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Role of Interleukin-10 in Hypertensive and Non-Hypertensive Stroke Patients

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ABSTRACT

Background: Stroke is a third leading cause of death and its impact is growing rapidly in developing countries despite significant improvements in the identification of its main contributing factors. Researchers are working to halt different steps and mediators of inflammation at different steps of stroke to reduce the size and volume of infarcted brain tissue. IL-10, an anti-inflammatory marker is thought to be neuroprotective. The objective is to determine the association of IL 10 in hypertensive and non-hypertensive stroke patients. **Methods:** Out of total 120 stroke patients, 60 patients each were categorized as hypertensive and non-hypertensive diagnosed based on history, physical examination and CT scan of brain. Patients recruited were from neurology and emergency wards of two public sector hospitals of Lahore. Blood samples were collected from these patients. **Results:** The average plasma IL-10 level was slight higher in normotensive stroke patients as compared to hypertensive subjects, recorded as 5.4±13.7 and 3.8±9.3 respectively. The medians were same with value 0.3 and the difference was insignificant with p-value 0.604. **Conclusion:** IL.10 is a potent anti-inflammatory mediator that perform protective role in stroke by inhibiting various proinflammatory mediators. Present study cannot reveal any association between IL.10 and hypertensive and non-hypertensive stroke patients.

Keywords: Ischemic Stroke, Haemorrhagic stroke, Hypertension, Interleukin 10.

INTRODUCTION

Stroke is a major cause of morbidity and mortality around the world. Other than proven risk factors, such as hypertension, hyperlipidaemia, and diabetes, there is increasing evidence showing that inflammation plays a key role for its progression, at least acutely. Hypoxic injury is the outcome of both types of stroke i.e ischemic as well as haemorrhagic stroke. Hypoxic injury to the brain tissue followed by reperfusion leads to a host of changes, collectively referred to as ischemic cascade. This cascade includes excitotoxicity, ionic imbalance around the affected area, oxidation stress, inflammation and eventually death.[1] The inflammatory response has cellular as well as molecular components. The cellular components include neutrophils, macrophages, lymphocytes as well as capillary endothelial cells.[2,3] As regard molecular components, these are up regulated during inflammatory process. These include adhesion molecules, chemokines and cytokines.

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Il-10 is also called human cytokine synthesis inhibiting factor (CSIF),[4] This protein is homodimer, with a molecular mass of 37KDa and each monomer consist of 160 amino acids with a mol. Mass of 18.5KDa and located on the chromosome (1). It is classified as class (2) cytokines (this class consist of IL-10, IL-19, IL-20, IL-22, IL24 and interferon like molecules). but IL-10 has the most potent anti-inflammatory and anti-immune activity).[5,6]

IL.10 has been shown to improve the neurological out come after CNS injury. It provides the antiappoptotic and proliferative property to the non-activated cells. It also directly increases the survival of both cortical and cerebellar neurons as well as astrocytes, glial cells and oligodendrocytes from apoptosis by inhibiting the mitochondrial initiated apoptotic death. Higher IL.10 concentration were associated with lower degree of patient disability and better outcome in stroke patients. The aim of this study was to determine the levels of IL-10 in stroke patients.

Hypertension is one of the major players that predispose the cause of haemorrhagic as well as ischemic stroke and other cerebrovascular complications. It causes numerous progressive alterations in cerebral blood flow and brain vessels that brings complex and dynamic relationship between B.P and cerebral function, by several mechanism. Components of the inflammatory response are activated within the vessel walls in many

cerebro vascular diseases with hypertension. Didion. S.P et al (2009) have studied that Angiotensin11 (that has very critical role in some forms of hypertension) activates multiple inflammatory mechanisms within the vascular cells. The IL.10 as an anti-inflammatory cytokine plays a major role in preventing deleterious effects of Angiotensin 11 hormone, thus IL.10 may be a key mediator of vascular protection during hypertension and during other forms of vascular diseases.[7,8]

MATERIALS AND METHODS

A written consent was taken from the conscious patients or their near relatives in case if patients were unconscious. The study was approved by the Institution Review Board (IRB), Sheikh Zayed Medical Complex.

This cross sectional, analytical study was carried out on 120 stroke patients that were diagnosed as having stroke based on clinical history, physical examination and computed tomography brain scan by neurologist within 12 hours of stroke onset. Subjects suffering from any condition that alter the levels of IL.10 e.g bacterial infections, viral infections, Diabetes mellitus, and any inflammatory condition except stroke were excluded. Three-(03) cc blood was drawn from antecubital vein from each stroke patient under aseptic techniques. The blood was transferred in a vacutainer containing anticoagulant, centrifuged and plasma was separated labelled and stored in eppendorfs at -20 degree centigrade till further analysis for IL.10 levels. The plasma IL.10 levels were measured by using standard ELISA method at NHRC, FPGMI, Sheikh Zayed Medical complex Lahore. All data was arranged and analysed by using SPSS version 17.0. Gender and stroke (ischemic as well as haemorrhagic stroke) were expressed as frequencies and percentages. Whereas plasma IL.10 and age were described by using Mean+-SD. All data was arranged and analysed by using SPSS (statistical package for social sciences) version 17.0.

All quantitative variables were expressed as Mean+-SD. All qualitative variables were described by using frequencies and percentages.

Analysis of IL.10 in hypertensive and non-Hypertensive patients was done by using Mann-Witney–U test. Association of IL.10 with hypertension was done by using Chi square test. P value ≤ 0 .05 was considered significant.

