Relationship Between High Sensitivity TNF-α WITH clinical outcome During Admission In Acute Ischemic Stroke

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Abstract

Background : Tumor necrosis factor alpha (TNF-α), together with other pro-inflammatory cytokines such as Interleukin-1b (IL-1b), IL- 6 and IL-8, play a role in the ischemic injury of the central nervous system. TNF-α has adverse effects on ischemic brain tissue. The mechanism generated is a multicomplex process. In other studies, an increase in TNF-α can actually have neuroprotective effects. This study aims to determine the relation between the levels of the High Sensitivity TNF-α with clinical outcome in acute ischemic stroke.

Method : Thirty patients with acute ischemic stroke patients who admitted in Dr. Soetomo hospital Surabaya during the period December 2011 to February 2012. 2 cc of vein blood for examination High sensitivity TNF-α was drawn during admission from acute ischemic stroke. Clinical outcome in acute stroke was measured by NIHSS score.

Results: From 30 research samples, the mean age of patients was 59.53 ± 11.51 years. The mean High Sensitivity TNF-α level in the study subjects was 2 ± 0.99 pg / ml. NIHSS examination showed the median value of the NIHSS was 5 with a range of 2-19. There is a correlation but not statistically significant with the strength is very weak between High Sensitivity TNF-α with the NIHSS in patients with acute thrombotic stroke ($r = 0.100$ and $p = 0.600$).

Conclusion: There is relationship between serum levels of High sensitivity TNF-α with clinical outcome in acute ischemic stroke patients.

Keywords: *TNF-α, HS TNF-α, clinical outcome , acute ischemic stroke.*

Introduction

At present, stroke is ranked as the second leading cause of death worldwide. In the first year after a stroke, about 20% of patients die.[1] The number of ischemic stroke sufferers is greater than hemorrhagic stroke. In western countries, the number of ischemic stroke sufferers is around 80-85% of all stroke sufferers. Ischemic stroke is caused by a decrease in cerebral blood flow resulting in death and brain cell dysfunction.[2] Other problems are associated with the risk of infection in stroke patients.[3]

Tumor necrosis factor alpha (TNF-α), together with other pro-inflammatory cytokines such as Interleukin-1b (IL-1b), IL-6 and IL-8, play a role in the ischemic injury of the central nervous system. Some experimental studies have shown that TNF-α has adverse effects on ischemic brain tissue. The mechanism generated is a multicomplex process.[4] In other studies, an increase in TNF-α can actually have neuroprotective effects.[5]

The problem that arises is whether there is a correlation between serum TNF levels and neurological deficits that occur in patients with acute thrombotic stroke. NIHSS is a score frequently used in the evaluation of stroke clinical outcome.[6]

Method

This research is an analytic study with cross sectional design. Inclusion criteria include: Patients with acute thrombotic strokes, having suffered a thrombotic stroke 4 hours until the 7th day and are willing to sign informed consent. Exclusion criteria include: Having an infection before an attack (eg, injury, heat), having acute

ischemic heart disease, having a history of malignancy, metabolic disorders (electrolytes, liver function and kidney function), using immunosuppressive drugs, NSAIDs. Based on the formula for calculating the correlation sample, the minimum sample size is 16.97 rounded up to 30 people.

All study subjects underwent the same clinical and laboratory examinations. High Sensitivity TNF-α serum examination was carried out in the Prodia Surabaya laboratory which was carried out by the ELISA-Sandwich method. The normality of data distribution was examined by the Saphiro Wilk test. Spearman's statistical test was used to determine the correlation between the two variables that were not normally distributed.

Results

This study involved a total sample of 30 acute ischemic stroke patients who came to the Emergency room Dr. Soetomo hospital who met the inclusion criteria and did not meet the exclusion criteria. General characteristics and laboratory tests are shown in Table 1.

