

Correspondence

Treatment of alcoholic fatty liver: is the metabolic effect of metadoxine the only reason for improved liver function?

To the Editor:

We read with interest the paper by Caballería et al. which recently appeared in the *Journal* (1). After a double-blind randomized multicentric study, the authors concluded that the improvement in steatosis and liver function tests observed in the metadoxine-treated group was due to the metabolic effect of the drug that accelerates ethanol and acetaldehyde catabolism.

We observed a similar improvement in steatosis and liver function tests in alcoholic patients treated with gamma-hydroxybutyric acid, a drug which acts on GABA receptors in the hypothalamus and in the basal ganglia cells, with an anti-craving effect (2), but lacks the liver metabolic effect of metadoxine (3). Since metadoxine also has anti-craving properties (4,5), and a specific evaluation of abstinence was not reported in the study by Caballería et al., the effect of metadoxine could merely be due to an undetected better compliance with alcohol abstinence in the treated group.

Caution is warranted in attributing metabolic "protection" to a substance, because of the strong likelihood of misinterpretation and misuse by patients with alcohol abuse, who are always looking for a pretext not to stop drinking, which remains the only therapeutic chance for them.

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Reply

To the Editor:

We would like to thank Dr Stefanini et al. for their interest in our paper published in the *Journal* (1). However, according to their letter, they have failed to understand the messages of our study. Thus, we would like to bring the following facts to their attention:

1. Contrary to the statement of Dr. Stefanini et al., we did not conclude that the effect of metadoxine was merely due to a metabolic effect that accelerates ethanol and acetaldehyde catabolism. What we hypothesized in the paper as a mechanism is that metadoxine restores hepatic glutathione content and prevents the decrease in hepatic ATP concentration and, consequently, attempts to maintain the intracellular redox homeostasis (2). It has also been demonstrated that metadoxine accelerates the hepatic oxidation of ethanol and acetaldehyde (3), probably by the maintenance of normal levels of alcohol dehydrogenase during chronic ethanol intake (4). We stated in the paper that this former mechanism could explain the improvement in the subgroup of patients who did not remain total abstainers during the study.

2. Neither is the statement true that "a specific evaluation of abstinence was not reported in the work by Caballería et al". By contrast, it is clearly mentioned in Patients and Methods that alcohol abstinence

during the treatment period was carefully controlled by questioning the patient and relatives, and by serial urine alcohol determination. As mentioned in the Results, we were able to identify 16 patients in the metadoxine group and 15 patients in the placebo group who continued drinking. Furthermore, the alcohol intake during the study was significantly lower than initially and was similar in both groups (47.7±39 g/day in the metadoxine group and 57.3±31 g/day in the placebo group). Thus, it seems that the effect of metadoxine, as suggested by Stefanini et al., could not be due to "an undetected better compliance with alcohol abstinence in the treated group".

3. We fully agree with Dr Stefanini et al. that alcohol abstinence is the first and most important therapeutic measure in patients with alcoholic liver disease, regardless of the severity. Our role as hepatologists is to encourage our patients to start a detoxication program as soon as possible and, at the same time, to look for new and more effective specific treatments.

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