

tory body that oversees herbal dietary supplements, the Center for Food Safety and Nutrition, they have a different statutory definition, as Dr Levy points out. Specifically, a medical food as defined by the Orphan Drug Act is “a food which is formulated to be consumed or administered enterally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation”.

The authors re-emphasize, as stated in the Guidelines, that medical foods are not subject to the same rigorous premarket review and approval as drugs. Given the derivation of flavocoxid from herbal (botanical) products, one must acknowledge that the potential exists for medical foods to be subject to variability in constitution as well as to contamination and adulteration. Paradoxically, although stipulated to be administered under the supervision of a physician, they do not require a prescription.

In response to Dr Levy's second issue in which he stated that flaxocoxid was used as the primary example of drug-induced liver injury (DILI) associated with herbal products, we wish to clarify that it was not proposed in this way. Rather, it was presented as an example of a medical food that has been linked to hepatotoxicity by some authors of the Guidelines (with cooperation and assistance from Dr Levy himself).

Finally, Dr Levy takes the issue with flavocoxid being singled out as an injurious substance when, in comparison, nonsteroidal anti-inflammatory drugs (NSAIDs) are more likely to lead to significant morbidity. We acknowledge that liver injury from flavocoxid and herbal dietary supplements is likely to be rare; however, the purpose of the Guidelines was not to compare the risks of injury from the agents discussed with those from commonly used over-the-counter medications, such as NSAIDs, or to weigh in on the overall risk to benefit of various medications. The purpose of the Guidelines was to suggest preferred approaches to the diagnosis and management of DILI.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Levy R. Response to Chalassani *et al.* *Am J Gastroenterol* 2015;110:471 (this issue).

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Adalimumab Trough Levels and Response to Biological Treatment in Patients With Inflammatory Bowel Disease: A Useful Cutoff in Clinical Practice

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To the Editor: We read with great interest the article by Roblin *et al.* (1) about the development of an algorithm incorporating pharmacokinetics of adalimumab in the management of patients with inflammatory bowel disease (IBD). The findings of their study emphasize the importance of therapeutic drug monitoring during biological therapy in IBD patients so as to improve the workup of loss of response to treatment. They confirm previous findings by showing that the absence of mucosal healing was associated with adalimumab trough levels below 4.9 µg/ml, and elaborate more by proposing to optimize adalimumab treatment schedule or to switch to another antitumor necrosis factor-α drug when antidrug antibodies are absent or present, respectively, and to switch to another therapeutic class when high adalimumab trough levels are found in patients who show loss of response during treatment (1,2).

We feel that these results may greatly improve the management of patients with IBD under adalimumab treatment, as they propose a pragmatic and evidence-based algorithm that can be used in clinical practice in order to optimize the available resources. However, before an algorithm can be generalized to clinical practice, its results need to be reproduced in independent series. Therefore, we sought of interest to evaluate how assessment of adalimumab trough levels were associated with loss of response in our series of patients with Crohn's disease on adalimumab treatment.

We assessed adalimumab trough levels during the follow-up of 23 patients with Crohn's disease who were infliximab-naïve and who responded to adalimumab induction therapy. In these patients, median Harvey-Bradshaw Index before starting adalimumab was 10 (range 5–17) and significantly decreased to 4 (range 3–8; $P < 0.0001$) following adalimumab induction dose at 160/80 mg. Median follow-up was 48 weeks, and during this period 13 patients (56.5%) showed loss of response to adalimumab. In these patients, adalimumab trough levels were assessed using an ELISA Kit (Matriks Biotek, Ankara, Turkey). We found that median adalimumab trough levels in patients who showed loss of response were 4.8 µg/ml (range 2.4–7.2 µg/ml), and 7.5 µg/ml (range 6.6–8.4 µg/ml) in patients who maintained remission ($P = 0.01$). Noteworthy, these results are quite similar to those obtained by Roblin *et al.* in their preliminary study, and further confirm the relevance of biologic drugs' pharmacokinetic assessment so as to improve the management of patients affected by IBD, and in order to tailor adalimumab treatment to individual patient's profile (2,3). In conclusion, our preliminary results support the usefulness of therapeutic drug monitoring as an on-treatment tool able to optimize therapy, and confirm that an adalimumab trough level of 4.9 µg/ml is a valid cutoff to assess loss of response to treatment.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Roblin X, Rinaudo M, Del Tedesco E *et al.* Development of an algorithm incorporating