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Lack of efficacy of inosine pranobex in the treatment of chronic hepatitis C

Inosine pranobex is an antiviral agent that inhibits the replication of RNA or DNA viruses (1). Prohaska et al. (2) treated a patient with chronic hepatitis C with 3 g per day of inosine and obtained alanine aminotransferase (ALT) normalization.

Recently, Laskus et al. (3) administered inosine to ten patients with chronic hepatitis C. The patients were treated with 1 g four times daily but none of them normalized ALT. Inosine was given daily for 60 days and then every other month for 12 months. It could be argued that the lack of efficacy in these patients was due to the intermittent administration of inosine, rather than to a lack of antiviral effect.

We conducted a pilot study with continuous oral administration of inosine at a dose of 3 g daily for 6 months. Forty-three patients with histologically proven chronic hepatitis C (42 chronic active hepatitis and one chronic persistent hepatitis), who had anti-HCV and RNA-HCV in serum were included. None of the patients had human immunodeficiency virus antibody or auto-antibodies. Other causes of liver disease were excluded. Seven patients had never been treated with antiviral agents. Thirty-six patients had been treated 1 year before with interferon (3–6 MU/tiw for 6–12 months) and seven (19%) normalized ALT during this therapy, but all of them had reactivation at the end of treatment. The others only had fluctuations in ALT during interferon (IFN) treatment without ALT normalization.

During inosine treatment, the mean ALT increased when comparing the basal with the final (end of treatment) level (163±92 UI/l vs 199±159 UI/l). With inosine administration only 4/43 patients (9%) normalized ALT within the first 4 months from the beginning of treatment (one patient in the 1st month, one in the 2nd month, one in the 3rd month, and the other in the 4th month). When the therapy had finished, an ALT increase was observed in these four patients. All patients still had serum RNA-HCV. No side effects were observed except for an increase of uric acid (8.9±0.28) in six patients, but without clinical consequences.

Thus the frequency of ALT normalization obtained in our study was only slightly higher than that observed without any treatment in chronic hepatitis C (9 vs 5%) (4). In light of these results it may be concluded that even the continuous administration of inosine is of little value in the treatment of chronic hepatitis C. Since 4/29 (13%) non-responders to IFN had normalization of ALT during inosine treatment, perhaps this drug may be useful in a small proportion of IFN-resistant patients. However, this needs to be proven in a controlled trial.

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Long-term response to interferon-alfa 2b re-treatment in chronic hepatitis C

About 50% of patients with chronic hepatitis C responding to interferon (IFN) relapse during follow up (1–5). While a second cycle of IFN seems effective in normalizing the alanine aminotransferase (ALT) values, the long-term efficacy of re-treatment has not been established.

The clinical consequences of the ALT relapses after therapy are also unclear; there is concern that repeated episodes of liver necrosis following therapy withdrawal could cancel the benefits of treatment.

In 1987, we started a randomized controlled trial on the efficacy of IFN-alpha-2b in chronic non-A, non-B hepatitis. The trial design, the first results and the histologic evaluation have been reported (6,7). Of the 80 patients who completed the study, 29 (Group 1) received subcutaneously 1 000 000 Units (MU) of IFN thrice weekly (t.i.w.) for 24 weeks and 26 (Group 2) received 3 MU of IFN t.i.w. subcutaneously for 24 weeks.

At the end of therapy, the response to IFN was considered complete when ALT levels had normalized and partial when ALT levels had decreased by more than 50% from baseline. Relapse after a complete response was defined as an ALT elevation confirmed by three consecutive biochemical controls performed every 30 days.