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Does active smoking really influence the course of Crohn's disease? A retrospective observational study

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Abstract

Background: Active smoking has been associated with a higher risk of developing Crohn's disease (CD). However, its impact on clinical outcomes has been controversial among studies.
Aims: To evaluate the influence of active smoking on initial manifestations of CD, the development of disease-related complications, and therapeutic requirements.
Methods: Patients diagnosed with CD within a ten-year period (1994–2003) were identified. Clinical and therapeutic features until October 2008 or loss of follow-up were recorded. Smoking status was assessed at each major disease-related event (e.g. penetrating and stricturing complications, perianal disease, intestinal resection, introduction of immunomodulators or biological agents).
Results: A total of 259 patients were included in the study with a median follow-up period of 91 months. At diagnosis, 50.5% were active smokers and only 12% of them quit smoking during follow-up, mostly after a major disease-related event occurred. Smoking at diagnosis was not associated with a particular CD presentation. Active smoking did not influence the development of strictures, intraabdominal and perianal penetrating complications, or increased resectional surgery, biological therapy or immunomodulators requirements.

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Conclusions: Patients who develop CD while smoking seem to have a similar disease course to those who never smoked.

1. Introduction

The current hypothesis for the pathogenesis in Crohn's disease (CD) suggests that genetic susceptibility in combination with environmental factors compose a complex pathogenic system that causes a characteristic dysregulation of mucosal immunity.[1] Among environmental factors, smoking has been the only one repeatedly associated with a higher risk for CD development[2,3] as well as with a worse disease prognosis as judged by increased clinical activity,[4] lower quality of life,[5] disease-related complications,[6] increased need for immunosuppressive drugs[7] and early post-operative recurrence.[8,9] Initial retrospective studies suggested that disease outcomes improved after giving up smoking when compared with continuing smokers.[10,11] These results were reproduced in the only prospective study assessing the effect of smoking cessation on the course of CD.[12]

The impact of smoking does not seem to be the same in all CD patients. It has been suggested that women and patients with small bowel involvement are particularly susceptible to the deleterious effects of tobacco.[7,8,10,13] Moreover, the impact of smoking seems to vary depending on the genetic background. In this regard, no effect of active smoking has been found among Jewish CD patients,[14] as well as in Hungarian population.[15]

The influence of active smoking on disease progression is poorly characterized mainly because of the heterogeneity of disease phenotypes and because smoking status has only been assessed at the time of disease diagnosis but not later on, leading to controversial results.[12,16–18] Therefore, the aim of our study was to evaluate the influence of active smoking on phenotypic changes based on the Montreal's classification basis as well as on the therapeutic requirements, in a cohort of CD patients who were followed-up right from disease diagnosis.

2. Patients and methods

2.1. Study population and data collection

CD patients diagnosed between January 1994 and December 2003 were identified from the Inflammatory Bowel Disease (IBD) databases of three Spanish tertiary centres. Only those patients who were diagnosed, treated, and followed in the same centre were included. Diagnosis of CD was based on the conventional Lennard-Jones criteria.[19] Demographic, epidemiological, and clinical features (including treatment with steroids, immunomodulators, biological agents, or surgery, as well as changes in the Montreal's classification during the follow-up period) were collected from diagnosis until October 2008, loss of follow-up, or patient's death. A careful history of smoking habit (recording dates of starting and stopping smoking) was obtained from medical records or by telephone call, if this was not available or for patients that had not visited in the outpatient clinic within 6 months prior to data compilation.

For the purpose of this study, we defined *non-smokers* as those patients who had never smoked or smoked less than 7 cigarettes/week,[7,8] and *former smokers* as those that had given up smoking at least 12 months before diagnosis in agreement with previous studies. Those patients who smoked at CD diagnosis or within the previous year but who quit smoking for more than 12 months during the follow-up period were considered as *quitters*. In all other situations patients were considered to be *active smokers*. In order to assess the influence of heaviness of smoking, the number of cigarettes per day was also recorded. *Heavy smokers* were those who smoked 15 or more cigarettes/day, taking into account the increased risk that has been found within this threshold in CD patients.[10] However, due to the retrospective design of the study, this variable was only available at CD diagnosis but not thereafter. Treatment requirements at baseline included all treatments started within the first three months after disease diagnosis.

2.2. Study outcomes

To assess the impact of smoking status on disease outcomes we arbitrarily defined some *major disease-related events* that included the development of any stricturing and/or penetrating disease complication (bowel strictures, intraabdominal penetrating complications, or perianal disease), and therapeutic requirements (introduction of immunomodulators -thiopurines or methotrexate-, biological agents -infliximab or adalimumab-, and intestinal resection). To define stricturing or penetrating disease behaviour at disease presentation or during follow-up, we used the Montreal's classification criteria.[20] For each of these events, patients were classified according to their smoking status at the time the event occurred. Patients were classified according to their smoking status at CD diagnosis if no event occurred by the end of the follow-up period. In agreement with smoking status definitions, for patients who quitted or started smoking during the study period, their follow-up finished one year after their change in smoking status. While steroids have been the widest used therapy in CD, we did not consider steroid use as a major-disease related event. Hence, we did not collect the time for the first course of steroids but the total time on steroids.

This was an observational study according to the 1975 Declaration of Helsinki (6th revision, 2008) and was approved by the Institutional Review Board of the steering centre (Hospital Universitari Germans Trias i Pujol).

2.3. Statistical analysis

Descriptive statistics are expressed as percentages for qualitative data and mean with standard deviation or median and interquartile range (IQR) for quantitative data. Univariate