
4-Aminopyridine in patients with multiple sclerosis: dosage and serum level related to efficacy and safety.

Van Diemen HA, Polman CH, Koetsier JC, Van Loenen AC, Nauta JJ, Bertelsmann FW.

Department of Neurology, Free University Hospital, Amsterdam, The Netherlands.

Abstract

In a recent randomized, double-blind, placebo-controlled crossover trial, we demonstrated efficacy of 4-aminopyridine (4-AP) in improving disability of patients with multiple sclerosis (MS). Here we describe the relationship between dosage, serum level, efficacy, and safety of intravenously and orally administered 4-AP in the same group of 70 MS patients. After both intravenous and oral administration there was a significant relationship between serum levels and 4-AP doses used (p < 0.001 and p < 0.01, respectively). The use of 4-AP in oral doses three times a day showed a large variation and fluctuation in serum levels. After 12 weeks of oral treatment (maximum daily dosage 0.5 mg/kg body weight), a statistically significant improvement was found for the smooth pursuit gain of the eye movements (estimated effect 0.14, 95% confidence interval 0.06-0.23, p < 0.001). The amount of improvement was significantly related to 4-AP serum levels (p = 0.0013). Side effects after intravenous 4-AP occurred frequently and were very troublesome (pain in infusion arm, dizziness). Side effects during oral treatment (dizziness, paresthesias) were very mild and occurred 30-45 min after intake of the medication and could be related to high serum levels.

PMID: 8504436 [PubMed - indexed for MEDLINE]

Pharmacotherapy. 2003 Jul;23(7):823-34.