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Role of Uric Acid Therapy in Prevention of Early Ischemic Stroke Progression

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Abstract

Objective: To study the role of uric acid (UA) in the outcome of thrombolysis after stroke. **Materials and Methods:** Our observational study was conducted over 5 years at the KMC Hospital, Mangalore from July 2011 to July 2016. All patients above the age of 18 years presenting to the hospital within 4.5 hours of stroke onset were included into the study. The patients' stroke severity was calculated by National Institute of Health Stroke Scale (NIHSS) score, whereas the outcome was measured by modified Rankin Scale (mRS) score. The patients were divided into good outcome, poor outcome, and expired groups of patients depending on the mRS score (<3, ≥3 but <6, and 6, respectively). UA in the blood was measured and recorded in all the included patients. At the end of the study, significance was calculated by standard statistical methods. **Results:** A total of 71.9% patients were found to have a good outcome, 24.2% patients had poor outcome, and the rest were in the expired group of patients. Among the good outcome patients, UA was found to be 4.6 ± 1.4 mg/dL, in the poor outcome group UA was 3.7 ± 1.1 mg/dL, and in expired group UA was 3.2 ± 0.6 mg/dL (P = 0.002). **Conclusion:** Our results suggest that UA has neuroprotective actions and can predict a good outcome among patients undergoing thrombolysis.

Keywords: High purine diet, mRS, neuroprotection, NIHSS, outcome of stroke, stroke, thrombolysis, uric acid

Introduction

Stroke is a common and devastating disease that has been one of the most common cause of mortality and disability in the past decade. While a decreasing trend has been noted in its incidence in the developed nations, developing nations still continue to record an increasing trend in stroke mortality. Therefore, the target to treat stroke early is important. Thrombolysis remains a main modality of treatment for these patients. However, despite thrombolysis, many patients do not show any improvement in stroke outcome.[1] Therefore, we studied the role of one of the endogenous antioxidant that protects the brain.

Materials and Methods

Our observational study was conducted at the KMC Hospital, Mangalore. We studied our patients who underwent thrombolysis for 5 years from July 2011 to July 2016. All patients above the age of 18 years presenting to the hospital within 4.5 hours of stroke onset, and who were willing to provide an informed consent were included into the study. The patients' stroke severity was calculated by the National Institute of Health Stroke Scale (NIHSS) score, whereas the outcome was measured by the modified Rankin Scale (mRS) score. The patients were divided into good outcome, poor outcome, and expired groups of patients depending on the mRS score (<3, ≥3 but <6, and 6, respectively). The blood investigation uric acid (UA) was measured and recorded in all our patients. At the end of the study, the significance was calculated by standard statistical methods.

Results

We were able to include 128 patients in our study. Eight patients were excluded because they did not wish to be a part of the study, and 4 patients were excluded because they did not complete the treatment in the hospital and their

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outcome could not be determined. None of our patients had a prior stroke.

The mean age of our patients was 62.5 ± 13 years. A slight male preponderance was noted in our patients, with 68 of the 128 (53.1%) patients being males. A majority of our patients, 114 of 128 (89.1%), were found to have middle cerebral artery territory stroke, followed by posterior cerebral artery stroke (8.6%) and anterior cerebral artery stroke. The mean time to presentation to our hospital was 120 ± 55 minutes with a door-to-needle time of 17 ± 4 minutes. The admission NIHSS of our patients was 22 ± 7.

After thrombolysis by the National Institute of Neurological Disease and Stroke criteria of 1995, 92 of the 128 (71.9%) patients were found to have a good outcome, 31 (24.2%) patients had poor outcome, and 5 patients were in the expired group of patients. Among the good outcome patients, UA was found to be 4.6 ± 1.4 mg/dL, in the poor outcome patients, UA was 3.7 ± 1.1 mg/dL, and in expired group, UA was 3.2 ± 0.6 mg/dL ($P = 0.002$).

Discussion

UA is a metabolic end product of purine nucleotides. The latter are chief constituents of DNA and RNA. The concentration of UA is usually higher in humans than in other animals. It is considered to have antioxidant properties.[2] The scavenging of hydroxyl radicals, peroxynitrite, hydrogen peroxide, and prevention of peroxidation of lipids may be among the mechanisms of its antioxidant property.[3] UA is an important endogenous antioxidant that has been shown to have neuroprotective effects.[4]

Ischemic penumbra is the oligemic zone where brain's autoregulation is ineffective. This is the critical area that may be successfully preserved to restore at least some of the functions, thereby providing the "window of opportunity." There is preservation of energy and cellular integrity. On development of stroke, there is energy failure. With sustained hypoxia, excitotoxicity, oxidative stress, and spontaneous waves of depolarization, mitochondrial damage may eventually lead to programmed neuronal death causing the infarct.[5]

Oxidative and nitrosative stress play a role in ischemic injuries. It modulates signal transduction tipping the balance in favour of cell death. Peroxynitrite especially may act as an executioner in cell death. The brain has limited antioxidant defences.[5]

In agreement with prior observations,[6] our study found an inverse correlation between the UA levels and the outcome of stroke.

Conclusion

Ischemic penumbra is an area that can be preserved. The oxidative and nitrosative stress inclusive of peroxynitrite cause neuronal damage. The brain has limited antioxidant defences. Few prior studies have been found regarding UA levels and stroke outcomes after thrombolysis, with none from India. UA can play a role in enhancing the antioxidant defences in brain. Therefore, we present our results suggesting that UA has neuroprotective actions and can predict a good outcome among the patients undergoing thrombolysis. It also supports the exploration of the benefits of newer therapeutic options in stroke management such as administration of exogenous UA in patients being treated with thrombolysis.[7] The role of diets rich in purine may also be suggested such as dried beans and legumes, mushrooms, cauliflower, spinach, and meat-based stews or soups.[8]

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Conflicts of interest

There are no conflicts of interest.

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