A Study of Lipid Peroxidation in Ischemic Stroke
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Abstrak
Telah dilakukan pengukuran malonil dialdehid serum (MDA) pada 25 kasus stroke iskemik dan 25 kelola untuk mengetahui hubungan beratnya stroke dengan hasil penanganan. Umur rata-rata kasus stroke adalah 53.08 ± 15.01 tahun, dan rasio laki/perempuan adalah 3:2. Penentuan MDA dilakukan dengan cara Placer dkk. MDA serum pada kasus lebih tinggi secara bermakna dibanding kelola (3.33 ± 0.75 μmol/L vs. 1.73 ± 0.48 μmol/L, p < 0.001). Angka ini lebih tinggi pada kasus yang pengukuran MDA nya dilakukan dalam 6 jam pertama serangan stroke. Tidak ada korelasi dengan keadaan-ubaan serangan stroke, dengan lokasi dan luasnya infark, atau dengan beratnya stroke sebagaimana ditentukan oleh Modified National Institute of Health Stroke Scale.

Abstract
Serum malonyl dialdehyde (MDA) level, an index of lipid peroxidation, was estimated in twenty five CT proved ischemic stroke subjects and 25 age and sex matched healthy controls, to find out its correlation with severity and outcome of stroke. Mean age of stroke patients was 53.08 ± 15.01 years and male-female ratio was 3:2. Estimation of serum MDA levels was done by the method of Placer et al. Serum MDA levels were found to be significantly high in ischemic stroke patients compared to controls (3.33 ± 0.75 μmol/L vs. 1.73 ± 0.48 μmol/L, p < 0.001). The levels were higher in those in whom MDA levels were estimated within 6 hours of onset of stroke. MDA levels had no correlation with the suddenness of the stroke, with site and extent of infarction or with the severity and outcome of stroke as determined by Modified National Institute of Health Stroke Scale.

Keywords: Lipid peroxidation, Cerebrovascular accident, Ischemic stroke, Malonyl dialdehyde

Stroke is the third leading cause of death after ischemic heart disease and cancer in the developed countries. Although mortality rates are declining, stroke continues to be a major cause of disability. Thus discovery of means to limit the ischemic injury caused to the tissues may help in decreasing the total burden on the society. Ischemic injury to tissues, e.g. myocardial infarction and cerebral stroke, is partially mediated by abundant production of free oxygen radicals. Lipid peroxidation has been broadly defined as the oxidative deterioration of polyunsaturated fatty acids, a process responsible for the production of free radicals.

Lipid peroxidation is a process normally occurring at low levels in all cells and tissues. Although a variety of antioxidant mechanisms control lipid peroxidation, but under certain conditions the protective mechanisms can be overwhelmed, leading to elevated steady state tissue levels of peroxidative products in tissues. Conditions that can stimulate lipid peroxida-

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correlation, if any, between serum MDA levels and the severity of neurological deficit.

MATERIALS AND METHODS

Twenty-five patients of ischemic stroke, irrespective of age and sex, admitted to our institute were included in this study. Another 25 healthy subjects matched for age & sex served as control. The study approved by the ethical committee of the hospital. The criteria laid down by WHO to establish the clinical diagnosis of stroke were followed and only CT proved cases of cerebral thrombosis were included. Patients suffering from TIA, AMI, liver and kidney diseases, poorly controlled Diabetes Mellitus and pregnant patients were excluded from the study.

All the patients were subjected to a thorough physical examination and investigations like Hb, TLC, DLC, ESR, urine analysis, blood urea & sugar, serum uric acid, lipids and electrolytes along with X-Ray chest and EKG. Other investigations like echocardiography, CT scan brain and serum MDA levels were also studied in all cases soon after admission.

Neurological status of each patient was assessed using a modified National Institute of Health Stroke (MNIHS) Scale at admission and after 3 weeks and was correlated with MDA levels.

RESULTS

Mean age of stroke patients was 53.08 ± 15.01 years and 32% patients were below the age of 45 years. Male-female ratio was 3:2. Onset of stroke was sudden in 24%, acute in 56% and progressive in 20% of patients. 80% of the patients reached the hospital within 24 hours of the onset of stroke. 96% patients presented with carotid territory and 4% with a basilar territory stroke. In the stroke group 24% of patients were hypertensive, 16% were suffering from COPD, 48% were smokers, 36% had dyslipoproteinemia, 12% were chronic alcohol drinkers and one case (4%) was of well-controlled NIDDM. None of the patients was suffering from any active coronary artery disease.

