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ORIGINAL ARTICLE

Serum albumin at admission for prediction of functional outcome in ischaemic stroke patients

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Abstract This study aimed to investigate the effect of serum albumin at admission, measured within 24 h after stroke onset, on the functional outcome in ischaemic stroke patients. The medical records of 76 first-ever hemiplegic ischaemic stroke patients were reviewed. Collected data included age, sex, initial stroke severity, cerebrovascular risk factors, lesion-related variables, aetiologic subtype of stroke and serum albumin at admission. The functional outcome was measured by functional independence measure (FIM) and modified Barthel index (MBI). Serum albumin at admission and initial National Institutes of Health Stroke Scale (NIHSS) score were correlated with the functional outcome, respectively. Serum albumin at admission was an independent predictor of MBI gain on multiple regression analysis. Serum albumin at admission would be a useful predictor of the functional outcome and trials for the correction of hypoalbuminaemia from the acute stage would be helpful to decrease the risk of poor outcome in ischaemic stroke patients.

Keywords Stroke · Albumin · Outcome · Assessment

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Introduction

Serum albumin level is one of the biochemical markers of nutritional status [1]. It is well known that protein-energy malnutrition after acute stroke is a risk factor for poor outcome and can worsen prognosis by decreasing cellular immunity [2, 3].

Recent experimental studies revealed a beneficial effect of albumin infusion in animal models of cerebral ischaemia and it was suggested that this neuroprotective effect was mediated by multiple specific actions of albumin including antioxidative properties and influence on endothelial functions and venular perfusion [4, 5].

Hypoalbuminaemia at admission may be associated with premorbid nutritional status of the patients because of long half-life of albumin [6]. We performed this study to investigate the effect of serum albumin at admission, measured within 24 h after stroke onset, on the functional outcome in ischaemic stroke patients.

Patients and methods

We reviewed the medical records of 76 first-ever hemiplegic patients, all of whom had been diagnosed with a cerebral infarction by brain magnetic resonance imaging (MRI). All patients visited the emergency room (ER) of our hospital within 24 h after the onset of the stroke. Patients with recurred stroke, serious medical illness leading to prolonged immobilisation, severe gastrointestinal diseases and liver disease were excluded from this study. This study was approved by the Institutional Review Boards of Chonnam National University Hospital.

Data collected for all patients included age, sex, initial stroke severity according to the National Institutes of Health Stroke Scale (NIHSS), cerebrovascular risk fac-

tors, lesion-related variables, aetiologic subtype of stroke according to the Trial Org 10172 in Acute Stroke Treatment (TOAST) classification and serum albumin at admission.

The NIHSS was used to assess the severity of neurological impairment. Mild, moderate and severe impairment were defined as: mild 1–6 points; moderate 7–12 points; severe 13–42 points. Cerebrovascular risk factors included hypertension, diabetes mellitus, hyperlipidaemia, smoking and heart disease. Lesion-related variables were the side, locations and volume of the brain lesion. Brain MRIs were performed with a 1.5-T whole-body superconducting imager (Signa Horizon®, GE Medical Systems) within 3 days after the onset of the stroke. Diffusion-weighted imaging was used for lateralisation, localisation and volumetric analysis of the brain lesion. Hemispheric involvement was checked and the lesions were categorised into middle cerebral arterial territory, brainstem, cerebellum and others. The volume of the lesion was calculated by summing up the area of the lesion on each slice of sectional images and multiplying it by the value of the slice thickness plus the interslice gap. The level of serum albumin at admission was measured at ER within 24 h after the onset of the stroke.

The functional outcome was measured by functional independence measure (FIM) and modified Barthel index (MBI) at 3 days and 3 months after the onset of the stroke. FIM gain is the difference between the follow-up FIM score and initial FIM score. MBI gain is the difference between the follow-up MBI score and initial MBI score. FIM gain and MBI gain indicate the functional improvement.

