The effect of 4-aminopyridine on clinical signs in multiple sclerosis: a randomized, placebo-controlled, double-blind, cross-over study.

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Abstract

To find out whether treatment with 4-aminopyridine is beneficial in multiple sclerosis (MS), 70 patients with definite MS entered into a randomized, double-blind, placebo-controlled, cross-over trial in which they were treated with 4-aminopyridine and placebo for 12 weeks each (maximum dose, 0.5 mg/kg of body weight). The estimated effect of the treatment as measured with the Kurtzke expanded disability status scale, which was the main evaluation parameter, was 0.28 point ($p = 0.001$). A significant decrease in the scale score (1.0 point or more) was encountered in 10 patients (16.4%) during oral treatment with 4-aminopyridine whereas it was not seen during placebo treatment (p less than 0.05). A significant subjective improvement (defined as an improvement that significantly affected the activities of normal daily life) was indicated by 18 patients (29.5%) during 4-aminopyridine treatment and by 1 patient (1.6%) during placebo treatment (p less than 0.05). Significant improvements related to 4-aminopyridine occurred in a number of neurophysiological parameters. No serious side effects were encountered. However, subjective side effects such as paresthesias, dizziness, and light-headedness were frequently reported during 4-aminopyridine treatment. Analysis of subgroups revealed that there was no difference in efficacy between those patients randomized to receive 4-aminopyridine and then placebo and those randomized to receive placebo and then 4-aminopyridine or between patients with and those without subjective side effects. Especially patients with temperature-sensitive symptoms and patients characterized by having a longer duration of the disease and being in a progressive phase of the disease were likely to show clear clinical benefit.

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