Prevalence of Apical Periodontitis in Patients with Inflammatory Bowel Diseases: A Retrospective Clinical Study

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Abstract

Aim: We evaluated the prevalence of apical periodontitis (AP) and the oral health status in patients with inflammatory bowel diseases (IBDs) treated with immunomodulators, with particular attention to biologic medications (BMs). **Methods:** One hundred ten patients, 49 men and 61 women (average age, 46 ± 13.8 years), from the Gastroenterology Unit of the University Hospital with IBDs who were treated with BMs or corticosteroids were included in the study. One hundred ten patients who registered for a dental check-up at the Dental Clinic were matched for age, sex, and physical characteristics with the study group without systemic diseases and not taking medications who were the control. Patients underwent a complete oral, dental, and radiographic examination. Decayed, missing, and filled teeth and periapical index score indexes were recorded. Student *t* test, χ^2, and Mann-Whitney *U* test were used as appropriate. **Results:** The prevalence of AP was 64% in IBD patients and 59% in the control; according to the gender-stratified analysis, the difference was not significant among the male groups, whereas the number of teeth with AP was significantly higher in female patients with IBDs than in the controls ($P \leq .05$). The prevalence of AP in patients treated with BMs was 65%; women showed 69% higher risk for AP and presented a significantly higher number of teeth with AP ($P \leq .05$). Decayed, missing, and filled teeth index was similar in both groups, whereas patients with IBDs had a higher periapical index score than the controls. **Conclusions:** Women with IBDs and taking immunomodulators had a higher prevalence of AP. All patients with IBDs had larger lesions than healthy subjects. These data emphasize the influence of the status of the immune system in the onset of AP and the need for further studies to confirm these findings. *(J Endod 2017;43:389–394)*

Key Words

Apical periodontitis, biologic medications, inflammatory bowel diseases

Significance

The development and evolution of apical periodontitis in patients affected by autoimmune diseases and in treatment with the new immunomodulators need to be considered carefully.

Inflammatory bowel diseases (IBDs) are multifactorial, idiopathic, chronic inflammatory disorders characterized by diffuse inflammation of the intestinal mucosa. They are associated with dysregulation and inappropriate response of the intestinal mucosal immune system to otherwise innocuous luminal antigens in a genetically susceptible host (1, 2). Crohn's disease (CD) and ulcerative colitis (UC) are 2 main phenotypes of IBD (3–5). Genetic predisposition (6–9) and deficiencies in the innate immune response can be linked to the development of IBDs. The pathogenesis of IBDs is the result of an imbalance of proinflammatory and anti-inflammatory factors (10, 11). UC is characterized by an upregulation of interleukin (IL)-5 and can be considered as a type 2 immune disease, whereas CD exhibits high levels of interferon-γ, IL-12, and tumor necrosis factor (TNF) and is classified as a type 1 immune disease prototype (12).

First-line treatment (13–15) for IBDs has been centered on immunosuppressive therapy such as disease-modifying anti-inflammatory drugs or corticosteroids (16). Nonsteroidal anti-inflammatory drugs are used to relieve pain and inflammation and treat the symptoms of extraintestinal manifestations of IBDs (arthralgia, arthritis) (17–19).

Patients who have not responded to standard therapies are currently being treated with biologic medications (BM), which are predominantly recombinant human proteins with immunoregulatory effects (20–28). Their target is mainly the modulation of proinflammatory cytokines. Anti-TNF agents have been reported to achieve remission of the disease, tapering of glucocorticoids (26, 29), and healing of the mucosa (30).

Oral manifestations of IBDs can be found in 4%–16% of patients and include persistent soft tissue swellings, edema of the mucosa, linear ulceration, angular cheilitis, and granulomatous gingivitis (31). Furthermore, IBD patients seem to have increased prevalence of caries and periodontitis (32–38).

Apical periodontitis (AP) is a chronic inflammatory disorder of the periradicular tissues caused by an infection of endodontic origin. It is the consequence of a dynamic encounter between root canal microbes and host defenses that results in a local inflam-

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mation, resorption of hard tissues, and destruction of other periapical tissues driven by complex interactions between immune-inflammatory cells and soluble mediators (39, 40). Prevalence of AP increases with age and varies from 33% to 62% (41).

Because no studies to date have investigated the association of IBDs with AP, the purpose of this investigation was to evaluate the prevalence of AP and the oral health status in patients with IBDs, with particular attention to the influence of BMs on AP.

Materials and Methods

Medical records of 110 patients affected by IBDs who were referred to the University Dental Clinic for a routine dental evaluation during the period of June 2012–July 2015 were retrospectively studied; data extrapolated were compared with those from 110 healthy patients not subjected to any pharmacologic therapy who visited at the Dental Clinic in the same period. The study was approved by the Institutional Ethics Committee and was in accordance with the Helsinki Declaration of 1975 (as revised in 2000). All participants gave their informed consent before inclusion in the study.

