Neuroprotective effect of an antioxidant, ebselen, in patients with delayed neurological deficits after aneurysmal subarachnoid hemorrhage.

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OBJECTIVE: The effect of ebselen, a seleno-organic compound with antioxidant activity through a glutathione peroxidase-like action, on the outcome of subarachnoid hemorrhage was evaluated in a multicenter placebo-controlled double-blind clinical trial. METHODS: Patients who suffered aneurysmal subarachnoid hemorrhages of Hunt and Kosnik Grades II through IV at admission and were able to start drug treatment within 96 hours of the ictus were enrolled. Early surgery was performed whenever possible. Oral administration of ebselen granules suspended in water (150 mg, twice a day) or placebo was started immediately after admission and continued for 2 weeks. The major end points were the Glasgow Outcome Scale at 2 weeks, 1 month, and 3 months after the start of treatment. The incidence of delayed ischemic neurological deficits clinically diagnosed as resulting from vasospasm and the incidence and extent of low-density areas on postoperative computed tomographic scans were also studied as secondary outcome measures. RESULTS: Intent-to-treat analysis of the 286 patients enrolled in the trial (145 patients administered ebselen and 141 administered placebo) revealed that the incidence of clinically diagnosed delayed ischemic neurological deficits was unaltered. There were 52 (receiving ebselen) and 58 (receiving placebo) patients with delayed deficits; however, a significantly better outcome was observed after ebselen treatment than after placebo (P = 0.005, chi2 test). There was a corresponding decrease in the incidence and extent of low-density areas (P = 0.032, Wilcoxon rank sum test). CONCLUSION: Ebselen reduced brain damage in patients with delayed neurological deficits after subarachnoid hemorrhage and may be a promising neuroprotective agent.

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