Combination therapy for ischemic stroke: potential of neuroprotectants plus thrombolytics.

許重義
Chen SD;Lee JM;Yang DI;Nassief A;Hsu CY.

Abstract

Thrombolysis improves clinical outcome in patients with acute ischemic stroke. However, only a small fraction of patients receive thrombolytic therapy due to the narrow therapeutic time window available for the treatment in patients with ischemic stroke. A better understanding of the mechanisms underlying ischemic injury may lead to the development of novel therapeutic strategies to reduce brain damage after stroke. Cerebral ischemia triggers a number of pathophysiological and biochemical changes in the brain that present potential targets for therapeutic intervention. Candidate pathways include those regulating cellular calcium influx, excitatory neurotransmitter uptake, and generation of reactive oxygen species, as well as activation of enzymes including kinases, proteases, and lipases. The end result of these pathophysiological pathways may be apoptosis (programmed cell death) or necrosis. The activation of inflammatory cascades following ischemia also contributes to brain injury. Several neuroprotective agents which block cell death pathways have been proposed to have therapeutic potential in patients with stroke including calcium channel antagonists, glutamate receptor antagonists, free radical scavengers, anti-inflammatory strategies, inhibitors for nitric oxide synthase, and growth factors. Although results from clinical trials to date have been disappointing, there is reason to believe that combination therapy involving both thrombolytics and neuroprotectants holds promise for stroke treatment and warrants further investigation.