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Utility of tolerance assays for real-time management of infliximab infusion reactions

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Authorship

RGL and CIN: conception and design of the study, acquisition, analysis and interpretation of data, drafting of the article and review and final approval of the version.

MRS, LRR and RAC: acquisition and review and final approval of the version.

INP and RGE: writing of the article, and review and final approval of the version

EUS: drafting of the article and review and final approval of the version.

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Conflicts of interest

The authors declare no conflict of interests

Statement of Generative AI and AI-assisted technologies in the writing process

To optimize the accuracy and style of my manuscript, I have utilized the capabilities of ChatGPT-4.0, an artificial intelligence language model developed by OpenAI. This tool has allowed me to receive suggestions and guidance on the structure, writing, and coherence of my scientific text. It is important to mention that, although I have used ChatGPT-4.0 as an assistant, all the content and ideas presented in the manuscript are the result of my own research and knowledge.

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Abstract

Failure of infliximab (IFX) therapy is often associated with pharmacokinetic challenges, frequently linked to the development of anti-infliximab antibodies (ATI). ATI formation is a key factor contributing to therapeutic failure and significant safety concerns, as these antibodies can trigger severe infusion-related reactions that may require treatment discontinuation. In Spain, most available ATI detection assays are sensitivity-based, identifying antibodies only in the absence of circulating IFX. In contrast, tolerance assays can detect ATI even in the presence of IFX, offering distinct advantages in managing immunogenicity.

We report the case of a 29-year-old female with corticosteroid-refractory ulcerative colitis undergoing IFX treatment. The patient experienced an infusion reaction during her sixth dose. Blood tests revealed IFX trough levels of 10.6 µg/mL, free ATI <0.2 UA/mL, and total ATI >250 UA/mL.

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This case highlights the utility of tolerance assays in promptly assessing ATI during infusion reactions, enabling real-time therapeutic adjustments. While measuring free ATI is generally more informative in clinical practice, total antibody levels may provide valuable complementary insights, particularly in cases of suspected immunogenicity during infusion reactions.

Keywords: Infliximab infusion reactions. Immunogenicity. Tolerance assays.

Dear Editor,

Failure of infliximab (IFX) therapy is frequently associated with pharmacokinetic challenges, often attributable to the presence of anti-infliximab antibodies (ATI). ATI formation is a significant factor contributing to therapeutic failure and safety concerns, as these antibodies have been implicated in infusion-related reactions. Some of these reactions can be severe, necessitating immediate discontinuation of treatment (1).

In Spain, most assays for ATI detection rely on sensitivity-based methodologies, which detect antibodies only in the absence of circulating IFX. In contrast, tolerance assays can detect ATI even in the presence of detectable IFX, offering potential advantages in managing immunogenicity (2).

Case Report

We report the case of a 29-year-old female diagnosed with ulcerative colitis, under treatment with topical mesalazine and oral beclomethasone. The patient presented with a corticosteroid-refractory flare characterized by 6-7 daily bloody stools, tenesmus, and nocturnal symptoms. Rectoscopy revealed a rectal ampulla with edematous, eroded mucosa and serofibrinous exudate. Clinical assessment of disease activity yielded a Mayo score of 6 and an UCEIS score of 2.

Induction therapy with IFX was initiated at 5 mg/kg at weeks 0, 2, and 6. Therapeutic drug monitoring performed at weeks 2 and 6 showed trough levels of 22.7 µg/mL and 7.7 µg/mL, respectively. Due to subtherapeutic levels at week 6, the regimen was

intensified to 5 mg/kg every 4 weeks. At week 10, trough IFX levels were 6.5 µg/mL, and the intensified schedule was maintained with follow-up planned for 4 months.

At week 18, during IFX administration, the patient experienced an infusion reaction characterized by pruritus and erythema. Given the severity of the reaction, the infusion was immediately discontinued. Blood samples obtained at the time of the reaction revealed infliximab trough levels of 10.6 µg/mL, free anti-infliximab antibodies (ATI) <0.2 UA/mL, and total ATI >250 UA/mL.

Discussion

This case highlights the importance of early detection in determining the cause of infusion reactions and guiding real-time treatment adjustments. Tolerance tests are particularly valuable for assessing ATI status during infusion reactions, even when IFX is detectable. In contrast, sensitivity-based assays require waiting until the next dose (trough level) to assess free ATI, leading to additional hospital visits and increased burdens on patients and healthcare resources (3).

In conclusion, measuring free ATI is generally more informative in clinical practice, providing a direct measure of immunogenicity. However, total antibody levels may offer complementary insights, particularly in cases of suspected immunogenicity during infusion reactions.

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