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The Role Of Plasma Interleukin 1 Beta Concentration, Body Temperature To The Extent Of Lesions In Ischemic Stroke Outcome Patients With And Without Hypertension

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Abstract

Aims: This study aims to analyze plasma interleukin's role with one beta concentration, body temperature to the extent of lesions in ischemic stroke outcome patients with and without hypertension.

Background : Stroke is a leading cause of disability and remains the second leading cause of death in the world. The proinflammatory cytokines interleukin-1β (Il-1β) and Tumour Necrosis Factor-alpha (TNF-alpha) play critical roles in the pathogenesis of ischemic stroke. Interleukin-1 (IL-1) is a prototype of inflammatory cytokines with a broad impact on nerve function. Inflammatory mediators of the IL-1 family show specific cell production, expression, and release patterns. Ligands are mainly produced by glia (and some neurons), while astrocytes and neurons express IL-1RI6 signal transduction receptors. Under normal conditions, the expression of IL-1 is deficient in the brain. The hyperthermia initiated within the first 24 hours from stroke onset was independently related to larger infarct volume and higher neurological deficit

Methods : The study subjects were recruited consecutively from this study population. We took blood samples to analyze IL-1β at three ± two days after the onset of stroke by medical laboratory officers. We separated plasma samples by centrifugation and stored them frozen at -70 ° C until analyzed. We measured IL-1β concentration from plasma EDTA samples with sandwich-type high-sensitivity ELISA. The test's sensitivity is 0.09 ng / L. Functional outcome of the patient assessed using the Barthel Index in a cross-sectional manner with laboratory analysis.

Results : The study results showed no significant difference in body temperature (p= 0.97) and the lesions' area (p= 0.61). Whereas we found that IL-1 beta levels (p= 0.02) and ischemic stroke outcomes (p=0.01) to have significant differences.

Conclusion : There is a correlation between plasma Interleukin -1β levels (Il-1β) and ischemic stroke outcomes with and without hypertension

Keywords: Interleukin -1β levels, body temperature, ischemic stroke outcome, hypertension

Background

Stroke is a leading cause of functional impairment. For patients who are >65 years of age, six months after stroke, 26% are dependent on their daily living activities, and 46% have cognitive deficits[1]. The stroke risk and severity have been associated with altered plasma concentrations of specific inflammatory mediators[2]. The

proinflammatory cytokines interleukin -1β (Il-1β) and Tumor Necrosis Factor-alpha (TNF-alpha) play critical roles in the pathogenesis of ischemic stroke. Interleukin 1 (IL-1) is a prototype of inflammatory cytokines with a broad impact on nerve function. The IL-1 cytokine family consists of six members, three receptor ligands [IL-1a, IL-1β, and IL-1 receptor antagonist (IL-1ra), two receptor subtypes (IL-1RI and IL-1RII), and protein accessory (IL-1AcP). Inflammatory mediators of the IL-1 family show specific cell production, expression, and release patterns[3]. The relative physiological outcome of increased IL-1β and TNF alpha signaling in ischemic stroke may depend on cytokines-producing cells' kinetics and location[3]. Increasing evidence implicates both cytokines in the early inflammatory response that precedes and accompanies ischemia-induced neuronal damage[3,4]. In this process. Interleukin- (IL-) 6 is one of the essential proinflammatory cytokines; it is expressed within a few hours after cerebral ischemia and is an acknowledged biomarker for long- and short-term neurological outcomes after ischemic stroke [3,4]. IL-18 is a proinflammatory cytokine that stimulates the production of a large number[5.6].

The enzymatic cleavage of inactive proIL-1β forms biologically active IL-1β by the protease, IL-1β was converting enzyme (ICE). ICE is a family of cysteine proteases, the caspases, several of which are associated with the apoptotic cell death pathway. This pathway has been implicated in ischemic brain damage. Thus, ICE inhibition could be a viable strategy for reducing brain damage after a stroke due to its role in IL-1β formation and neuroinflammation, or apoptosis, or both. Testing this hypothesis has been difficult because selective ICE inhibitors have been unavailable. Recently, mutant mice deficient in a functional gene for ICE have been produced. In the present study, we tested the hypothesis that these mutant mice, unable to make mature IL-1β, would have minor brain damage than their wild-type controls in response to a focal ischemic insult[7]. In humans with stroke, there is no data about IL-1 β. The hyperthermia initiated within the first 24 hours from stroke onset was independently related to larger infarct volume and higher neurological deficit[7,10].

Methods

The study subjects were recruited consecutively from this study population. We took blood samples to analyze IL-1β at three ± two days after the onset of stroke by medical laboratory officers. We separated plasma samples by centrifugation and stored them frozen at -70 ° C until analyzed. We measured IL-1β concentration from plasma EDTA samples with sandwich-type high-sensitivity ELISA. The test's sensitivity is 0.09 ng / L. Functional outcome of the patient assessed using Barthel Index in a cross-sectional manner with laboratory analysis. Ethical approval received from the Health Research Ethical Committee, Faculty of Medicine Universitas Sumatera Utara, Medan-Indonesia. The research was conducted from April 2019 to June 2019 at Adam Malik General Hospital, recruiting 45 consecutive samples of patients diagnosed with Acute Ischemic Stroke. We confirmed an ischemic stroke diagnosis by Head Computed Tomography Scan[7]. This study's exclusion includes sepsis, no confirmed Head CT Scan, prior fever, leucocytosis, and hyperglycemia [7,8]. Data were collected and calculated using SPSS Statistic for Windows.