Table 1 General Characteristics

Variable	n (%)	Mean ± SD	Range
Sex			
Male Female	20 (66,7) 10 (33,3)		
Age (years)		59.53 ± 11.51	35 – 80
Systolic blood pressure (mmHg)		162.67 ± 25.18	110 – 210
Dyastolic blood pressure (mmHg)		96.33 ± 14.96	60 – 140
Onset of attack (days)		3.4 ± 1.57	1 – 7

Serum TNF-α levels in research subjects

The mean High Sensitivity TNF-α level in the study subjects was 2 ± 0.99 pg / ml. The mean High Sensitivity TNF-α levels can be seen in table 2.

Table 2 Mean High Sensitivity TNF-α levels

Variable	Mean ± SD	Range
High Sensitivity TNF-α levels (pg/ml)	2.00 ± 0.99	0.55 – 4.79

NIHSS results in research subjects

The results of the NIHSS examination showed the median value of the NIHSS was 5 with a range of 2 - 19, this data can be seen in table 3.

Table 3 Average NIHSS values

Variable	Median	Range
NIHSS	5	2 – 19

Correlation between High Sensitivity TNF-α levels with NIHSS value

A positive correlation was obtained with the strength of a very weak correlation between High Sensitivity TNF-α levels and NIHSS values and not statistically significant with p = 0.600 and the correlation coefficient of 0.100. This can be seen in table 3.

Table 3 Correlation between High Sensitivity TNF-α levels and NIHSS values

Variable	Correlation coefficient	p
High Sensitivity TNF-α levels vs NIHSS values	0.100	0.600

Discussion

The design of this study was cross sectional. Selection of consecutive sampling as a method of selecting research subjects because this method is the best non-probability sampling and easy to do.[7]

During approximately 4 months of research, 30 subjects were found to meet the research criteria. Of these 30 subjects, 20 (66.7%) of them were male and 10 (33.3%) were female. The ratio between male and female subjects is 2: 1 (table 1). This research shows that men experience more acute thrombotic strokes than women. In accordance with the epidemiological data of stroke, men suffer more strokes than women.[8,9] Other literature studies state that the percentage of thrombotic strokes in women in India and Southeast Asia is 33% to 36%.[10]

From 30 research samples, the mean age of patients was 59.53 ± 11.51 years (table 1). In accordance with the epidemiological data of stroke that many stroke suffered by patients aged over 45 years.[10,11] Baseline data that has been collected is then tested for normality first with the Kolmogorov-Smirnov test (KS test). This test aims to determine the distribution of normal or abnormal data.[12]

Analysis using the KS test found that the distribution of the study data was normal. Therefore an analysis to determine the correlation between High Sensitivity TNF-α and NIHSS levels in acute strokes was performed using Pearson correlation analysis.

A positive correlation was seen with a very weak correlation strength of 0.100 between High Sensitivity TNF-α and NIHSS levels in patients with acute stroke, which was not statistically significant at p = 0.600. This means that the higher the High Sensitivity TNF-α level, the greater the NIHSS value, but not statistically significant.

The results of this study are supported by other studies [13] which state that the increase in TNF-α in liquor fluids and serum of patients in acute stroke has a correlation with the severity of stroke as measured by the SSS (Scandinavian Stroke Scale) and BI (Barthel Index)). In addition there are other studies that show a TNF-α correlation with stroke outcomes using mRS (modified Rankin Scale) and BI (Barthel Index) in the first week of stroke.[14]

Conclusions and Recommendations

There is a positive correlation with the correlation coefficient (r = 0.100) between High Sensitivity TNF-α and functional expenditure as measured by NIHSS in acute ischemic strokes even though it is not statistically significant (p = 0.600). Further research is needed to measure High Sensitivity TNF-α levels with NIHSS 1, 7 and 30th day of stroke sufferers. So that it can be known the actual neurological outcome level, as well as with a larger sample size so that it can provide more representative results.

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Ethical Clearance: This study is ethically approved by the Institutional ethical Committee.

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