Original Article

Capsula Eburnea

GASTROINTESTINAL COMPLICATIONS DURING USE OF ANTI-INFLAMMATORY DRUGS FOR ORTHOPEDIC DISEASES

Giuseppe Margiotta[1], Antonio Sanfilippo[1], Maurizio Filippo Accardo[2], Provvidenza Damiani[3], Alessandro Geraci[4], Giovanni Tomasello[5]

SUMMARY

Non-Steroidal Anti-inflammatory Drugs (NSAIDs) are molecules that inhibit the functionality of cyclooxygenase, resulting in suppression of prostaglandin production. Primary physicians and specialist clinics frequently prescribe NSAIDs for the treatment of osteoarticular diseases such as tendinitis, bursitis, synovitis, spondylitis and osteoarthritis. This analysis aims to study gastrointestinal complications in orthopedic patients, caused by the use of NSAIDs, employing esophagogastroduodenoscopy and colonoscopy.

INTRODUCTION

Inflammation can be triggered by infectious, chemical and physical causes. Several factors contribute to its development, such as E-, P-, L-selectin, intercellular adhesion molecules (ICAM-1), vascular adhesion molecules (VCAM-1), soluble mediators such as interleukins (IL)-1, (IL)-2, (IL)-6 and (IL)-8, as well as tumor necrosis factor, whose concentration increases significantly in the synovium of patients with joint diseases. The soluble inflammation mediators are responsible for the production of PGE_1 and PGE_2 that instigate the development of clinical signs of inflammation. The use of Non-Steroidal Anti-inflammatory Drugs (NSAIDs) is essential for reaching therapeutic goals. The main effects of NSAIDs derive from their ability to inhibit the synthesis of prostaglandins by blocking the function of cyclooxygenase. There are two isoforms of cyclooxygenase (COX); the first, COX-1[1], is the constitutive isoform found in most tissues, while the second, COX-2, is induced under conditions of phlogosis by cytokines and inflammatory mediators. For the purposes of this study, it is important to note that only COX-1 is constitutively expressed in the stomach. Patients with inflammatory bone and joint problems (tendinitis, bursitis, synovitis, spondylitis, osteoarthritis) are turning to their primary physicians or specialists for pain management in order to improve function and quality of life. Chronic pain occurs frequently, having a negative impact on the patient and society; therefore, it should be seen as an important public health problem [2] deserving more attention. The treatment of choice in such cases is usually nimesulide or diclofenac in a bi-daily dose, with continued monitoring of the patient over time to ensure better care and avoid self-medication abuse. Complications [3] such as hemorrhagic gastritis, peptic ulcer or “non-erosive gastro-esophageal reflux disease”, cause symptoms

Address of the authors

[1] Orthopedic and Traumatology Unit, University of Palermo, Italy.

[2] Department of National Accounts and Analysis of Social Processes, University of Palermo, Italy.

[3] Department of Internal Medicine and Specialist - DIMIS, University of Palermo, Italy.

[4] Orthopedic Unit, Santa Maria del Prato Hospital, Feltre, Italy.

[5] Department of Oncology and Surgical Disciplines, University of Palermo, Italy.

***Send correspondence to**: Dr. Giuseppe Margiotta,* margiotta.gius@gmail.com

***Received**: August19th, 2011 — **Revised**: September 08th, 2011 — **Accepted**: September 22th, 2011*

and signs including belching, nausea, pyrosis, heartburn, gastro-esophageal reflux and haematemesis. Abdominal colic, stools with bloody mucus, diarrhea and melena have been reported by patients suffering from nonspecific colitis and hemorrhagic colitis.

MATERIALS AND METHODS

From April to June of 2010, 103 patients (64 women and 39 men) seen at the Orthopedics and Traumatology Unit of the Polyclinic of Palermo, Italy, were included in this study; average age was 73 years (range 62 to 84 years). Through anamnesis and physical examinations, symptoms such as inflammation of tendons, serous membranes and synovium, as well as spondylitis were observed; these can all be considered exacerbations of osteoarthritis, a disease common among the study subjects.

IN ORDER TO IMPROVE the functional impairment of the joint involved and eliminate the pain, patients received anti-inflammatory therapy twice a day; the drugs used were nimesulide (100 mg orally) for 50 patients and diclofenac (100 mg orally) for the remaining 53 patients. When patients returned for a clinical reassessment, 70% reported symptoms and signs compatible with gastrointestinal disease. Symptomatic patients were treated with proton pump inhibitors [4] for 15 days; a few continued to suffer from gastrointestinal symptoms, so it was decided to perform endoscopic examinations in these patients. The first group reported belching, nausea, heartburn, gastro-esophageal reflux, pyrosis and melena, and we decided to refer some of these patients to esophagogastroduodenoscopy for an accurate diagnostic analysis. The second group reported abdominal colic, stools with bloody mucus and diarrhea, and it was decided to refer some of these patients for a colonoscopy for an accurate diagnostic analysis.