All statistical analyses were carried out with the Statistical Package for the Social Sciences (SPSS version 14.0) for Windows. Descriptive statistics were used to investigate general characteristics of the patients. The correlation between the variables with continuous data and the functional outcome was ascertained by Pearson's correlation. Student's *t*-test and one-way analysis of variance (ANOVA) were performed to assess the relationship between the variables and the functional outcome. All the predictive variables were first examined by simple regression analysis to assess the importance of each of them on the functional outcome. Multiple linear regression analysis was performed to identify independent influence on the functional outcome. The analysis was performed by "enter method" among selection methods of variables. A *p*-value of less than 0.05 was considered statistically significant.

Results

We included 76 ischaemic stroke patients, 49 men and 27 women, in this study. Patients were aged between 22 and 83 years, with a mean of 62.5 years (standard deviation 13.0 years). The prevalence of cerebrovascular risk factors was: hypertension (55.3%), diabetes mellitus (35.5%), hyperlipidaemia (59.2%), smoking (38.2%) and heart disease (43.4%).

The stroke lesions were on the right side in 44.7% of the patients. The locations of the lesions were middle cerebral arterial territory in 55.3%, brainstem in 23.7%, cerebellum in 5.2% and others in 15.8%. The most common aetiologic subtype of stroke was large artery atherosclerosis (65.8%), followed by small vessel occlusion (26.5%) and cardioembolism (7.7%).

Initial stroke severity was assessed as mild impairment in 16 patients, moderate impairment in 23 patients and severe impairment in 37 patients. The mean serum albumin level was 3.7 g/dl. The scores of FIM gain and MBI gain were 14.0±10.7 and 14.0±10.6 points, respectively (Table 1).

FIM gain was significantly correlated with serum albumin at admission (r=0.236, p=0.040) and initial NIHSS (r=–0.268, p=0.019), respectively. MBI gain was significantly correlated with serum albumin at admission (r=0.404,

Table 1 General characteristics of the patients

Variables	All patients (n=76)
Age (years)	62.5±13.0
Sex (n)	
Male	49
Female	27
Risk factors (n)	
Hypertension	42
Diabetes mellitus	27
Hyperlipidaemia	45
Smoking	29
Heart disease	33
Lesion side (n)	
Right	34
Left	42
Lesion volume (cm^3)	109.8±188.8
Lesion locations (n)	
MCA territory	42
Brainstem	18
Cerebellum	4
Others	12
TOAST classification (n)	
Large artery atherosclerosis	50
Cardioembolism	6
Small vessel occlusion	20
Stroke of other determined aetiology	0
Stroke of undetermined aetiology	0
Albumin (g/dl)	3.7±0.6
Initial NIHSS	13.9±7.5
Initial FIM	54.2±26.3
Follow-up FIM	68.1±28.0
FIM gain	14.0±10.7
Initial MBI	37.1±26.6
Follow-up MBI	51.1±28.7
MBI gain	14.0±10.6

Values are mean±standard deviation
FIM gain=follow-up FIM – initial FIM; MBI gain=follow-up MBI – initial MBI
MCA, middle cerebral artery

p=0.000) and initial NIHSS (r=–0.317, p=0.005), respectively (Table 2). Demographic variables including age and sex, cerebrovascular risk factors, lesion-related variables and aetiologic subtype of stroke were not related to the functional outcome, respectively (Tables 2 and 3).

On simple regression analysis, the significant variables associated with the functional outcome were serum albumin at admission and initial NIHSS score (Table 4). Using multiple regression analysis, the significant independent factor associated with the functional outcome was serum albumin at admission (Table 5). In the model of MBI gain, 16.2% of the variance (adjusted R^2=0.162) was explained by the model, which was statistically significant (F=8.250, p=0.001).

Table 2 Correlation between variables and functional outcome

	FIM gain		MBI gain	
	r	*p*	*r*	*p*
Serum albumin	0.236	0.040*	0.404	0.000*
Age	–0.142	0.223	–0.114	0.328
Lesion volume	–0.053	0.651	–0.004	0.975
Initial NIHSS	–0.268	0.019*	–0.317	0.005*

FIM gain=follow-up FIM – initial FIM; MBI gain=follow-up MBI – initial MBI
*p<0.05

Table 3 Relations between variables and functional outcome

	FIM gain (p value)	MBI gain (p value)
Sex	0.917	0.615
Hypertension	0.122	0.872
Diabetes mellitus	0.138	0.388
Hyperlipidaemia	0.327	0.478
Smoking	0.634	0.420
Heart disease	0.666	0.596
Lesion side	0.536	0.416
Lesion locations	0.758	0.836
TOAST	0.297	0.590