The severity of stroke as assessed by MNIHS scale at presentation revealed that 44% patients were cases of mild stroke, 24% of moderately severe stroke and 32% were suffering from very severe type of stroke. All the patients received need-based therapy, but steroids were not used. 32% of patients died, 40% were left with residual deficit and only 28% recovered completely.

88% of patients were seen to be suffering from lobar infarct and only 12% had deep seated infarcts.

Mean serum MDA levels were 1.73 ± 0.43 μmol/L in control group and it was 3.33 ± 0.75 μmol/L in the stroke group. The difference was highly significant (< 0.001). Serum MDA levels were significantly higher in those cases who were admitted to the hospital within 6 hrs compared to those who were admitted after 24 hrs of onset of stroke (3.45 ± 0.8 vs 3.04 ± 0.9). MDA levels were raised in all cases of stroke irrespective of presentation of stroke. The levels were also similarly high in all the groups, irrespective of severity of stroke. No statistically significant difference in serum MDA levels was observed in stroke patients who recovered completely, partialy or died.

DISCUSSION

Free oxygen radicals are formed during normal cellular metabolism. Cell injury associated with free radical occurs either in situation in which the scavenging system is overwhelmed or in disease states in which the protective antioxidant system is impaired. Goto suggested three possible mechanisms by which lipid peroxide could cause vascular damage. High serum lipid peroxide may inhibit endothelial prostacycline production, may directly injure endothelial cells or may increase platelet aggregation. Dzhandzhava and Shakarishivili studies activity of antioxidant protective enzymes and found decreased levels corresponding significantly to severity of impairment and were of the opinion that these patterns can be used for diagnostic and prognostic purposes. Skochii et al and Yamasaki and Kogure studies lipid peroxidation in patients of ischemic stroke and concluded that lipid peroxide levels may be used for evaluation of treatment efficacy and prognosis of the disease.

Kibata et al found raised serum lipid peroxide levels in patients with recent onset stroke and the values did show a fall when the levels were estimated a few days later. Santos et al estimated plasma malonyldialdehyde like material (MDA-LM) in 57 stroke patients and detected values above 50 mol/L in 30% of patients suffering from SAH, in 68% of patients of cerebral thrombosis and in only 17% of patients with TIA. The plasma MDA-LM level and the cerebral damage did not show any correlation, as determined by CT scan. Similar findings were reported by Huang et al who did not find any difference in the levels between those having small or a large cerebral lesion.
Figure 1. Serum MD levels in the stroke and control groups
On the other hand, Dzhandzhgava and Shakarishvili studied the activity of anti-oxidant protective enzymes-superoxide dismutase catalase, glutathione peroxidase and glutathione reductase in blood, serum and CSF in patients suffering from all types of ischemic insult to brain and found an early decrease in the activity of antioxidant enzyme as well as contents of lipid peroxidation products and these patterns were seen to normalise within 14-15 days. The degree of alteration was found to correspond significantly with the severity of impairment and he concluded that these patterns can be used for diagnostic and prognostic purposes. Skochii et al in a study on 89 patients of cerebral stroke found a clear correlation between serum lipid levels and the severity of stroke and concluded that lipid peroxidation may be used for evaluation of treatment efficacy and prognosis of the disease.

In the present study, serum MDA levels were estimated in 25 patients of ischemic stroke at the earliest after hospitalisation and they were found to be significantly higher compared to age and sex matched controls, specially in patients hospitalised within 6 hours of onset of stroke. No significant difference as found in the levels in patients with sudden, acute or progressive onset stroke. Similarly no correlation could be established of serum MDA levels with the severity of neurological deficit, or with the outcome of stroke. These findings were in agreement with those of the other workers.

Thus we could not detect any prognostic usefulness of determination of serum MDA levels in ischemic stroke patients as assessed by their neurological score. On the other hand, rise in serum MDA levels in the stroke patients as compared to age and sex matched controls was highly significant (p < 0.001), more so during first 6 hours of the onset of stroke. This stresses the role of lipid peroxidation in the damage caused during cerebral ischemic infarction and implies that antioxidant measures may be useful in limiting this ischemic injury.

REFERENCES