online survey was open from 4th November 2019 to 11th March 2020 on the European Federation of Crohn's and Ulcerative Colitis Association website.

Research results

This survey enrolled 1050 IBD patients speaking nine different languages. Among them, 807 declared to have ever smoked or consumed an alternative smoking product. More than half were current cigarette smokers (59.0%). This proportion was significantly higher in CD than in UC patients. There were no significant differences in the use of any nicotine-containing product between CD and UC patients. The perception of the impact of cigarette smoking significantly differed between CD and UC patients. Similarly, the perceived impact of using alternative smoking products on disease activity significantly differed between CD and UC patients. Among patients having ever smoked cigarettes, 31.7% did not receive any information from their physician on the effect of smoking on disease activity, while 45.4% of them received the information that smoking is detrimental to disease activity. These proportions were significantly different in CD and in UC patients.

Research conclusions

We found significant differences between CD and UC patients in both awareness and perception of the impact of smoking on their disease. Further efforts should be done to encourage smoking cessation for all IBD patients, including UC patients, because of the well-established beneficial effects of smoking cessation on general health.

Research perspectives

In light of the increasing use of alternative nicotine-containing products, like e-cigarettes, further studies are mandatory to explore the safety and impact of these products in patients with IBD.

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