FIM gain=follow-up FIM – initial FIM; MBI gain=follow-up MBI – initial MBI

Table 4 Simple regression analysis of functional outcome

Variables	FIM gain		MBI gain	
	Adjusted R^2	p value	Adjusted R^2	p value
Age	0.007	0.223	0.000	0.328
Sex	–0.013	0.917	–0.010	0.615
Hypertension	0.022	0.106	–0.013	0.872
Diabetes mellitus	0.016	0.138	–0.003	0.388
Hyperlipidaemia	0.000	0.327	–0.007	0.478
Smoking	–0.010	0.634	–0.005	0.420
Heart disease	–0.011	0.666	–0.010	0.596
Lesion side	–0.008	0.536	–0.004	0.416
Lesion volume	–0.011	0.651	–0.013	0.975
Lesion location	–0.013	0.933	–0.006	0.467
TOAST	0.001	0.307	–0.013	0.918
Albumin	0.043	0.040*	0.152	0.000*
Initial NIHSS	0.059	0.019*	0.088	0.005*

FIM gain=follow-up FIM – initial FIM; MBI gain=follow-up MBI – initial MBI
*p<0.05

Table 5 Multiple regression analysis of functional outcome

	FIM gain (adjusted R^2=0.063, F=3.506, p=0.035)				MBI gain (adjusted R^2=0.162, F=8.250, p=0.001)			
	Unstandardised coefficient		t	p value	Unstandardised coefficient		t	p value
	B	SE			B	SE		
Albumin	2.477	2.202	1.125	0.264	5.647	2.059	2.743	0.008*
Initial NIHSS	–0.288	0.180	–1.601	0.114	–0.232	0.168	–1.380	0.172

SE, standard error; FIM gain=follow–up FIM – initial FIM; MBI gain=follow-up MBI – initial MBI
*p<0.05

Discussion

The level of serum albumin has been acknowledged to be a marker of nutritional status. It can be a useful measure when acute changes in nutrition need to be assessed. However, it is sometimes difficult to distinguish between changes in serum albumin as a result of nutrition vs. underlying disease processes [2, 6]. Baseline measurements of serum albumin (<24 h) may not be affected by the acute stress response after stroke [7]. Hypoalbuminaemia at admission may be associated with premorbid nutritional status attributable to the long half-life of albumin [6].

A large number of factors such as admission functional ability, hemineglect, incontinence, age and others may influence the functional outcome of stroke patients [8]. Hypoalbuminaemia appears to be a predictor of poor prognosis in different clinical settings [9]. Aptaker et al. [10] suggested that the level of serum albumin appears to be related to medical complication rate and the functional outcome in geriatric stroke patients. Hypoalbuminaemia worsens the prognosis by decreasing cellular immunity, and increasing the risk of infection and pressure sores in stroke patients [2]. Dziedzic et al. [1] also demonstrated that the level of serum albumin remains an independent predictor of poor outcome and a relatively high serum albumin level in acute stroke patients decreases the risk of poor outcome. In this study, each serum albumin at admission and initial NIHSS score among various predictive variables was correlated with the functional outcome. However, other variables such as age, sex, aetiologic subtype, lesion-related variables and others were not associated with the functional outcome. According to the results of regression analysis, serum albumin at admission was the only predictive factor of the functional outcome assessed by MBI gain in this study.

Albumin has multifaceted intravascular effects. It not only reduces haematocrit level but also influences erythrocyte aggregation by increasing low shear viscosity and decreasing erythrocyte sedimentation under no-flow conditions [5, 11]. To rescue the ischaemic penumbra area and reduce harmful injury associated with the postischaemic reperfusion, there is a need for haemodilution to increase cerebral blood flow and neuroprotective agents that are proven to reduce secondary brain injury. Albumin infusion reduces the haematocrit acutely, has a haemodiluting action and is the most common intravascular volume expander.

