Efficacy and safety of 4-aminopyridine in patients with long-term spinal cord injury: a randomized, double-blind, placebo-controlled trial.

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Abstract

OBJECTIVES: To study the efficacy and safety of 4-aminopyridine (4-AP), and to document sensorimotor changes after discontinuation of the drug in patients with long-term spinal cord injury. DESIGN: Randomized, double-blind, placebo-controlled trial. SETTING: Clinical research unit. PATIENTS: Twenty-seven patients with long-term spinal cord injury. INTERVENTION: Patients were randomized to receive either oral 4-AP 5 mg/day, which was increased by 5 mg/week to a maximum dosage of 30 mg/day, or placebo for 12 weeks. They switched to the opposite treatment for the next 12 weeks. MEASUREMENTS AND MAIN RESULTS: Twenty-five patients finished the study. The results from the first 12 weeks were used to test efficacy. Positive gains in motor function, sensation, and independence occurred more frequently in patients receiving 4-AP (69%) than those receiving placebo (46%). Significant functional improvement was also noted in those treated with 4-AP (chi2, p=0.042). When each evaluation scale was considered separately, significant improvement was seen only in motor function (4-AP 92% vs placebo 46%, Fisher exact test, p=0.03). Persistent effects of the drug were assessed at week 24 in the group that initially received 4-AP. A persistent, significant 4-AP effect was observed in evaluations of sensation and independence (67% and 83% of patients, respectively; Wilcoxon signed rank test, p=0.032 and 0.042, respectively). Fourteen (56%) patients had 26 adverse reactions. One moderate adverse reaction--posterior tibial artery vasospasm--and 25 mild adverse reactions, such as dry mouth, dizziness, nausea, gastritis, oral and peripheral paresthesia, resolved adequately. Six (24%) patients experienced transitory alterations of enzyme levels (alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, and creatine kinase) and thrombocytopenia. CONCLUSION: Patients who received 4-AP showed significant improvement in motor function, and a persistent effect on sensation and independent function occurred. The drug is safe; however, after starting 4-AP therapy, patients must be carefully monitored for the possible occurrence of peripheral vasospasm. PMID: 12885095 [PubMed - indexed for MEDLINE]

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