Response to the comments on the article ''Good clinical practice recommendations for proton pump inhibitor prescription and deprescription. A review by experts from the AMG''

Respuesta al comentario del artículo «Recomendaciones de buena práctica clínica en la prescripción y deprescripción de inhibidores de la bomba de protones. Revisión por expertos de la AMG»

We have read the comments by Salvador and Rivera[1] on the recommendations by Valdovinos-García et al. (2025), regarding the prescription and deprescription of proton pump inhibitors (PPIs),[2] with great interest, in particular, the therapeutic algorithm proposed for PPI use in the intensive care unit (ICU). After reviewing the algorithm with the published recommendations, we believe it reflects the indications of the original consensus, especially with respect to the clinical conditions and risk factors that justify prophylaxis with PPIs in the ICU. According to our consensus, ''*PPI use as a prophylactic measure is recommended in patients admitted to the intensive care unit with risk factors for stress ulcers*'' which lays the groundwork for restricting PPI use in intensive care, limiting their use to only high-risk cases. The algorithm presented by Salvador and Rivera correctly incorporates the main risk factors described in the consensus: prolonged mechanical ventilation (more than 48 h) and the presence of coagulopathy. Those 2 factors have been identified by experts as the most important for precipitating gastrointestinal bleeding due to stress ulcers in critically ill patients, with estimated relative risks of 15.6 for ventilation > 48 h and 4.3 for coagulopathy. In this sense, the algorithm is in line with the original recommendations, by requiring the presence of mechanical ventilation > 48 h or coagulopathy for indicating PPIs in the ICU.[3] Notably, the original article reports that clinically significant gastrointestinal bleeding in the ICU occurs in ∼1% of critically ill patients without prophylaxis, but despite its low frequency, is an important cause of death. Precisely for that reason, prophylaxis with PPIs is indicated in high-risk patients in the ICU because it can reduce the incidence of bleeding by around 60%. If the abovementioned algorithm considers additional factors (e.g., other comorbidities or situations of extreme physiologic stress in the ICU), it should be clarified that the original article does not mention them explicitly as primary indications for prophylaxis. The consensus authors focused their recommendation on the 2 factors with the most solid statistical support (prolonged mechanical ventilation and coagulopathy). This does not exclude other clinical contexts that increase the risk of bleeding (such as septic shock, severe burns, brain trauma, high-dose corticosteroid use, etc.),[3–5] but instead, indicates that the available evidence confers special importance upon prolonged ventilation and coagulopathy. In practice, those other factors tend to be considered relevant when they accumulate or are added to the major ones. The consensus did not list them, perhaps in an effort to prioritize conciseness and higher quality evidence. At any rate, the nucleus of the algorithm –to restrict PPI prescription in the ICU to patients at a significant risk for bleeding– concurs with the spirit of the original recommendations.

In addition, we wish to reinforce the validity of the algorithm regarding PPI *deprescription*, once the patient is no longer exposed to risk factors in the ICU. In the recommendations, we clearly state that there is no significant difference between different PPI doses or administration routes for purposes of prophylaxis, for which the standard dose is recommended and the treatment maintained, only while the patient presents with risk factors, suspending it once the risk factors are resolved. This indication is fundamental for preventing unnecessarily prolonged treatments with PPIs in the critically ill patient. In fact, the consensus authors emphasize the fact that PPIs are among the most overused drugs: up to *two-thirds* of the patients that take them lack an appropriate indication for their chronic use. Therefore, suspending the PPI in the absence of a clear indication (such as prophylaxis in a patient no longer intubated or coagulopathic) is considered good clinical practice.

In conclusion, the therapeutic algorithm proposed by Salvador and Rivera for PPI use in patients in the ICU is consistent with the recommendations by Valdovinos-García et al. (2025). Said algorithm adequately reflects the recommendation that the indication for prophylaxis with PPIs should be limited to critically ill patients at a confirmed high risk (mainly mechanical ventilation > 48 h or coagulopathy) and coincides with the original consensus in discouraging PPI use when there are no such risk factors. That congruence, supported by data in the original article, strengthens the validity of the algorithm and contributes clarity in the practical application of the recommendations, emphasizing the judicious use of PPIs in the ICU, as well as their timely deprescription, once the conditions of risk are overcome.

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Declaration of competing interest

The authors declare that there is no conflict of interest.

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Fecal microbiota transplantation in recurrent *Clostridioides difficile*: Is greater methodological rigor and the analysis of other populations relevant?

Trasplante de microbiota fecal en *Clostridioides difficile* recurrente: ¿es pertinente mayor rigor metodológico y el análisis de otras poblaciones?

Dear Editors,

We have read with particular interest the study by Quera et al.[1] titled ''Fecal microbiota transplantation through colonoscopy in the treatment of recurrent *Clostridioides difficile*: Experience at a university center'', whose aim was to describe the clinical results of fecal microbiota transplantation (FMT) performed as treatment for recurrent *Clostridioides difficile* infection (CDI). We would like to make the following observations.

An adequate and detailed description of the methodological aspects of the study by Quera et al.[1] should be emphasized. The use of statistical normality tests has been widely discussed. Each has its clear indications, but the Shapiro-Wilk test is recommended over the Kolmogorov-Smirnov test, given that it has been demonstrated to be more powerful and exact. However, we believe it would have been relevant to have given more statistical data on the use of the test employed and the possible limitations for its implementation. For example, for applying the Shapiro-Wilk test, probabilistic sampling is recommended, and the authors provided no further information about their sampling and selection decisions.[2]

In their study, Quera et al.[1] conducted a clinical follow-up of the patients of at least 3 months, post-FMT, and the percentage of successful FMT was defined as the absence of a new episode of CDI for 8 weeks after the procedure. In contrast, Gupta et al.[3] describe definitions for clinical and general cure, for evaluating the effectiveness of the procedure. Clinical cure is defined as diarrhea and/or *Clostridioides difficile* (*C. difficile*) toxin resolution within a period of 12 weeks or years, and general cure is defined as cure after a single or repeated FMT. One of the inclusion criteria for that study was CDI diagnosis, based on clinical symptoms and *C. difficile* confirmed through the polymerase chain reaction (PCR) test for toxins A and B, which could be considered post-management control, but is not mentioned in the study by Quera et al.[1]

Quera et al.[1] refer to the limitation in sample size, but it is important to consider special populations, such as immunocompromised patients. In the study by Alrabaa et al.,[4] a group of immunocompetent patients was compared with an immunocompromised group and found that all the immunocompetent patients achieved successful cure with FMT, whereas 3 immunocompromised patients experienced failure. A second FMT in those 3 patients was successful in one and failed in the other two. An important predictor of failure in FMT for CDI in immunocompromised patients was pre-FMT antimicrobial exposure.

In conclusion, the relevance and quality of the authors' research, their findings, and conclusions should be highlighted. We believe a collaborative effort by centers that are highly specialized in surgery and gastroenterology is necessary to develop better and more robust management guidelines in CDI and FMT. The aim of the methodological and population analyses we have made herein is to promote the ongoing implementation of methodological analyses, enabling the journal's continuous improvement and positioning in the scientific field in Latin America.

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