Albumin constitutes a major antioxidant defence against oxidising agents. Actually albumin traps the plasma's oxygen radicals and retards the formation of highly reactive hydroxyl radical species [12]. By avidly binding to copper ions, albumin inhibits copper ion-dependent lipid peroxidation at cell membrane [13]. A component of the neuroprotective effect of human albumin in acute ischaemic stroke resides in its antagonism of stagnation, thrombosis and leukocyte adhesion within postcapillary microcirculation in the early reperfusion phase [1]. In an experimental study of focal cerebral ischaemia, Belayev et al. [14] have shown that high-dose human albumin therapy, if administered promptly after stroke onset, is highly effective in improving neurological status and in reducing infarction volume and extent of brain swelling. They have reported that human albumin therapy has the beneficial effect of reversing stagnation, thrombosis and corpuscular adherence in the cortical venules of a rat model of middle cerebral artery occlusion [4].

Hypoalbuminaemia at admission may cause negative influences on neuroprotection in acute stroke patients. Some clinical trials have been performed to verify whether albumin therapy could be beneficial and therapeutic for acute stroke patients. Palesch et al. [15] demonstrated the safety and feasibility of administering high-dose albumin therapy to patients with acute ischaemic stroke and suggested that high-dose albumin therapy may be neuroprotective after ischaemic stroke.

Our results revealed that the serum albumin at admission is an independent predictive factor of the functional outcome in ischaemic stroke patients. It suggests that patients with low serum albumin level within 24 h after the onset of stroke may have a poor functional outcome and it may be caused by low neuroprotective effects. Therefore, active therapeutic trials for the correction of hypoalbuminaemia from the acute stage would be helpful in decreasing the risk of poor outcome in ischaemic stroke patients.

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References

1. Dziedzic T, Slowik A, Szczudlik A (2004) Serum albumin level as a predictor of ischemic stroke outcome. Stroke 35:156–158
2. Dávalos A, Ricart W, Gonzalez-Huix F et al (1996) Effect of malnutrition after acute stroke on clinical outcome. Stroke 27:1028–1032
3. Franch-Arcas G (2001) The meaning of hypoalbuminemia in clinical practice. Clin Nutr 20:265–269
4. Belayev L, Pinard E, Nallet H et al (2002) Albumin therapy of transient focal cerebral ischemia: in vivo analysis of dynamic microvascular responses. Stroke 33:1077–1084
5. Belayev L, Liu Y, Zhao W et al (2001) Human albumin therapy of acute ischemic stroke: marked neuroprotective efficacy at moderate doses and with a broad therapeutic window. Stroke 32:553–560
6. Baker JP, Detsky AS, Wesson DE et al (1982) Nutritional assessment. N Engl J Med 306:969–972
7. Davis JP, Wong AA, Schluter PJ et al (2004) Impact of premorbid undernutrition on outcome in stroke patients. Stroke 35:1930–1934
8. Jongbloed L (1986) Prediction of function after stroke: a critical review. Stroke 17:765–775
9. Phillips A, Shaper AG, Whincup PH (1989) Association between serum albumin and mortality from cardiovascular disease, cancer, and other causes. Lancet 2:1434–1436
10. Aptaker RL, Roth EJ, Reichhardt G et al (1994) Serum albumin level as a predictor of geriatric stroke rehabilitation outcome. Arch Phys Med Rehabil 75:80–84
11. Reinhart WH, Nagy C (1995) Albumin affects erythrocyte aggregation and sedimentation. Eur J Clin Invest 25:523–528
12. Halliwell B (1998) Albumin – an important extracellular antioxidant? Biochem Pharmocol 37:569–571
13. Hallenbeck JM, Dutka AJ, Tanishima T et al (1986) Polymorphonuclear leukocyte accumulation in brain regions with low blood flow during the early postischemic period. Stroke 17:246–253
14. Belayev L, Busto R, Zhao W et al (1997) Effect of delayed albumin hemodilution on infarction volume and brain edema after transient middle cerebral artery occlusion in rats. J Neurosurg 87:595–601
15. Palesch YY, Hill MD, Ryckborst KJ et al (2006) The ALIAS pilot trial: a dose-escalation and safety study of albumin therapy for acute ischemic stroke-II: neurologic outcome and efficacy analysis. Stroke 37:2107–2114