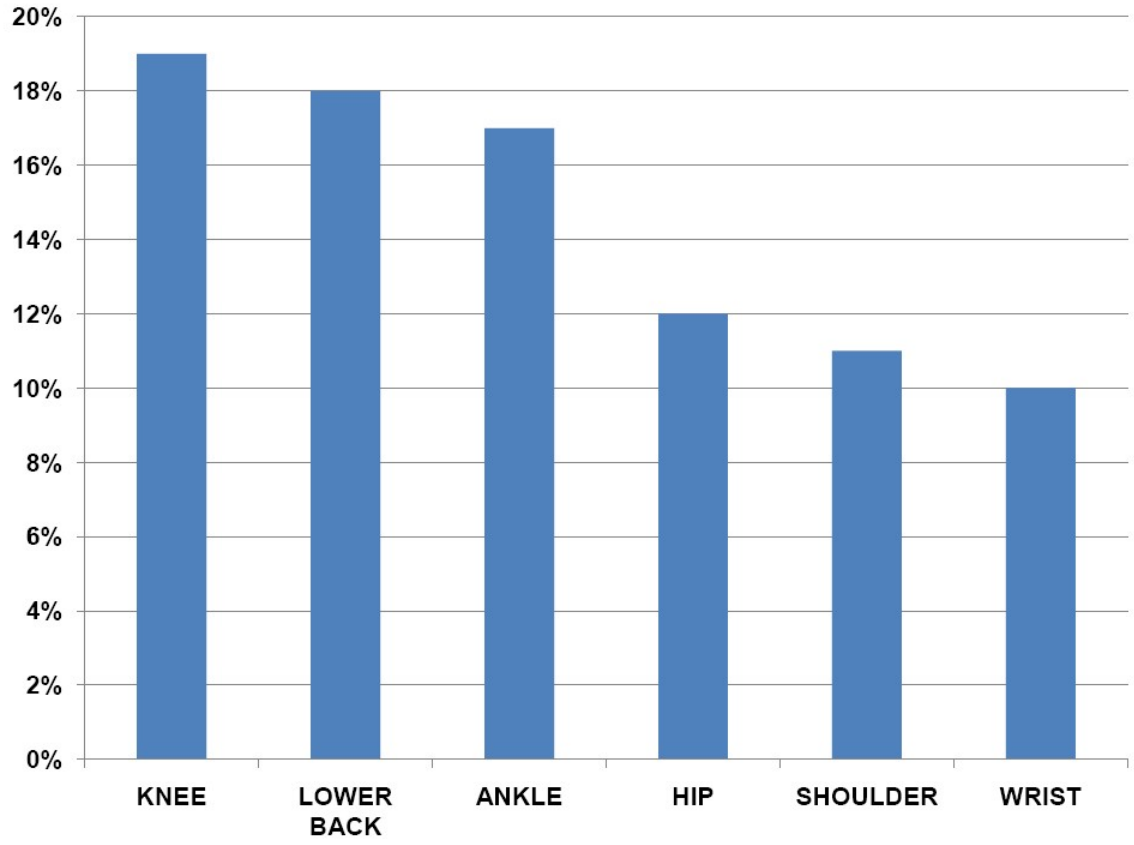

Figure 1. Level of Joint Involvement: In this figure, the abscissa illustrates the joints affected, and the ordinate the percentage of affected patients. The joints subjected to more physical stress seem to be more prone to developing inflammatory diseases.

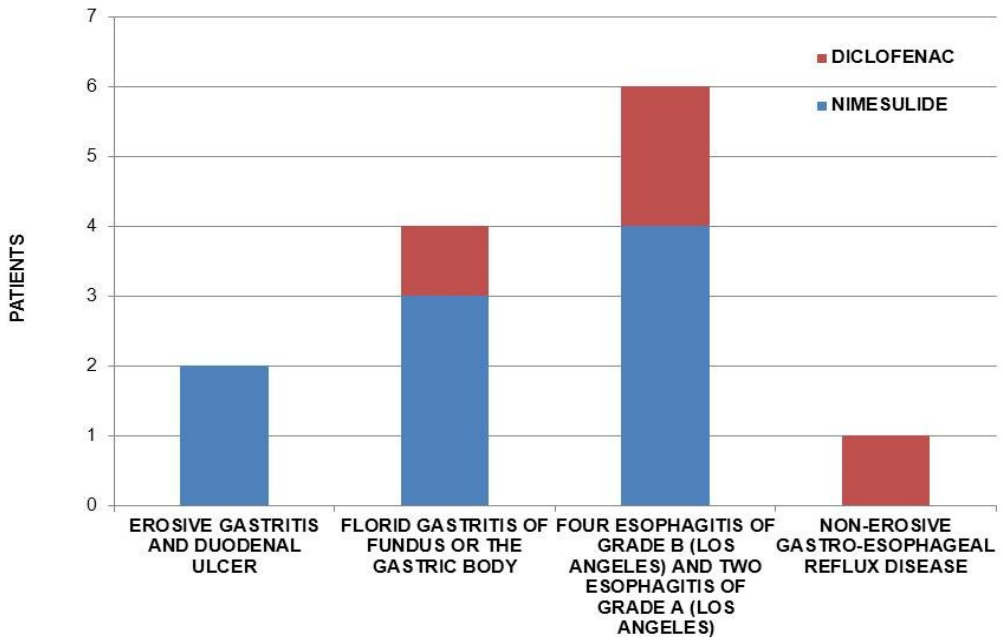

Figure 2. Esophagogastroduodenoscopy findings: The enteric and gastric mucosal lesions were detected by EGD examination, and this figure illustrates that among patients treated with nimesulide, lesions were more common and also more severe, while patients treated with diclofenac presented fewer lesions which were also less severe.

