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

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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.

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