

## **Effects of the combination therapy with candesartan and alpha tocopherol on brain injury and neurological outcome following brain ischemia in experimental model of transient focal cerebral ischemia in rats**

### **Abstract**

**Background & objective:** Stroke is third leading cause of death and disability in the most of human communities. Single neuroprotective drugs have so far failed because ischemic stroke has complex pathophysiology and multiple interactive processes. Several experimental studies have shown that combination therapy with drugs that act via different mechanisms can produce amplified protective effects. In addition, combination therapy may reduce doses of drugs and decrease incidence of adverse effects. We examined the effects of post-ischemic combination therapy with candesartan and alpha tocopherol on cerebral infarction, formation of edema and oxidative stress biomarkers.

**Materials and methods:** Male Sprague-Dawley rats were divided into five groups, sham, control ischemic, candesartan treated (0.3 mg/kg), alpha tocopherol treated (30 mg/kg) and combined treated ischemic groups. Transient focal cerebral ischemia was induced by 90-min-long occlusion of the left middle cerebral artery followed by 24-h-long reperfusion. Neurological deficit score was evaluated at the end of the reperfusion period. Thereafter, the animals were randomly selected and used for three projects: (i) Measurement of the infarct volumes, (ii) investigation of ischemic brain edema formation using a wet/dry method, and (iii) assessment of the malondialdehyde (MDA) and reduced glutathione (GSH) concentrations using a HPLC technique.

**Results:** Induction of cerebral ischemia in the control group produced considerable brain infarction in conjunction with severely impaired motor functions. Combined treatment with

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candesartan and alpha tocopherol significantly reduced the infarct volume and improved the above functions. The water content in the left (lesioned) hemisphere was considerably elevated in the control ischemic group. Combined treatment significantly lowered the water content in the ischemic lesioned hemisphere, retained tissue GSH level, and led to a lower MDA production. These effects on brain edema and oxidative stress biomarkers were significantly more than the monotherapy with candesartan.

**Conclusion:** The combination therapy with candesartan and alpha tocopherol can noticeably decrease ischemic brain injury and attenuate edema formation likely via increasing the antioxidant activity.

**Keywords:** Stroke, brain edema, candesartan, alpha tocopherol, malondialdehyde, glutathione.