Increased Blood Viscosity in Ischemic Stroke Patients with Small Artery Occlusion Measured by an Electromagnetic Spinning Sphere Viscometer

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Background and Purpose: High blood viscosity causes blood stagnation and subsequent pathological thrombotic events, resulting in the development of ischemic stroke. We hypothesize that the contribution of blood viscosity may differ among ischemic stroke subtypes based on specific pathological conditions. We tried to verify this hypothesis by measuring blood viscosity in acute ischemic stroke patients using a newly developed electromagnetic spinning sphere (EMS) viscometer. *Methods:* Measurements in acute ischemic stroke patients were performed 4 times during admission and data were compared with those obtained from 100 healthy outpatient volunteers. *Results:* We enrolled 92 patients (cardioembolism: 25, large artery atherosclerosis: 42, and small artery occlusion [SAO]: 25) in this study. Comparisons of blood viscosity between the ischemic stroke subgroups and control group revealed that blood viscosity at the date of admission was significantly higher in the SAO group (5.37 ± 1.11 mPa·s) than in the control group (4.66 ± .72 mPa·s) ($P < .01$). Among all subtype groups showing a reduction in blood viscosity after 2 weeks, the SAO group showed the highest and most significant reduction, indicating that SAO patients had the most concentrated blood at the onset. *Conclusions:* Blood viscosity was significantly increased in the SAO group at the date of admission, which indicated the contribution of dehydration to the onset of ischemic stroke. The importance of dehydration needs to be emphasized more in the pathogenesis of SAO. The clinical application of the EMS viscometer is promising for understanding and differentiating the pathogenesis of ischemic stroke. **Key Words:** Blood viscosity—ischemic stroke—small artery occlusion—pathogenesis—rheology—dehydration.

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Introduction

Blood viscosity, one of the important rheological parameters, is determined by blood components and varies with the shear rate as a non-Newtonian fluid.[1,2] The determining factors of blood viscosity are the concentration of blood cells, erythrocyte deformability and aggregation, and the concentration of plasma components. Blood viscosity increases when the concentrations of blood cells and plasma components become elevated and also with the low deformability and high aggregation of erythrocytes. Among these factors, the concentration of blood cells contributes the most to determining blood viscosity.[3-5] A strong correlation has been demonstrated between blood viscosity and the concentration of blood cells.[5] Shear rate is an important factor regulating blood viscosity with non-Newtonian characteristics in the circulatory system. While blood viscosity increases exponentially with reductions in the shear rate, it decreases and converges to a certain value with elevations in the shear rate, which exhibits shear-thinning behavior.[6] The important rheological function of blood viscosity is to control the resistance to blood flow in combination with the characteristics of vessels (length and radius).[7] Therefore, blood viscosity measurements have been performed in thrombotic diseases since the 1960s and previous studies have demonstrated that increased blood viscosity is related to cardiovascular events.[8-10] Furthermore, relationships have been reported between blood viscosity and some cardiovascular risk factors, such as hypertension, dyslipidemia, smoking, and obesity.[11-14] An increase in blood viscosity has been identified in the acute phase of ischemic stroke, similar to other thrombotic diseases.[15-19] However, actual measurements of blood viscosity have not been performed because of the stereotypical belief that blood viscosity increases equally in all ischemic stroke subtypes, which is within expectations and with less clinical value. However, since the measurement of blood viscosity may provide useful information on differential diagnoses, treatments, and the prevention of stroke, it needs to be examined more extensively. Ischemic stroke consists of a number of subtypes with different pathogeneses, and, thus, we hypothesize that the contribution of blood viscosity may differ among ischemic stroke subtypes due to specific pathological conditions.

A newly developed electromagnetic spinning sphere (EMS) viscometer has the ability to measure a small amount of samples quickly and sequentially in a noncontact disposable manner and skips the time-consuming washing process after each sample measurement.[20,21] We previously introduced the measurement of blood viscosity with the EMS viscometer and reported our findings on control volunteers.[22] In the present study, we measured blood viscosity in acute ischemic stroke patients and discussed the importance of blood viscosity measurements in terms of differential diagnoses and the treatment of ischemic stroke.

Methods

Patient Population and Blood Sampling

We herein conducted a prospective study with the recruitment phase between June 2014 and August 2015 in a comprehensive stroke center hospital. Patients (≥20 years) diagnosed with cardioembolism (CE), large artery atherosclerosis (LAA), and small artery occlusion (SAO) were eligible for the study if they were admitted for more than 2 weeks. Ischemic stroke subtypes were determined according to the classification of the Trial of Org 10172 in Acute Stroke Treatment with the aid of the findings of magnetic resonance imaging or computerized tomographic scans. Measurements were performed 4 times (date of admission, a couple of days after, 1 week after, and 2 weeks after) during admission. As a control group to compare blood viscosity with the stroke subtype groups, we used the 100 healthy outpatient volunteers (58.0% male, mean age 65.5 ± 14.8 years) recruited in our previous study.[22] All participants provided written informed consent prior to inclusion in the study, which was approved by the hospital's ethics committee. Blood sampling was performed to measure blood cells and biochemical parameters as a routine clinical examination, and residual EDTA (ethylenediamine tetraacetic acid) anticoagulated blood after the completion of blood cell counts was then used in this study.

Measurement of Blood Viscosity by the EMS Viscometer

Blood viscosity was measured using the EMS viscometer (Kyoto Electronics Manufacturing Co., Ltd, Kyoto, Japan) as previously described.[22] Briefly, .3 ml of a 37°C prewarmed EDTA-anticoagulated blood sample in a disposable glass tube containing a 2-mm aluminum sphere was set in the EMS viscometer, and its viscosity was measured at 37°C in accordance with the following measurement sequence. The measurement sequence was programmed to measure blood viscosity at 6 different rotational speeds of a driving magnetic field (1000, 800, 640, 500, 400, and 300 rpm) sequentially in 1 measurement cycle, and the cycle was set to repeat 5 times at 30-second intervals. The sample was shaken at every interval of the 5 measurement cycles to prevent sedimentation. The shear rate of blood typically ranges from 30 to 110 s^{-1} under this experimental condition. After the exclusion of outliers (greater than 20 mP·s), the mean value of 5 measurements was calculated to obtain the representative value of each rotational speed. Blood viscosity at 100 s^{-1} was used as a representative value for comparisons and data analyses.

Statistical Analysis

Data are given as the mean ± standard deviation. Statistical analyses were performed using the commercially