RESULTS

The patients' problems can be grouped according to the location of the pain, with the following breakdown: pain in lower back, wrist or shoulder, respectively in 18%, 10% and 11% of patients; pain in knee, ankle or hip, respectively in 19%, 17% and 12% of patients [5] (fig. 1). 43 patients reported gastric symptoms, and of these 13 suffering from heartburn, gastro-esophageal reflux and melena were subjected to esophagogastroduodenoscopy (EGD). The results of endoscopic examinations showed the following situations: of two patients with melena, one had an erosive gastritis and the other a duodenal ulcer; four patients with heartburn had florid gastritis; of six patients with gastro-esophageal reflux and pyrosis, four were found to have a B grade esophagitis, and two an A grade esophagitis (the Los Angeles Classification system was used). One patient who reported symptoms for gastro-esophageal reflux disease did not show signs of injury in the EGD examination and was therefore classified as having a "non-erosive gastro-esophageal reflux disease". Three patients refused to undergo EGDs and were asked to undergo treatment for heartburn and epigastric pain (fig. 2). Other 29 patients showed signs of colic, and of these only nine were submitted to a colonoscopy. The endoscopic examinations found six patients suffering from stools with bloody mucus and diarrhea to have a proctosigmoiditis, while three patients with abdominal colic were found to have a non-specific colitis. Two patients refused to undergo colonoscopy, regardless of having reported abdominal colic and stools with bloody mucous. In one patient undergoing colonoscopy, it was not possible to complete the examination beyond the sigmoid due to the presence of a semi-solid stool (fig. 3).

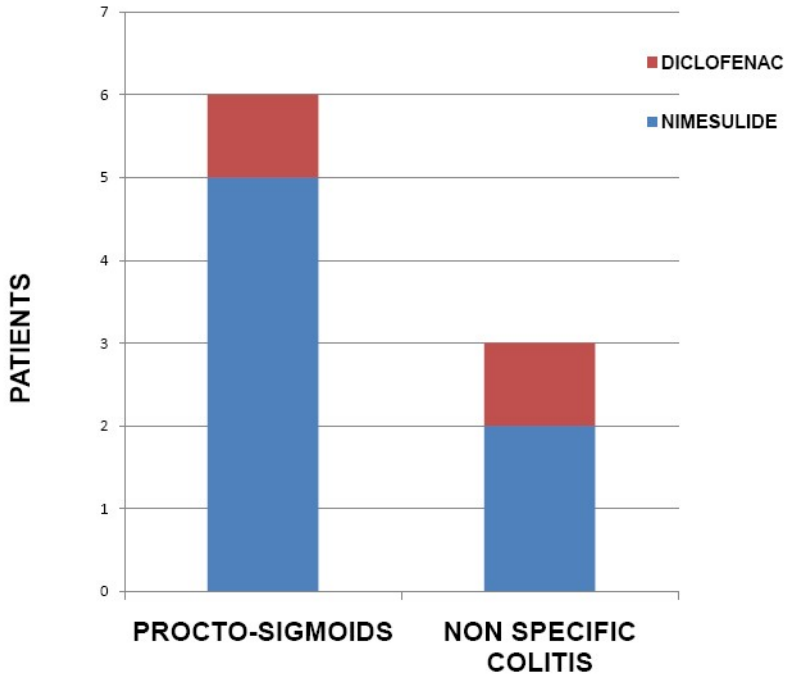

Figure 3. Colonoscopic Findings: The number of patients with Procto-sigmoids and non-specific colitis is higher among the nimesulide group than the diclofenac one.

DISCUSSION

Joint inflammation affects approximately 50% of people over 65 with a basic osteoarthritic disease, and average physical efforts necessary for leading a normal daily life can easily induce the inflammation of tendons, serous membranes and lumbar muscles in these patients. The use of Non-Steroidal Anti-inflammatory Drugs (NSAIDs) is being increasingly demanded by patients themselves, and encouraged by physicians, in order to reach the main therapeutic goals, such as functional improvement [6] and elimination of pain. The study we conducted shows that the gastrointestinal complications caused by NSAID abuse is sometimes so severe as to lead to an exacerbation of co-morbidities often present in patients over 65. In this study, nimesulide and diclofenac were administered. Nimesulide was found to be primarily responsible for the onset of gastrointestinal complications, with diclofenac being responsible for more minor complications. Considering that the use of NSAIDs is often inevitable, in patients over 65 years old, cox 2 inhibitor drugs should be used, in association with a proton pump inhibitor to ensure a complete protection of the gastrointestinal mucosa.

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