RESULTS

In this study 120 stroke patients were enrolled with 60 hypertensive cases and 60 normotensive. There were 29 males and 31 females in hypertensive group with average age 61.3±9.9 and 60.9±15.1 years respectively. Among normotensive there were 39 males and 21 females with average ages 56.8±16.5 and 60.8±12.3 years respectively [Table 1] the average plasma IL-10 level was little higher in normotensive stroke patients as compare to hypertensive which were recorded 5.4±13.7 and 3.8±9.3 respectively. The medians were same with value 0.3 and the difference was insignificant with p-value 0.604. [Table 2] The cases were categorized on the basis of IL-10 level raised and not raised and its relation was explored with presence of hypertension and it was revealed that there was no difference for the percentage of cases with hypertension in cases with raised and not raised IL-10 level with p-value 0.666. [Table 3] Where as the standard value of IL.10 was taken as3pgm/ml which are minimum detectable level of IL.10, and the normal level of plasma IL.10 is 4.8-9.8pgm/ml with the mean of 7.1pgm/ml.35

Table 1: Age and gender distribution of hypertensive and normotensive stroke patients

Age	Hypertensive				Normotensive			
	Male		Female		Male		Female	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent
< 40	0	.0	1	3.2	6	15.4	1	4.8
40 - 49	0	.0	5	16.1	1	2.6	1	4.8
50 - 59	12	41.4	8	25.8	14	35.9	6	28.6
60 - 69	11	37.9	5	16.1	6	15.4	6	28.6
70 - 79	4	13.8	8	25.8	9	23.1	5	23.8
80 +	2	6.9	4	12.9	3	7.7	2	9.5
Total	29	100.0	31	100.0	39	100.0	21	100.0
Mean ± SD	61.3 ± 9.9		60.9 ± 15.1		56.8 ± 16.5		60.8 ± 12.3	
			Normotensive		**0.674**		**59**	**< 0.001**
Plasma IL-10 at admission			Hypertensive		0.467		59	< 0.001
			Normotensive		0.433		59	< 0.001

Table 2: Comparison of Plasma IL-10 level between hypertensive and normotensive stroke patients

	Plasma IL-10 at admission						
	Mean	SD	Min	Max	Q1	Median	Q3
Hypertensive	3.8	9.3	0.0	50.0	0.0	0.3	2.0
Normotensive	5.4	13.7	0.0	50.0	0.0	0.3	2.7
Total	4.6	11.7	0.0	50.0	0.0	0.3	2.1
	Mann Whitney U =1702.5			Z-Approximation = -0.518		P-value 0.604	

Table 3: Distribution of cases by IL-10 level raised or not raised between hypertensive and normotensive stroke patients

Status	IL10				Total	
	Raised		Not Raised			
	Number	Percent	Number	Percent	Number	Percent
Hypertensive	13	46.4	47	51.1	60	50.0
Normotensive	15	53.6	45	48.9	60	50.0
Total	28	100.0	92	100.0	120	100.0

Chi-square likelihood ratio = 0.19. P-value = 0.666. Odd ratio = 0.83 (0.36 - 1.94)

DISCUSSION

In this study, interestingly no significant association of IL.10 in hypertensive and non-hypertensive stroke patients was found.

IL.10 is a potent anti-inflammatory cytokine that has multiple actions. Endogenously produced IL.10 is a potent immunosuppressant and important modulator of acute and chronic inflammation. Munshi. A et al (2010) have shown in their genetic study that there is significant association of the polymorphism of IL.10 gene (IL.10-1082 promoter polymorphism) with the stroke of undetermined aetiology. Moreover hypertensive and diabetic individual bearing A. allele of IL.10 gene in high frequency were found to be more predisposed to stoke.[9] This study determined the association of plasma IL.10 in hypertensive and non-hypertensive stroke patients

Vanja et al have studied that reduced IL.10 levels are present in early stroke period and are significantly associated with a degree of neurological deficient or stroke outcome.[10] They showed that higher IL.10 concentration were associated with lower degree of patient disability, thus indicating the patients who require certain therapeutic interventions. Evan. Exel et al (2002) have shown that low IL.10 production levels have an increased risk of stroke.[11] IL.10 production level 558pgm/ml in stroke versus 764pgm/ml with a p-value of .047. Similarly Vila. N et al (2003) have shown in their study that early worsening was independently associated with lower IL.10 (p-.05) in pts with sub cortical infarcts or lacunar stroke.[12]

In the same line Dirnagl.U et al,[13] (2004) have studied that significantly lower concentration of IL.10 were found in pts with neurological worsening(p-.05). Similarly Park et al (2013) conducted a study in a Korean population, and they found that IL-10 gene polymorphism would contribute to the development of ischemic stroke with hypertension Lieu.X et al (2017) suggests that IL-10 gene polymorphism contribute to the development of ischemic stroke.[14,15] In contrary to these studies Chang. L. T et al (2010) has studied that IL.10 levels were significantly higher in pts with severe neurological impairments (p-.0001). Further higher Sr.IL.10 was strongly and independently correlated with severe neurological impairment.[15]

CONCLUSION

In conclusion among various inflammatory mediators IL.10 is a potent anti-inflammatory mediator that performs protective role in stroke by inhibiting various pro inflammatory mediators.. Though the present study cannot revealed any significant association between IL.10 and hypertensive and non-hypertensive stroke patients, further studies should be done for evaluating the long term effects of neuroprotection from inflammation by IL.10

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