Results

Table 1 and Table 2 provide information on the general characteristic and frequency distribution of ischemic stroke without or with hypertension. Table 1 shows the characteristics of age, gender, education, works, plasma Il-1 beta concentration, and body temperature. Only 25 (0.55%) subjects were female and age 29 (0.64%) were > 60 years old. At the educational level, there were 7 primary school (0.15%), 7 elementary school (0,15%), 17 high school (0.37%), 14 university (0.02). The lowest plasma IL-1 β concentration was at 26

(0,57%), and It found the highest body temperature as much 41 (0.91%). Only plasma IL 1 β concentration is significant (p = 0.05).

Table 2 shows that the lesion's extent didn't significantly differ between < 50 mm2 and > 50 mm2 based on hypertension status. There are significant differences between a good outcome and a lousy outcome according to hypertension status (p= 0.01).

Table 3 shows that IL-1 beta levels (p= 0.02) and ischemic stroke outcomes (p=0.01) were significantly different.

Discussion

In this study, the female was highest 25 (55%), and age 29 (64%) were > 60 years old. The lowest plasma IL-1β concentration was 26 (57%), and It found the highest body temperature as much 41 (91%). Only plasma IL 1β concentration is significant with and without hypertension (p = 0.05). There are significant differences between a good outcome and a lousy outcome according to hypertension status (p= 0.01)

In another study by Asare et al. (2010), the plasma IL-1β concentration about stroke in sickle cell disease, the male was 8 (61%) and in the mean age of 8,7 years old[2]. Hidayat et al. (2011) the plasma IL-1β concentration is associated with central obese men and show on 62 male subjects aged 30-60 years old with waist circumference > 90 cm[9].

Castillo et al (1998) show hyperthermia initiated within the first 24 hours from stroke onset, but not afterward, was independently related to larger infarct volume (odds ratio [OR]=3.23, 95% CI=1.63 to 6.43; p<0.001) and higher neurological deficit (OR=3.06, 95% CI=1.70 to 5.53; P<0.001) and dependency (OR=3.41, 95% CI=1.69 to 6.88; p=0.002) at 3 months. The infectious origin of hyperthermia was not associated with poorer outcomes or greater infarct volume[10]. In this study, hyperthermia was highest as much 41 (0.91%), and the body temperature was not significantly (p >0,05)

In this study, plasma IL-1β concentration levels (p=0.02) and ischemic stroke outcomes (p=0.01) were significant with and without hypertension differences. Protti et al. (2013) show patients with IL-10 <925.0 pg/mL presented with neurological deterioration within the first 72 hours[6]. Schielke et al. (1998) show IL-l β is a proinflammatory cytokine with numerous brain actions that could account for its influence on ischemic brain damage. For example, brain temperature is a critical variable in ischemia studies, and IL-113 is pyrogenic[8]. Another study by Pires et al. (2013) shows hypertension causes blood-brain barrier breakdown by mechanisms involving inflammation, oxidative stress, and circulating vasoactive molecules. It exposes neurons to cytotoxic molecules, leading to neuronal loss, cognitive decline, and impaired recovery from ischemic[11]. In conclusion, there is a correlation between plasma IL-1β concentration levels and ischemic stroke outcomes with and without hypertension

Conclusion

There is a correlation between plasma Interleukin -1β levels (Il-1β) and ischemic stroke outcomes with and without hypertension.

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Competing interests

No potential conflict of interest was reported by the authors

Tables and figures

Table 1. Frequency distribution of ischemic stroke with and without hypertension based on characteristics

Ischemic Stroke					
Variable	Categori	Hypertension	Non Hypertension	Total	P value
Age	< 60 years old	15	1	16	0.06
	≥60 years old	20	9	29	
Gender	Male	16	4	20	0.52
	Female	19	6	25	
Education	Primary school	7	0	7	0.06
	Elementary school	7	0	7	
	High School	11	6	17	
	University	10	4	14	
Work	work	18	3	21	0.202
	retired	17	7	24	
Plasma IL-1 Beta Concentration	Low	23	3	26	0.05
	High	12	7	19	
Body Temperature	Hyperthermi	31	10	41	0.53
	Normothermi	3	0	3	
	Hypothermi	1	0	1	

Table 2. Frequency distribution of ischemic stroke with and without hypertension based on the extent of the lesion and outcome

Ischemic Stroke					
Variable	Categori	Hypertension	Non Hypertension	Total	P value
Extent of the lesion	< 50 mm^2	17	6	22	0.61
	≥ 50 mm^2	18	5	23	
Outcome	good ≥60	13	10	23	0.01
	bad < 60	22	0	22	

Table 3. Correlation of plasma IL 1 beta levels, body temperature, ischemic stroke outcome with and without hypertension

Variable	B	OR	OR (95% CI)	p value
Plasma IL-1 Beta Concetration	0.006	0.002	0.001- 0.010	0.02
Body Temperature	0.005	0.143	-0.284 – 0.294	0.97
Outcome	-0.417	0.109	-0.636- -0.198	0.01
Constant	1.733	0.169	1.392 – 2.075	

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