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Muhammad Faisal Wadiwala

*National Institute of Neurologic Disorders and Stroke*

Ambreen Sonawalla

*Aga Khan University*

Ayeesha Kamran Kamal

*National Institute of Neurologic Disorders and Stroke*

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## What is the role of free radical scavengers in acute stroke?

Muhammad Faisal Wadiwala,<sup>1</sup> Ambreen Sonawalla,<sup>2</sup> Ayeesha Kamran Kamal<sup>3</sup>

Stroke Service and Vascular Fellowship Program, International Cerebrovascular Translational Clinical Research Training Program (Fogarty International Center and National Institute of Neurologic Disorders and Stroke),<sup>1,3</sup> Medical College,<sup>1</sup> Aga Khan University, Karachi, Pakistan.

Corresponding Author: Ayeesha Kamran Kamal. Email: ayeesha.kamal@aku.edu

Effects of Edaravone, a Free Radical Scavenger, on Serum Levels of Inflammatory Biomarkers in Acute Brain Infarction.

### Why is this study important and noteworthy?

Stroke may lead to functional disability. Much of this tissue injury is a result of the release of free radicals, which directly damage cells and also initiate other reactions which lead to cerebral oedema. Free radicals, through lipoperoxidation, cause increases in inflammatory cells and mediators, and matrix metalloproteinases (MMP) in the brain which leads to disruption of the blood-brain-barrier, increase in vascular endothelial permeability and vasogenic brain oedema.

Edaravone, a free radical scavenger, has been shown to reduce the free radicals which are produced during reperfusion in ischaemic cerebral injury, and inhibit expression of MMP-9 in ischaemic brain models. However, its effects on serum levels of inflammatory biomarkers have

not been sufficiently studied.

This study was a prospective observational study, aimed at investigating the effects of Edaravone treatment on serum levels of inflammatory biomarkers, in patients with acute cerebral infarction.

### Who were the participants?

This study was a prospective observational study, conducted in Japan, enrolling 69 patients (39 men and 30 women) who were admitted to the hospital within 12 to 36 hours of suffering an acute brain infarction, between April 2007 and September 2008. Edaravone was administered to all the patients who had come within 12-24 hours of onset of symptoms, whereas those admitted after 24-36 hours of symptoms served as the control group.

This study excluded patients below 18 years, or those with contraindications to edaravone treatment such as serious kidney dysfunction, liver disorder, or hypersensitivity to ingredients in edaravone. Patients with

recurrent cerebral infarction (<6 months between episodes), or previous history of heart disease such as heart failure or ischaemic heart disease, were also excluded, as were those with a disability having a modified Rankin scale (mRS) score  $\geq 2$  before onset or those who required surgical or endovascular interventions during hospitalization. Patients with infections, inflammatory diseases, haematologic disorders, malignancy requiring treatment, or pregnancy were also excluded.

### **What was the intervention and what were the measurements?**

Patients who were admitted 12-24 hours after onset of symptoms were administered 30 mg of edaravone diluted in 100 mL of saline, every 12 hours for the next 14 days. The edaravone was administered intravenously via drip-infusion over a 30 minute period.

Diagnosis of acute cerebral infarction was made by neurologic examination and computed head tomography and/or MRI. Serial blood samples were obtained from the patients at admission, at 48 hours, 7 days and 14 days after onset of symptoms and tested using ELISA for high-sensitivity C-reactive protein (hs-CRP), Interleukins IL-6, IL-10, IL-18, tumour necrosis factor (TNF)- $\alpha$ , MMP-2 and MMP-9.

### **What was the outcome?**

Over the 14 days, there was no significant change in MMP-9 levels in the edaravone group ( $p=0.564$ ) whereas in the control group MMP-9 levels increased from 3.857 to 4.538 ng/mL ( $p=0.027$ ).

Unpaired t tests for other serum biomarkers showed no significant differences between the two groups over the observation period. There was also no significant difference seen in the NIHSS score at 14 days, in the mRS score at 3 months, after onset of symptoms, or in the duration of hospitalization.

### **What were the conclusions?**

In patients with acute cerebral infarction, edaravone

significantly suppressed circulating serum levels of MMP-9. However, since in humans, the contribution of brain tissue to the circulating levels of MMP-9 within 14 days after onset of a stroke is unknown, these findings should not be taken to reflect the effects of edaravone on ischaemic brain per se. Edaravone did not significantly affect serum levels of any other inflammatory biomarker. Further, edaravone did not significantly affect functional outcomes in patients.

### **How does this impact our clinical practice?**

This study does not conclusively demonstrate that the suppression of circulating MMP-9 levels by edaravone correlates with improved outcomes in relation to stroke pathophysiology. However, the use of edaravone may help combat the neurotoxicity following tPA-based revascularization, since tPA is known to cause neurotoxicity by many pathways, including increasing MMP-9 levels. However, further studies need to be done to confirm this beneficial effect. We should stay tuned for the effects of edaravone which appear exciting in these 'preclinical studies'.

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### **References**

1. Isahaya K, Yamada K, Yamatoku M, Sakurai K, Takaishi S, Kato B, et al. Effects of Edaravone, a Free Radical Scavenger, on Serum Levels of Inflammatory Biomarkers in Acute Brain Infarction. *J J Stroke Cerebrovas Dis* 2010; 21: 102-7.