Effect of combination of endothelin receptor antagonist (TAK-044) and aspirin in middle cerebral artery occlusion model of acute ischemic stroke in rats.

Methods Find Exp Clin Pharmacol 29(4):257-63, 2007.

Briyal S, Gulati A, Gupta YK.

The present study was carried out to investigate the effect of the combination of an endothelin antagonist TAK-044 and an antiinflammatory agent aspirin in middle cerebral artery (MCA) occlusion model of acute ischemic stroke in rats. Male Wistar rats were pretreated with TAK-044 (5 mg/kg, i.p.) and aspirin (50 mg/kg, i.p.) for 7 days individually and in combination in different groups, and were thereafter subjected to focal ischemia for 2 h by occlusion of MCA using intraluminal thread. Twenty-four hours later, the rats were subjected to motor performance tests and killed subsequently for estimation of markers of oxidative stress malondialdehyde (MDA), reduced glutathione (GSH) and superoxide dismutase (SOD). The control group received the vehicle and the same protocol was followed. In vehicle-treated MCA occluded rats, significant ($p < 0.01$) motor impairment, with elevated levels of MDA (600.8 +/- 14.4 nmol/g tissue) and decreased levels of GSH (61.1 +/- 3.1 microg/g tissue) and SOD (8.5 +/- 0.5 U/mg protein,) was observed. Pretreatment with TAK-044 and aspirin for 7 days significantly improved motor function and attenuated the raised levels of MDA (475 +/- 14 and 538 +/- 17.3 nmol/g tissue, respectively) and the decrease in GSH (101 +/- 5 and 100 +/- 4.5 microg/g tissue, respectively) and SOD (12.1 +/- 0.5 and 10.5 +/- 0.6 U/mg protein, respectively), as compared to vehicle-treated MCA occluded rats. Combination of both the agents did not show a significant difference as compared to the individual drugs alone. The present study demonstrates that, although protection was observed with both the drugs (TAK-044 and aspirin), there was no enhanced effect when both agents were given in combination.