Triple therapy with amantadine in treatment-naive patients with chronic hepatitis C: a placebo-controlled trial

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The antiviral efficacy of amantadine in patients with chronic hepatitis C is controversial. In this randomized, prospective, placebo-controlled, multicenter trial, triple therapy with interferon alfa (IFN-alpha)-2a plus ribavirin and amantadine (amantadine group) was compared with combination therapy IFN-alpha plus ribavirin (control group). Four hundred previously untreated patients with histologically proven chronic hepatitis C were randomly allocated to treatment with amantadine sulphate (100 mg twice daily orally) or a matched placebo together with IFN-alpha induction plus ribavirin (1,000-1,200 mg/day orally) for 48 weeks. The primary end point was sustained virologic response (SVR) defined as undetectable serum hepatitis C virus (HCV) RNA (<100 copies/mL) 24 weeks after the end of treatment. SVR was observed in 52% of the amantadine group and in 43.5% of the control group (P = .11). Among patients with HCV genotype 1 infection, the corresponding SVR rates were 39% and 31%, respectively. The virologic on-treatment response rate in week 24 was significantly higher in the amantadine group as compared with the control group (70% vs. 59%, respectively, P = .016). This beneficial effect was mainly related to HCV type 1-infected patients (63% vs. 47%, respectively, P = .012). Independent factors associated with SVR, according to multiple logistic regression analysis, were amantadine treatment, low baseline HCV RNA, platelet counts (>=250/nL), pretreatment ALT quotient >=3, and GGT level (<28 U/L) as well as HCV genotypes other than 1. In conclusion, although we could not demonstrate a significant advantage of the triple regimen in univariate analysis, multivariate analysis offers arguments that amantadine should be considered as a potential anti-HCV drug in future studies.