Correlation of Interleukin-10 with Glasgow Coma Scale in Patients of Stroke

SANA SABIR1, NAIMA UMER2, MOHAMMAD SHOAIB3, SIBGHA ZULFIQAR4

ABSTRACT

Background: Interleukin-10 is an anti-inflammatory cytokine that has multiple functions. Its anti-inflammatory properties suggest its neuro-protective role in stroke patients. Glasgow Coma Scale (GCS) is a clinical scoring system to evaluate the severity of brain damage in stroke. In the present study, we tried to find out any correlation between a clinical assessment tool and a related biochemical parameter in patients of stroke.

Methods: A total number of 120 consecutive patients of stroke were included in this study. They were subdivided on the basis of their blood pressure at admission into hypertensive (n=60) and non-hypertensive (n=60) groups. Clinical assessment of severity of brain damage due to stroke was evaluated by using GCS on admission. At the same time, a blood sample was taken to estimate plasma level of IL-10. Correlation coefficient was calculated between GCS and IL-10 levels to find out any relationship between the two.

Results: In the hypertensive group, mean±SD of IL-10 was 3.8±9.3 pg/ml and of GCS was 10.98±3.55. In the non-hypertensive group, mean±SD of IL-10 was 5.4±13.7 pg/ml and of GCS was 10.45±4.01. Correlation coefficient between IL-10 & GCS of all stroke pts was -0.305 with p-value<0.001.

Conclusion: It is concluded that IL-10 plays a protective role in patients of stroke.

Key words: Interleukin-10, Glasgow Coma Scale, Stroke

INTRODUCTION

Stroke a growing epidemic, is a significant cause of morbidity and mortality. It is the third leading cause of death, and long term disability. Besides the physical and emotional burden on patients and their families, this represents an enormous economic burden as well. The impact of stroke is growing rapidly in developing countries despite significant improvements in the identification of its main contributing factors. Pakistan is the sixth most populous country in the world, with an estimated population of 165 million. Out of total disease burden in Pakistan, stroke including non-communicable diseases accounts for 41%. According to a survey, 4.8% may be suffering from stroke1-3.

Stroke can be subdivided into two categories; Ischemic stroke and Hemorrhagic stroke. In addition to these two main categories, stroke may manifest as silent stroke, transient ischemic stroke and lacunar stroke. Neurobiology of the stroke is one of the most challenging field in the neurology and neuroscience research. Irrespective of the type of the stroke, compromised vascular supply to the tissues is the primary event.

Hypoxic injury is the outcome of both types of stroke i.e., ischemic as well as hemorrhagic 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 death4.

The balance between the pro and anti-inflammatory cytokines determines the severity of inflammation. Examples of pro inflammatory cytokines are the IL-1, and tumor necrotizing factor alpha (TNF alpha), these appear to exacerbate the injury. While anti-inflammatory cytokines like IL-6, IL-10 and transforming growth factor beta (TGF beta) may be neuroprotective5,7.

There is strong evidence from an experimental model study that co-administration of anti-inflammatory agents with tissue plasminogen activator (rtPA) increases its efficacy and effective therapeutic time window.

IL-10 is also called human cytokine synthesis inhibiting factors (CSIF), and has been first discovered by Mosman and co-workers in 1989. This protein is homodimer, with a molecular mass of 37Kda8 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 2 alpha helical cytokines consist of IL-10, IL-19, IL-20, IL-22, IL-24 and interferon like molecules These

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members have similar genomic organization and all these activate JAK/STAT signaling pathway but IL-10 has the most potent anti-inflammatory and anti-immune activity. IL-10 is mainly produced by the macrophages but other cells like keratinocytes, monocytes, mast cells, CD4 and CD8 T cells. Eosinophils and epithelial cells are also involved in its secretion. This cytokine has pleotropic effect in the immune regulation and inflammation. It down regulates the TH1 cytokines, MHC class11 antigen and co stimulatory effect on macrophages. It also increases the B cell survival, proliferation and antibody production. It can block natural factor K beta(NFKB) and synthesis of proinflammatory cytokines like interferon gamma (IFN-gamma), IL-2, IL3, TNF alpha and granulocyte monocyte colony stimulating factor(GM-CSF) by macrophages and regulatory T-cells. IL-10 also has the ability to suppress the antigen-presentation capacity of antigen presenting cells. As regard the regulation of its secretion, the IL-10 promoter contain various transcription factor responsive elements, so the macrophages the major source of IL-10 are stimulated to produce IL-10 by several exogenous as well as endogenous factors such as endotoxins (via toll like receptors, NFKB beta dependent), TNF alpha, CAMP elevating drugs (via protein kinase A).

