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Editorial

Lesson from epidemiology of paediatric Crohn's disease

Recent epidemiological evidences indicate a tremendous increase in incidence and prevalence of the chronic multifactorial non-communicable diseases (NCDs) in the western countries as well as in other geographical areas [1]. These disorders result from an abnormal interplay between environment factors and host immunity, on a genetic susceptibility background [2]. Among NCDs, the inflammatory bowel diseases (IBD), including Crohn's disease (CD), ulcerative colitis (UC) and unclassified IBD (U-IBD), have become a global problem leading to serious morbidity, with a negative impact on health-related quality of life and a considerable economic burden on National Health Services [3]. About 25% of all diagnosed IBD occur in the paediatric age (PIBD): this is extremely important considering the negative effects of a chronic and disabling disease on the current and future health status of affected children and adolescents, primarily on their nutrition and growth patterns. Knowledge of the PIBD natural history and course is therefore of great significance, both for patients and physicians caring for them [4].

Most epidemiological surveys show rather homogeneous PIBD incidence data in western countries, with north–south gradient in the northern hemisphere. It is estimated that the current incidence of PIBD in the western world is around 10–12 new cases/100,000/year. Interestingly, the increase in the incidence of PIBDs is also affecting newly developed countries [5]. Recently, paediatric Scottish data showed a 66% rise in incidence of CD diagnosed <16 years of age from 2.9/100,000/year in 1990–1995 to 4.8/100,000/year in 2003–2008, indicating a 500% rise in paediatric CD over just 40 years, and a further marked increase from 2009 to 2014 [6].

In this issue of Digestive and Liver Disease a North French research group, well known for promoting the EPIMAD epidemiological registry, presents the results on the evolution of CD in a group of 535 paediatric patients, diagnosed with definite or probable CD between January 1988 and December 2004, less than 17 years at diagnosis, with at least two-year follow up [7]. The major strength of the study comes from including a patient population resident in the author's region at diagnosis, with data deriving from adult and paediatric gastroenterologists' files and from regional hospital records.

Several variables were analysed and data from the study can be summarized as follows:

1. At the end of follow up, extension of the disease was reported in 47% of patients who had a solely ileal or colonic disease at diagnosis, with an ileo-colonic involvement in 83%; moreover, upper gastrointestinal (GI) was documented in 42% of patients and perineal locations in 16% of patients, compared with 31% and 10% at baseline, respectively.
2. A complicated behaviour (structuring and/or penetrating phenotype) occurred in 58% of patients compared to 27% at baseline, indicating an evolution from uncomplicated to complicated phenotype in 42% of patients. Interestingly, among several variables analysed, only ileal or ileo-colonic pattern and perianal disease at the baseline were associated with a subsequent complicated course.
3. Of 466 patients receiving at least a course of corticosteroids, 42% and 15% were steroid-dependent and steroid-resistant at 1-year, respectively. The cumulative probability to receive immunomodulators (IM) (thiopurines, methotrexate) was 22%, 50% and 65% at 1, 5, 10 years, respectively. The cumulative probability to receive anti-TNFα was 2%, 16% and 29% at 1, 5, 10 years, respectively.
4. The cumulative probability to undergo surgery (ileo-cecal or ileal resection, sub-total or total colectomy with ileo-rectal or ileo-anal anastomosis) markedly increased from 9% at 1 year to 30% and 43% at 5 and 10 years, respectively.
5. While extraintestinal features were evident at baseline in 23.5% of patients, de novo extraintestinal manifestations occurred in almost 30% at the end of the follow-up.
6. The overall death rate was 0.93% with a standardized mortality rate around 1.6%. The authors report 5 cancers after a mean duration of 15 years: the crude cancer rate was 0.93% with a standardized incidence ratio of 3.3%.

The data presented in this study confirm powerfully that paediatric CD (PCD) is characterized by a high degree of evolution toward more complex clinical forms, both as a disease localization and course [8]. The EPIMAD group in a previous report and other European groups have affirmed, through accurate epidemiological studies, that a third of PCD patients commonly evolves toward a complicated disease phenotype (penetrating, stricturing) during a period of less than ten-year follow-up [9]. Interestingly, the same groups have shown a progression in the extension of the disease (including involvement of the upper GI tract) in 30% of cases at 2–9 years of follow-up [10].

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By examining this study and other epidemiological surveys, we should remark that the great majority of the patients studied had been recruited in an era where biologics (either alone or in combination with IM) had not been introduced in the early stages of the disease and in a scheduled fashion [11]. It is widely agreed that the introduction of biologics has allowed to achieve and maintain mucosal healing and that the latter is convincingly associated with a change in the natural history of CD in terms of reduction of hospitalization and surgical rates [12]. Thus, we await with interest future epidemiological reports on PCD to appreciate if the disease course will be improved by a more widespread and precocious use of IM and biologics.

Epidemiological studies in PIBD should also be focused on patients with so-called "very early onset IBD" (VEOIBD), that is defined as IBD occurring in children less than 6 years of age. Noticeably, VEOIBD is characterized by an aggressive phenotype and a peculiar resistance to standard medical and surgical therapy. The study of the evolution of this disease should be of great scientific and clinical interest [13].

Finally, from the epidemiological studies on PIBD a deeper knowledge is expected on the intrinsic and extrinsic variables that can predict the evolution of the disease. The ensuing advancement of knowledge should help in planning the best approach to PIBD patients, with the final goal of slowing or neutralizing the evolution of the disease and optimizing the quality of life.

Conflict of interest

None declared.

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