Contents lists available at www.innovativejournal.in

INNOVATIVE JOURNAL OF MEDICAL AND HEALTH SCIENCE

Journal homepage: http://www.innovativejournal.in/index.php/ijmhs

ISSN No. 2277-4939

S-100β PROTEIN AS A BIOMARKER IN ACUTE ISCHEMIC STROKE-A REVIEW ARTICLE

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ARTICLE INFO

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Key words: S-100β, acute ischemic stroke, CT scan

ABSTRACT

Acute ischemic stroke, a major subtype of acute stroke is one of the leading cause of death and disability throughout the world. At present, the diagnosis of acute ischemic stroke is mainly based on Computer Tomography or Magnetic Resonance Imaging. This article is a critical and descriptive review on S100β protein as a biomarker in acute ischemic stroke. We searched Pubmed database with key words or terms such as "S100β protein", 'Acute ischemic stroke' and the articles were analyzed for the results. S-100β level in plasma increase in response to the acute ischemic stroke. The plasma S-100β level increases significantly in acute ischemic stroke patients when compared to the normal subjects. Beside, the plasma S-100β can be significantly correlated to the volume of infarction in brain measured by plane CT scan. Plasma S-100β is an useful biomarker in acute ischemic stroke. It can be used for estimation of volume of infarction in brain in acute ischemic stroke patients. Thus, S-100β can be used as an alternative to CT scan/ MRI in diagnosis and in taking therapeutic decision in acute ischemic stroke management.

INTRODUCTION

Acute ischemic stroke, a major subtype of acute stroke is one of the leading causes of death and diability throughout the world. Ischemic stroke occurs due to loss of blood supply to part of brain initiating ischemic cascade [1].

S-100β is a member of S-100 super family of proteins which are called so because they are 100% soluble in ammonium sulfate. S-100 is an acidic protein and has a molecular weight of 21 kilodalton .It consists of two subunit α chain and β chain. It is known that combination of these subunits is different from the location in human body. S-100β is located in glial cell and schwann cell, S-100αβ in glial cell, and S-100αα in striated muscle, heart and kidney.S-100β is a Ca^{2+} binding protein with four calcium binding sites [2]. S-100 superfamily of proteins is located mostly in the cytoplasm and nucleus of wide ranges of cells. S-100 protein is normally present in the cells derived from neural crests, like schwann cells, melanocytes, glial cells, chondrocytes, adipocytes, myoepithelial cells, langerhans cells, dendritic cells etc. There are at least 21 different types of S-100 proteins of which S-100β is glial specific and thus can be a brain specific protein marker. It is expressed primarily by astrocytes. Unfortunately, not all the astrocytes express S-100β .It was shown that S-100β is only expressed by a subtype of mature astrocytes that unsheathe blood vessels and by NG-2 expressing cells. Physiologically S-100β protein functions in neurite extension, melanoma cell proliferations, stimulation of calcium influxes, inhibition of PK-C mediated phosphorylation, astrocytosis and axonal proliferation, inhibition of microtubule assembly etc. In developing CNS, it is a neurotropic factor and neuronal survival protein. In adult human, it is usually elevated due to nervous system damage which makes it potential clinical marker [3]. S-100β concentrations is correlated well with the extent of brain damage occurring in acute ischemic stroke, traumatic brain injuries, focal vascular insults, strokes and cerebral ischemia following cardiac surgeries [6]. Brain trauma and ischemia is associated with increased S-100β concentrations probably due to destruction of astrocytes. The protein may be elevated in focal vascular insult, neuronal ischemia, or brain ischemia due to S-100β secreted or released from damaged astrocytes. Because of its predominant location in astroglial cells, any CNS(central nervous system) insults as in traumatic injuries of head, cerebral ischemia, hemorrhagic stroke etc, which can damage astroglial cellular structure causes leakage of S-100β into extracellular matrix and into CSF and finally further into blood stream. Thus measurement of S-100β protein can be used for monitoring traumatic brain injury, cerebral ischemia, stroke etc. and in giving diagnosis and prognosis

of the clinical outcome[2]. S-100β protein can be detected in very low amount in blood in normal healthy individuals. Studies have also shown that S-100β in CSF can be useful marker for the diagnosis of the degree of brain damage after head injury, cerebral hemorrhage and ischemic stroke. Another recent study also shown that increasing S-100β in blood can be well correlated to the degree of brain damage after cerebral ischemia, infarction, hemorrhage and severe head injury[5].

MATERIALS AND METHODS

This article is a critical and descriptive review on S100β protein as biomarker in acute ischemic stroke. The articles so collected from pubmed database had been reviewed and analysed extensively.

RESULTS AND DISCUSSION

Stroke is defined by the abrupt onset of a neurological deficit that is attributable to a focal vascular cause. Ischemic stroke occurs due to loss of blood supply to part of brain initiating ischemic cascade resulting in loss of structural integrity of brain tissue and blood vessels releasing matrix-metalloproteinase which are calcium and zinc dependent enzymes that break down brain tissues[1].

Plasma S-100β level in healthy individuals ranges from 0.02 to 0.15 µg/l (i.e. 20-150 pg/ml) as determined by immunoluminometric analytic method and the reference value for S-100β protein depend on the race of the individuals [6]. In a study, Buttner Th and his company [7] showed that serum concentration of S-100β were significantly higher in patients with middle cerebral artery(MCA) infarction when compared to the normal healthy control($p<0.001$). Similarly, results of various studies also shows the elevated level of plasma and cerebrospinal fluid (CSF) S-100β level in acute ischemic stroke patients when compared to the normal subjects [8,9,10].