The data from lot of investigation on IL-10 suggest that major physiological importance of IL-10 seems to be the limitation of inflammation, support of humoral responses and prevention of uncontrolled non adequate immunologic reactions. Wang, et al(1995) have studied that IL-10 inhibits cytokine synthesis by acting mainly at the level of cytokine gene transcription, they observed in their study that IL-10 inhibited transcription of IL1beta, IL6 and TNFalpha genes in LPS stimulated peripheral blood mononuclear cells. IL-10 has been shown to improve the neurological out come after central nervous system(CNS) injury.

IL-10 provides the antiapoptotic 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. Assessment of conscious level is an essential component of neurological examination. Systemic assessment of the unconscious patient by the application of the GCS provides a grading of coma by using a numerical scale that allows serial comparison and may provide prognostic information. The objective of the study was to find correlation between IL-10 and Glasgow Coma Scale in stroke patients.

**METHODOLOGY**

Approval of this study was obtained from the research ethic committee, Institution Review Board (IRB), Sheikh Zayed Medical and Dental Complex Lahore. This study was carried out in the department of physiology, Federal Post graduate Medical institute, Sheikh Zayed Medical complex, Lahore in collaboration with medical and neurological wards of Jinnah hospital. This cross sectional, analytical study was carried out on 120 stroke patients 60 hypertensive cases and 60 normotensive. There were 29 males and 31 females in hypertensive group with mean age 61.3±9.9 and 60.9±15.1 years respectively. Among normotensives there were 39 males and 21 females with mean ages 56.8±16.5 and 60.8±12.3 years respectively. Demographic data was collected on a proforma along with history of patients. They were diagnosed on the basis of history, physical examination and CT scan of brain. Any condition that alters the levels of IL-10 e.g., bacterial infection, viral infection, diabetes mellitus and any inflammatory condition other than stroke was excluded. The Glasgow coma scale was employed to assess the conscious state of the stroke patient at the time of admission and subsequently at the time of discharge from the hospital Lahore. Blood samples were also collected from these stroke patients; and these samples were then centrifuged, plasma was separated and aliquots of plasma were kept frozen at -80°C. The IL-10 levels were, later, estimated in plasma using commercially available ELISA kit.

**RESULT**

All data was arranged and analysed by using SPSS (statistical package for social sciences) version 17.0. In the hypertensive group, mean ± SD of IL-10 was 3.8±9.3pg/ml and of GCS was 10.98±3.55. In the non-hypertensive group, mean ± SD of IL-10 was 5.4±13.7pg/ml and of GCS was 10.45±4.01. Correlation coefficient between IL-10 and GCS of all stroke patients was -0.305 with p-value<0.001.

Table 1: The correlation of plasma IL-10 level with age, Glasgow coma score and body mass index

<table>
<thead>
<tr>
<th>Spearman’s rho</th>
<th>Correlation Coefficient</th>
<th>Sig. (2-tailed)</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.055</td>
<td>0.554</td>
<td>120</td>
</tr>
<tr>
<td>GCS Score at admission</td>
<td>-0.305</td>
<td>0.001*</td>
<td>120</td>
</tr>
<tr>
<td>BMI</td>
<td>-0.185</td>
<td>0.044</td>
<td>120</td>
</tr>
</tbody>
</table>

*Correlation is significant at the 0.01 level (2-tailed). Correlation is significant at the 0.05 level (2-tailed).
DISCUSSION

For the best of my knowledge this is the first study conducted in Pakistan with the aim to investigate the correlation of IL.10 with the Glasgow coma scale in hypertensive and non-hypertensive stroke patients. In our study, we observed the correlation of increasing levels of IL.10 with the increase score of GCS. This is consistent with the studies showing the protective role of IL.10 in stroke. Previous studies show the significant association of IL.10 and stroke by proving the protective role of IL.10. Evan.Exel et al (2002) have shown that low IL.10 production levels have an increased risk of stroke\(^1\). IL.10 production level 558pgm/ml in stroke versus 764pgm/ml with a p-value of .047.

Similarly Vila. et al (2003) have shown in their study that early worsening was independently associated with lower IL.10 (p-.05) in patients with subcortical infarcts or lacunar stroke\(^2\).

In the same line Dirnagl. et al (2004)\(^3\) have studied significantly lower concentration of IL.10 were found in patients with neurological worsening.

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\(^4\). They showed that higher IL.10 concentration were associated with lower degree of patient disability, thus indicating the patients who require certain therapeutic interventions.

Limitations of the study: This study was conducted on a relatively small size. Samples should be taken in serial wise i.e., two consecutive samples should be taken for comparison. IL.10 should have been measured by HPLC instead of Elisa.

CONCLUSION

In conclusion, signs of inflammation are present throughout the different stages of stroke. IL.10 is a potent anti-inflammatory mediator that possesses a protective role in stroke by inhibiting various pro-inflammatory mediators.

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Conflict of interests: The authors have no conflict of interest to report.

REFERENCES