



**Effect of endothelin antagonist (TAK-044) on cerebral ischemic volume, oxidative stress markers and neurobehavioral parameters in the middle cerebral artery occlusion model of stroke in rats.**

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Stroke causes brain injury in millions of people world wide each year. Despite the enormity of problem, currently there is no established therapy, which can restore the blood flow at infarcted area and also improve the neurological deficit. The present study was carried out to investigate the effect of an endothelin antagonist (TAK-044) 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.) for 7 days and thereafter subjected to focal ischemia by occlusion of MCA using intraluminal thread for two hours. 30 min after reperfusion the animals were subjected to diffusion-weighted imaging (DWI) for assessment of protective effect. Twenty-four hours later the motor performance was tested and subsequently the animals were sacrificed for estimation of markers of oxidative stress; malondialdehyde (MDA), glutathione (GSH) and superoxide dismutase (SOD). Control group received vehicle (saline) and similar experimental protocol was followed. In the TAK-044 pretreated group, percent hemispheric lesion area (% HLA) in DWI was significantly attenuated 17.5 +/- 0.5% as compared to control group 61.2 +/- 5.9%. Significant motor impairment, with significant elevated levels of MDA, decrease in GSH and SOD were observed in the vehicle treated MCA occluded rats. Pretreatment with TAK-044 prevented the motor impairment and significantly reversed the changes in markers of oxidative stress (MDA, GSH and SOD). In addition to well-known vasodilatory effect, TAK-044 has recently been documented to have antioxidant and anti-inflammatory properties. These effects can contribute to the protection afforded by TAK-044 in the present study.