

Changes in Serum Growth Factors in Stroke Rehabilitation Patients and Their Relation to Hemiparesis Improvement

Hideto Okazaki, MD, PhD,* Hidehiko Beppu, PhD,† Kenmei Mizutani, PhD,†
Sayaka Okamoto, MD, PhD,* and Shigeru Sonoda, MD, PhD*

Predicting recovery from hemiparesis after stroke is important for rehabilitation. A few recent studies reported that the levels of some growth factors shortly after stroke were positively correlated with the clinical outcomes during the chronic phase. The aim of this study was to examine the relationships between the serum levels of growth factors (vascular endothelial growth factor [VEGF], insulin-like growth factor-I [IGF-I], and hepatocyte growth factor [HGF]) and improvement in hemiparesis in stroke patients who received rehabilitation in a postacute rehabilitation hospital. Subjects were 32 stroke patients (cerebral infarction: 21 and intracerebral hemorrhage [ICH]: 11). We measured serum levels of VEGF, IGF-I, and HGF and 5 items of the Stroke Impairment Assessment Set (SIAS) for hemiparesis on admission and at discharge. Age-matched healthy subjects (n = 15) served as controls. Serum levels of VEGF and HGF in cerebral infarct patients on admission were higher than those in control subjects, and the serum levels of IGF-I in stroke patients were lower than those in controls. The level of HGF in ICH patients on admission was negatively correlated with gains in SIAS, and higher outliers in HGF concentration were correlated with lower gains in SIAS. Focusing on the extremely high levels of these factors may be a predictor of the low recovery from hemiparesis after stroke. **Key Words:** Growth factor—stroke—hemiparesis—rehabilitation.

© 2014 by National Stroke Association

Introduction

Stroke is one of the major diseases causing disabilities, such as hemiparesis or dysphagia. Hemiparesis is the major symptom from which stroke patients seek recovery. There are many recent reports of new treatments, including robot-assisted therapy and constraint-induced

therapy; however, recovery is still limited.^{1,2} Hence, it is important that the recovery from hemiparesis be accurately estimated, and rehabilitation strategies are designed based on the prognosis for recovery. However, it is difficult to predict to what degree the hemiparesis will improve. In clinical practice, it is not uncommon that stroke patients show more or less recovery from hemiparesis than physiatrists expected. Stroke patients requiring rehabilitation are usually admitted to the subacute rehabilitation hospital about 2-4 weeks after stroke onset in Japan.³ Therefore, if some data collected on admission to the rehabilitation hospital can be used to predict prognosis of hemiparesis, such data would be very useful for evaluation in a clinical context.

It is known that growth factors contribute to neuroprotection and neurogenesis and, moreover, that some of these factors contribute not only to neurons but also to muscle cells as well.⁴⁻⁷ This led us to the hypothesis that higher levels of growth factors may lead to higher recovery from hemiparesis. Some researchers reported positive relationships between blood levels of growth

From the *Department of Rehabilitation Medicine II, School of Medicine, Fujita Health University, Tsu Mie; and †Division of Biochemistry, Fujita Memorial Nanakuri Institute, Fujita Health University, Tsu Mie, Japan.

Received October 31, 2013; revision received January 9, 2014; accepted January 16, 2014.

Grant support: This study was supported by a Grants-in-Aid for Scientific Research No.1765017, No.1870046.

Address correspondence to Hideto Okazaki, MD, PhD, Department of Rehabilitation Medicine II, Fujita Health University, School of Medicine, 424-1 Ootorichou Tsu Mie 514-1295, Japan. E-mail: hideto@fujita-hu.ac.jp.

1052-3057/\$ - see front matter

© 2014 by National Stroke Association

<http://dx.doi.org/10.1016/j.jstrokecerebrovasdis.2014.01.015>

Table 1. Characteristics of each group

Characteristic	Cerebral infarction (n = 21)	Intracerebral hemorrhage (n = 11)
Age (y)	71.0 ± 9.0	58.5 ± 14.0
Gender (male)	13	6
Side of stroke (right)	10	7
Handedness (right)	21	11
Stroke subtype	Large-artery atherosclerosis (n = 7) Cardioembolism (n = 6) Small-vessel occlusion (n = 8)	Putamen (n = 5) Thalamus (n = 4) Frontal subcortex (n = 2)
Time from onset to admission (d)	31.7 ± 16.2	37.2 ± 15.4
Length of stay (d)	70.5 ± 17.2	81.8 ± 26.3
SOP on admission	10.5 ± 7.1	10.9 ± 8.4
SOP on discharge	14.3 ± 6.7	13.8 ± 7.8

