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Thiopurines are an independent risk factor for active tuberculosis in inflammatory bowel disease patients

Thiopurines and active tuberculosis in IBD

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Abstract
The use of thiopurines is an independent risk factor for active tuberculosis in patients with inflammatory bowel disease.

Key Words: Tuberculosis; Inflammatory bowel disease; Thiopurines; Therapy; Risk.

Fortes FML, Rocha R, Santana GO. Thiopurines are an independent risk factor for active tuberculosis in inflammatory bowel disease patients. *World J Gastroenterol* 2023; In press

Core Tip: Inflammatory bowel disease (IBD) patients recommended for anti-TNF therapy need to be tested for latent tuberculosis (TB) prior to treatment. Azathioprine monotherapy is also an independent risk factor for active TB in patients with IBD. However, the recommendations of the Brazilian Public Health Guideline for Tuberculosis Prevention do not include patients who are receiving immunosuppressive therapy in the risk group for screening for latent TB. We evaluated 301 patients with IBD, and the use of azathioprine treatment increased the risk by 6.87-fold compared to patients without this treatment. The use of anti-TNF therapy had a 10.34-fold increased risk of TB, and the combination of both increased the risk by 17.81-fold.

TO THE EDITOR

It is known that immunosuppression increases the risk of tuberculosis, especially in countries with a high frequency of active tuberculosis. We read with interest the article published by Fortes *et al*.[1], who performed a retrospective cohort study among IBD patients at a reference center in Brazil, which is a country with a moderate incidence of TB. A total of 301 IBD patients were evaluated; 61.8% had ulcerative colitis, and 38.2% had Crohn's disease. One hundred thirty-one (43.6%) patients were using immunosuppression, being 27 (9.0%) with anti-TNFα, 31 (10.3%) using anti-TNFα associated with azathioprine and 3(1.0%) patients received anti-TNFα combined with methotrexate. It was observed that 70 (23.3%) patients were on azathioprine monotherapy. The use of azathioprine treatment increased the risk by 6.87-fold in comparison to patients without this treatment. The use of anti-TNF therapy showed a 10.34-fold increased risk of TB in this sample, and the association of both increased the risk to 17.81.

Advances in the treatment of inflammatory bowel disease (IBD) have been adopted worldwide. Some postmarketing adverse events have been reported, including active tuberculosis (TB) during anti-TNF therapy. It has already been established that the incidence of active TB in this scenario is associated with the TB burden in the geographic region of the study. Brazil is one of the 20 countries in which TB presents a high incidence along with countries from Africa and Asia[2].

IBD patients with a recommendation for anti-TNF therapy need to test for latent TB before treatment. The TNF alpha blocking mechanism, which is critical in stabilizing granulomas during TB infection, would explain this increase in risk. An unanswered question is whether azathioprine in monotherapy is an independent risk factor for active TB in IBD patients[1,3]. A case report published by Van Wijngaarde and Meijssen already drew attention to the development of pleural tuberculosis in a patient with Crohn’s disease while receiving azathioprine as the sole immunosuppressive treatment [4].

Considering that transplant recipients need substantial immunosuppression and azathioprine is one of the drugs used, studies among transplant recipients receiving immunosuppressive therapy helped guide physicians in the care of IBD patients. A Spanish group evaluated the risk factors for active TB after lung transplantation and concluded that the use of azathioprine was identified as an independent risk factor[5].

The recommendations of the Brazilian Public Health Guideline for Tuberculosis Prevention, reviewed in 2020, did not include patients receiving immunosuppressive therapy in the risk group for screening of latent TB[6]. However, consensus from endemic countries suggests investigation and treatment of latent TB before starting immunosuppressive therapy[7-9].

These findings suggest that in areas with a high burden of TB, the use of thiopurines is an independent risk factor for active TB in IBD patients. This evidence needs to be considered when using this therapy for these patients, especially those from countries with a high TB burden. We suggest giving attention to and treating patients with latent tuberculosis and guiding prevention with possible contacts with active tuberculosis. New studies reporting the risk of active TB among IBD patients receiving immunosuppressive therapy from countries with different incidence rates of TB are needed.

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