Selection of Cases

The patients with gastrointestinal (GI) chronic immune diseases, CD, or UC were recruited for this retrospective study. The eligibility criteria for inclusion were the following:

1. Male and female patients
2. Age range 18–70 years
3. Affected by a GI chronic immune disease
4. Taking corticosteroids or BM for at least 6 months for the GI disease

Exclusion criteria included the following:

1. Patients presenting with other systemic pathologies
2. Patients taking more than 1 medication for the major pathology
3. Patients who did not allow their data to be used

A total of 110 records from patients with IBD, 49 men and 61 women (average age, 46 $\pm$ 13.8 years), were recruited; 74 patients in treatment with BMs and 36 patients in treatment with corticosteroids who agreed and met the inclusion/exclusion criteria constituted the study group. All these individuals were outpatients attending the Department of Gastroenterology at D. Casula Hospital of the University of Cagliari, Italy.

In IBD patients the average period of time in which the disease was present was 12 $\pm$ 7.5 years. Diagnosis of CD and UC were performed according to the international investigational protocols (42–46).

An additional 110 subjects, 53 men and 57 women (average age, 41 $\pm$ 13.1 years), who reported no history of IBD or any clinical sign of ongoing systemic diseases, were matched for age, gender, and socioeconomic status (education, occupation, income), and who also met the inclusion criteria constituted the control group. Patients in the control group were randomly recruited in this retrospective study among the patients from the same health district seeking routine dental examination at the same Dental Clinic for the first time.

Clinical Data Collection and Radiographic Examination

All medical records comprised a questionnaire covering demographic data including age, gender, medical history, and medications taken. The medical history records were focused on the collection of relevant information regarding the major IBD disease, the time of onset of the disease, and the previous and current medications taken to treat the disease. A written informed consent for the dental examination, the panoramic radiograph, the additional periapical radiographs, and the use of the clinical data were included in all medical records. The medical record review was used to collect the data. The following parameters were assessed: number of teeth in the dental arches, presence of caries, presence of conservative restorations, presence of extensive restorations (conservative/prosthetic), presence of endodontic treatment, presence of apical periodontitis, evaluation of periodontal probing depth, and presence of lesions in the soft tissues (sinus tracts/abscesses/other). The teeth were examined according to the decayed, missing, filled teeth (DMFT) index by using the World Health Organization criteria (47). The evaluation of the panoramic radiographs (used as initial screening) and of all of the selective intraoral radiographs (taken in upper anterior teeth, when scarcely visible, in all teeth that presented restorations, prosthetic restorations, AP, or suspected AP in the panoramic radiograph) available in the medical records were used for the assessment of the periapical status.

Acquisition of Data

Medical history, diagnostic, and treatment information for each patient were entered on a collection form and coded for computer entry. At the initial visit, after the evaluation of the panoramic radiograph and the clinical examination, standardized periapical radiographs were taken. Conventional radiographs were obtained by using a film holder for paralleling technique. Exposure times and kilovoltage were adjusted according to the film manufacturer's instructions. The periapical radiographs were scanned, saved in JPEG format, and transferred to the Image J software (version 1.41; National Institutes of Health, Bethesda, MD) for measurement and recording of the results. The plug-in application TurboReg (Biomedical Imaging Group, Swiss Federal Institute of Technology, Lausanne, VD, Switzerland) was used to mathematically minimize any dimensional changes that might have been incorporated into the preoperative or postoperative radiographs as a result of angulation differences to the x-ray central beam at the time of image acquisition (48). The periapical status was assessed by using the periapical index score (PAI) (49) by 2 trained and calibrated endodontists (weighted kappa values, $\kappa = 0.8$) (50). For multirooted teeth, the highest of the PAI scores given to the individual roots was used. If the 2 examiners did not agree, the highest of their scores was assigned. The quality of coronal restorations and root canal treatments was assessed by the same 2 examiners on the basis of the criteria described by Ng et al (51). When 1 of the components was not satisfactory, the entire tooth was judged as inadequate.

Statistical Analysis

The prevalence of AP was evaluated on the total number of individuals and the total number of teeth. Statistical analysis was also differentiated by sex to investigate the possible confounding role of gender on the risk of AP. Descriptive analysis was performed, and the differences between groups were evaluated with Student t test for normal distributed variables, χ^2, or Mann-Whitney U test as appropriate. A further analysis was performed to assess possible differences between patients treated with BMs and controls; P value $\leq .05$ was considered statistically significant. STATA version 13 (STATA Corp, College Station, TX) was used.

Results

The prevalence of AP was 64% in the IBD group and 59% in the control (Table 1) ($P > .05$); the same happened with the number of teeth with AP, which was higher in patients with IBDs compared with the controls ($P > .05$). Gender-stratified analyses showed a higher