Abbreviation: SOP, sum of scores on 5 items of SIAS.
Data were mean ± SD.

factors at particular time points after stroke and clinical outcomes in ischemic stroke patients.⁸⁻¹² Serum levels of vascular endothelial growth factor (VEGF) at acute stroke were proportional to improvement in National Institutes of Health Stroke Scale (NIHSS) scores after 3 months.⁸ Insulin-like growth factor-I (IGF-I) levels at the acute phase of stroke and after 3 months were positively correlated with improvements in the modified Rankin scale (mRS) between 3 and 24 months.⁹ IGF-I levels were positively correlated with gains in the Functional Independence Measure between admission and discharge¹⁰ and negatively correlated with mRS scores at 1-3 months and 12-15 months after stroke.¹¹ Hepatocyte growth factor (HGF) levels within 3 hours of symptom onset were negatively correlated to NIHSS scores at 2 hours and 12 hours after onset.¹² However, except for 1 study,¹⁰ there are no reports of serial changes in growth factors between admission and discharge from the rehabilitation hospital.

The aim of this study was to evaluate serum levels of VEGF, IGF-I, and HGF in stroke patients undergoing rehabilitation in a postacute rehabilitation hospital and then to evaluate the relationships between the changes in serum growth factor levels on admission and at discharge and the clinical outcomes.

Methods

Subjects

Stroke patients whose admission is requested by other hospitals and for whom improvement is expected by the physician are admitted to rehabilitation hospitals from about 2-4 weeks after onset in Japan.³ Our subjects comprised 32 patients (19 men and 13 women) with stroke and hemiparesis hospitalized in the postacute rehabilitation ward of our hospital from July 2004 to October 2006. Patients who had a medical history of stroke, stroke involving the brain stem, cognitive dysfunction such as dementia, or other neurologic or muscular diseases that could

cause hemiparesis or motor weakness were excluded. The mean age was 66.7 ± 12.4 years. The mean time from onset to admission was 33.6 ± 15.9 days, and the mean hospitalization stay was 74.4 ± 21.1 days. The strokes were because of cerebral infarction (CI) and intracerebral hemorrhage (ICH). See Table 1 for descriptions of the patients in these 2 groups. The CI strokes were because of large-artery atherosclerosis, cardioembolism, and small-vessel occlusion. The ICHs were located in the putamen, thalamus, and frontal subcortex. All the subjects underwent Full-time Integrated Treatment designed for rehabilitation patients during hospitalization.¹³ All patients had 40 minutes of physical therapy (gait training) and 40 minutes of occupational therapy (activity of daily living training) per day daily during hospitalization. The aim of the rehabilitation was improvement in daily living and walking, so the patients did not have any specific exercises for hemiparesis. Fifteen normal healthy volunteers (3 men and 12 women; mean age: 63.0 ± 7.6 years) participated as control subjects for the serum growth factors. All subjects provided written, informed consent before participating in the study, and the ethics committee of our hospital approved all protocols.

Blood Samples and Clinical Outcomes

We measured serum levels of VEGF, IGF-I, and HGF on admission and at discharge (VEGF-Ad, VEGF-Dis, IGF-I-Ad, IGF-I-Dis, HGF-Ad, and HGF-Dis). As these particular growth factors display diurnal fluctuations,¹⁴ medical laboratory technicians drew blood at the time of awakening in the morning (7:00 AM). VEGF, IGF-I, and HGF were measured by enzyme-linked immunosorbent assays (VEGF: BioSource Immunoassay Kit; IGF-I and HGF: R&D Quantikine Set).

The severity of hemiparesis was evaluated by the Stroke Impairment Assessment Set (SIAS)¹⁵ on the same day as the blood withdrawals. SIAS is a 22-item evaluation of stroke impairment designed to comprehensively assess motor

Download English Version:

<https://daneshyari.com/en/article/5873362>

Download Persian Version:

<https://daneshyari.com/article/5873362>

[Daneshyari.com](https://daneshyari.com)