A group of researcher observed in their study that peak plasma levels of S-100 protein are well correlated with infarct volume($r=0.75$, $P<0.001$) in acute stroke patients[11]. From their study Fessbander et al [8] reported that patients with volumes of brain lesion>5 cubic centimeter(cc) exhibited significant increased serum levels of S-100 compared to those with lesion volumes of< 5 cubic cm. Michael T Wunderlich and his team[12] in their study on 58 acute stroke patients reported that S-100β protein concentrations were significantly correlated with both volume of infarction in brain($p< 0.001$). Manfred Hermann and his company[13] investigated 32 acute ischemic stroke patients and reported that plasma level of biochemical markers like S-100β is highly correlated with the volume of brain lesions as estimated by CT scan brain ($r=0.957$,$P<0.0001$). Another group of researcher also reported the well significant correlation between the S-100β level and infarct size in brain[14]. Beside, several studies also confirmed the positive correlation between the plasma S-100β level and volume of infarction in brain in acute ischemic stroke patients [15, 16, 10, 17].

CONCLUSIONS

Plasma S-100β rises in blood and CSF in respose to the acute neuronal injury and acute ischemic stroke [4]. From the results of the present study it can be concluded that plasma S-100β level increases significantly in acute ischemic stroke when compared to the normal healthy controls. Beside, the plasma S-100β level correlates to the volume of infarction in brain in acute stroke patients. However, the role of S-100β in differentiating acute ischemic and hemorrhagic stroke is not clear. So, we need further research on this area and also to confirm the sensitivity and specificity of S-100β in diagnosing acute stroke. But, till now costly imaging techniques like CT or MRI are used as gold standards in diagnosis and monitoring the acute stroke patients [1]. S-100β estimation which is much cheaper when compared to imaging technology, can be used in diagnosis, monitoring and rough estimation of volume of infarction in acute ischemic stroke patients, as an alternative to CT scan or MRI in a setup where costly imaging technologies are lacking.

REFERENCES

[1] Smith WS, English JD, Johnson SC. Cerebrovascular Diseases. In: Favei AS, Bravnald E, Kasper DL, Hsusor SL, Longo DL, Joneson J, et al, editors. Harrison's principles of internal medicine.17th ed.USA: McGraw Hills;2008.p.2513-35.

[2] Rothermundt M, Peters M, Prehn HMJ, Arott V. S-100β in brain damage and neurodegeneration. *Micros Res Tech* 12 Mar 2003; 60(6):614-32.

[3] J Sen, A Belli.S-100β in neuropathologic states: the CRP of the brain? *J Neurosci Res* 2007 May 15;85(7):1373-80.

[4] Heizmann WC. S-100β protein in clinical diagnostic assay specificity. *Clin chem* 2004;50:249-51.

[5] Nygaard O, Langbakk B, Rommer B. Age and sex related changes of S-100 protein concentrations in cerebrospinal fluid and serum in patients with no previous history of neurological disorder. *Clin chem*. 1997;43:541-3.

[6] Abdesselam OB, Vally J, Adem C, Foglietti MJ, Beaudeux JL. Reference values for serum S-100β protein depend on the race of individual. *Clin Chem* 2003;49:836-7.

[7] Buttner Th, Weyers S, Postert Th, Sprengelmeyer R, Kuhn W. S-100 protein; Serum marker of focal brain damage after ischemic territorial MCA infarction. *Stroke* 1997;28:1961-5.

[8] Fassbender K, Schmidt R, Scheriner A, Fatar M, Miihihanser F, Daffertshofer M. Leakage of brain-originated proteins in peripheral blood temporal profile and diagnostic value in early ischemic stroke. *J Neurol Sci* 1997 May 1;148(1):101-5.

[9] Danuta K , Piotr W, Robert P, Jerzy J, Przemyslaw J, Jerzy S. The diagnostic utility of S-100β protein and TPA in patients with ischemic stroke. *Neuro Endo Lett* 2007;28(5):693-8.

[10] Petzold A, Michel P, Stock M, Schluep M. Glial and axonal body fluid biomarkers are related to infarct volume severity and outcome. *J Stroke Cerebrovasc Dis* 2008 Jul-Aug;17(4):196-203.

[11] Missler U, Wiesman M, Friedrich Ch, Kaps M. S-100 protein and neuron specific enolase concentrations in blood as indicators of infarction volume and prognosis in acute ischemic stroke. *Stroke* 1997; 28:1956-60.

[12] Wunderlich MT, Ehert AD,Kraz T, Goertler M, Jost S, Hermann M. Early neurobehavioural outcome after stroke is related to release of neurobiochemical markers of brain damage. *Stroke* 1999; 30:1190-5.

[13] Hermann M, Vos P, Wunderlich MT, Bruijn CHMM, Laners KJB. Release of glial tissue specific protein after stroke. *Stroke* 2000;3: 2670-7.

[14] Kenangil G, Yalcin AD ,Haklar G, Cacina H, Forta H. Relation of serum S-100 protein to infarct size and clinical prognosis. *Marmara Med J* 2004;17(3):105-8.

[15] Foerch C, Singer OC, Neumann HT , Rochemont RDM, Steinmetz H, Siber M. Evaluation of serum S-100β as a surrogate marker for long term outcome and infarct volume in acute middle cerebral infarction. *Arch Neurol* 2005 July; 62:1130-4.

[16] Weglewski A, Ryglewicz D, Mular A ,Jurynczyk J. Changes of protein S-100β serum concentration during ischemic and hemorrhagic stroke in relation to the volume of stroke lesion. *Neurol neurochir* p 2005;39(4):310-7.

[17] Xiulong J, Xiaolin J, Xu Z. Changes and clinical significance of serum IL-6, TNF-α, and S-100β in patients with acute cerebral infarction. *JNeurolNeurorehab*. 2008;4:40-4.