Colonic Side Effects of Nonsteroidal Antiinflammatory Drugs

Key words: colonic ulcer, lower gastrointestinal bleeding, colitis

Non-steroidal anti-inflammatory drugs (NSAIDs) are a widely prescribed group of drugs, known to be responsible for many cases of gastroduodenal ulcers by inhibiting cyclo-oxygenase (1). The incidence of side effects while taking NSAID therapy is high, and has been reported to approach 70% in patients receiving long-term therapy. The most frequent complications are those involving the gastroduodenal mucosa, and they range from nonspecific gastritis to peptic ulceration. Although mucosal injury by NSAIDs does not seem to be particularly more frequent in elderly patients, they experience more severe complications (bleeding and perforation).

Colonic side effects of NSAIDs are rare, but they have increasingly been reported since the advent of colonoscopy (2-4). New NSAIDs, formulations with enteric coating or slow release may prevent gastroduodenal ulceration, but increase the risk of colonic damage. Colitis in previously asymptomatic patients has been associated with a number of NSAIDs; it has been estimated that as many as 10% of newly diagnosed cases of colitis may be secondary to NSAID use. Most of these patients present with diarrhea and macro or microscopic lower gastrointestinal bleeding. Gibson et al reviewed 40 cases of NSAID related colitis (2); endoscopy revealed a varied range of inflammatory changes, and solitary or multiple ulcers can occur. Interestingly all patients rechallenged with NSAIDs (after previous withdrawal of the medication) experienced relapse.

Several other conditions have been described in patients taking NSAIDs: ischemic colitis, colonic hemorrhage and perforation, perforation of colonic diverticula, proctitis (related to suppository use), eosinophilic colitis, diaphragm-like stricture formation and colonic ulcer. Behçet's disease may affect the gastrointestinal tract, especially the ileocecal area; it is more prevalent in Japan than in Western countries. An ileo-colonic ulcer in a patient with the typical manifestations of recurrent oral aphthous ulcers, ulcerating genital lesions and ocular lesions can be easily diagnosed with Behçet's disease; on the other hand in the absence of the triple symptom complex, such lesion is called "simple ulcer". Such nonspecific ulcers are found predominantly in the cecum. Their etiology is unknown, and therefore can not be diagnosed before having ruled out other causes of colonic ulceration. Several hypotheses have been suggested to explain the origin of these ulcerations. A possible ischemic injury has been proposed in view of the identification of vascular abnormalities in areas adjacent to nonspecific colon ulcers; however the discordance between the usual location of nonspecific ulcers and ischemic colitis makes this hypothesis improbable. Nonspecific ulcers originating from the ulceration of cecal diverticula might explain nonspecific ulcers, as it has been confirmed in some cases. However, it is evident that most diverticula never ulcerate; moreover cecal diverticula are usually located on the mesenteric side of the cecum, whereas cecal ulcers are found on the antimesenteric border.

The use of NSAIDs and other drugs has been correlated with the occurrence of colonic ulcers. Not only local, but also systemic effects, may play a role in the development of colonic ulceration, as this complication has also been reported after intramuscular administration of NSAIDs (5). Clinical manifestations of NSAIDs-induced colonic ulcer include abdominal pain, diarrhea or constipation, hematoquezia. Endoscopically the lesions may show shaggy elevated borders with a deep ulcer, or only clean-based areas of inflammation. The diagnosis is based on the characteristic gross appearance of the lesion, together with a history of NSAID use, and the absence of other apparent causes of cecal ulceration. Colonoscopy is especially helpful in the identification and evaluation of such lesions. Most ulcers heal with simple cessation of the offending agent. The report by Nakase et al (6) in this issue of Internal Medicine is one more evidence that colonic ulcers may occur as a complication of NSAID therapy.

As the authors remark, the differential diagnosis with simple ulcer is difficult, and it is established by monitoring the evolution after withdrawal of the drug. In all cases with simple ulcer an exhaustive investigation of NSAID use should be carried out, in order to allow cessation of the medication and prevent unnecessary therapeutic actions. On the other hand, NSAID-induced colitis should be considered in patients presenting with signs or symptoms (abdominal pain, diarrhea, hematoquezia, anemia etc.) of inflammatory bowel disease.

In long-term NSAID therapy, the lowest effective dosage should be sought and particular attention should be paid to the appearance of adverse effects, especially in elderly patients. Although gastroduodenal side effects are more frequent, we should be aware of the potential colonic injury by NSAIDs. With an early diagnosis rapid complete healing is the rule, but unrecognized or misdiagnosed cases may result in serious, or even life threatening complications.

See also p 249.
Norihiro Kaminaga, MD, Adolfo Parra-Blanco, MD and Rikiya Fujita, MD
Division of Gastroenterology, Showa University Fujigaoka Hospital, Tokyo 227-0043

References

2) Gibson GR, Whitacre EB, Ricotti CA. Colitis induced by nonsteroidal anti-inflammatory drugs. Report of four cases and review of the literature.