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P541

Diagnosis, management, and evolution of acute pancreatitis secondary to thiopurines in patients with Inflammatory Bowel Disease: an ENEIDA registry study.

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Background: Treatment with thiopurines in patients with Inflammatory Bowel Disease (IBD) may be associated with different adverse effects, including acute pancreatitis. Our aims were to evaluate the clinical presentation, severity and management of acute pancreatitis related to thiopurines in patients with IBD.

Methods: IBD patients with acute pancreatitis secondary to treatment with thiopurines for IBD were identified from the prospectively maintained ENEIDA registry of the Spanish Working Group on Crohn's Disease and Ulcerative Colitis (GETECCU). We included those patients who met the Atlanta diagnostic criteria and had an imaging test that ruled out biliary origin of pancreatitis. Investigators at each participating centre provided additional information on pancreatitis clinical evolution and management.

Results: We included 290 patients with pancreatitis in 34 centres; 54% were women, 84% had Crohn's disease and 56% were smokers. Five (1.7%) had had pancreatitis before, but no patient met criteria for chronic pancreatitis. The median age at pancreatitis was 36 years (IQR 27-50). In 94% of cases, pancreatitis occurred after the first thiopurine drug. Azathioprine was the thiopurine used in 97% of cases (median dose 2.3 mg/kg/day (IQR 2-2.5)), and 6% were treated with mercaptopurine (1.5 mg/kg/day (IQR 1-1.5)). Pancreatitis was diagnosed after a median of 23 days (IQR 14-35) since the start of the treatment with thiopurines. 81% required hospitalization for pancreatitis for a median of 5 days (IQR 4-7). Four (1.4%) were severe pancreatitis, 16 (5.5%) moderate, and the rest mild, according to the Atlanta classification. No epidemiological or treatment factors were associated with the severity of pancreatitis. Thiopurine was withdrawn in all patients upon diagnosis of pancreatitis. After 2 months (IQR 1-28) of pancreatitis, 16 patients (5.5%) received thiopurines again (5 the same, 11 a different thiopurine), suffering a new episode of pancreatitis in 12 (75%) after a median of 12 days (IQR 5-34). Pancreatitis occurred in all smokers that were treated again with thiopurines (n=7), compared to 5 of the 9 (56%) non-smokers or former smokers (p=0.04, RR 1.8; 95% CI 1.1-3.2).

Conclusion: Acute pancreatitis secondary to treatment with thiopurines is mild in most patients, usually appearing during the first month of treatment. The reintroduction of thiopurines, although feasible in some cases, is not recommended due to the high risk of developing a new pancreatitis, especially in smokers.