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Citicoline: pharmacological and clinical review, 2006 update.

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Abstract

Cytidine 5'-diphosphocholine, CDP-choline, or citicoline is an essential intermediate in the biosynthetic pathway of structural phospholipids in cell membranes, particularly phosphatidylcholine. Following administration by both the oral and parenteral routes, citicoline releases its two main components, cytidine and choline. Absorption by the oral route is virtually complete, and bioavailability by the oral route is therefore approximately the same as by the intravenous route. Once absorbed, citicoline is widely distributed throughout the body, crosses the blood-brain barrier and reaches the central nervous system (CNS), where it is incorporated into the membrane and microsomal phospholipid fraction. Citicoline activates biosynthesis of structural phospholipids of neuronal membranes, increases brain metabolism, and acts upon the levels of different neurotransmitters. Thus, citicoline has been experimentally shown to increase norepinephrine and dopamine levels in the CNS. Owing to these pharmacological mechanisms, citicoline has a neuroprotective effect in hypoxic and ischemic conditions, decreasing the volume of ischemic lesion, and also improves learning and memory performance in animal models of brain aging. In addition, citicoline has been shown to restore the activity of mitochondrial ATPase and membrane Na+/K+ATPase, to inhibit activation of certain phospholipases, and to accelerate reabsorption of cerebral edema in various experimental models. Citicoline has also been shown to be able to inhibit mechanisms of apoptosis associated to cerebral ischemia and in certain neurodegeneration models, and to potentiate neuroplasticity mechanisms. Citicoline is a safe drug, as shown by the toxicological tests conducted, that has no significant systemic cholinergic effects and is a well tolerated product. These pharmacological characteristics and the action mechanisms of citicoline suggest that this product may be indicated for treatment of cerebral vascular disease, head trauma (HT) of varying severity, and cognitive disorders of different causes. In studies conducted in the treatment of patients with HT, citicoline was able to accelerate recovery from post-traumatic coma and neurological deficits, achieving an improved final functional outcome, and to shorten hospital stay in these patients. Citicoline also improved the mnesic and cognitive disorders seen after HT of minor severity that constitute the so-called post-concussional syndrome. In the treatment of patients with acute ischemic cerebral vascular

disease, citicoline accelerates recovery of consciousness and motor deficit, achieves a better final outcome, and facilitates rehabilitation of these patients. The other major indication of citicoline is for treatment of senile cognitive impairment, either secondary to degenerative diseases (e.g. Alzheimer disease) or to chronic cerebral vascular disease. In patients with chronic cerebral ischemia, citicoline improves scores in cognitive rating scales, while in patients with senile dementia of the Alzheimer type it stops the course of disease, and neuroendocrine, neuroimmunomodulatory, and neurophysiological benefits have been reported. Citicoline has also been shown to be effective in Parkinson disease, drug addictions, and alcoholism, as well as in amblyopia and glaucoma. No serious side effects have occurred in any series of patients treated with citicoline, which attests to the safety of treatment with citicoline.