Detection of Reverse Flow by Duplex Ultrasonography in Orthostatic Hypotension

Toshiro Yonehara, MD; Yukio Ando, MD; Kazumi Kimura, MD; Makoto Uchino, MD; Masayuki Ando, MD

Background and Purpose The aim of this study is to elucidate the effect of orthostatic hypotension on changes in cerebral blood flow.

Methods Blood flow velocities of both the common carotid artery and vertebral artery were measured using duplex ultrasonography in 12 patients: 6 with familial amyloidotic polyneuropathy, 3 with Shy-Drager syndrome, 2 with pandysautonomia, and 1 with senile orthostatic hypotension. Simultaneously, peripheral blood flow was also evaluated by laser-Doppler flowmetry.

Results The patients showing dizziness or syncope when tilted to a 70° upright position exhibited characteristic reverse flow at the end-diastolic phase on the Doppler flow image of both the common carotid and vertebral arteries, which was effectively treated by infusion of 2.5 μg/min norepinephrine for 10 minutes. This end-diastolic reverse flow was not seen in any patients who did not have dizziness or syncope. After subjects were tilted from a supine to a 70° upright position, decrease in the peripheral blood flow of the patients with orthostatic hypotension remained unchanged for at least 5 minutes, whereas that of control subjects was recovered within 2 minutes. However, no significant difference between the patients with and without clinical symptoms was observed.

Conclusions These results suggest that detection of this specific echographic pattern may be quantitatively useful in examination of clinical symptoms accompanying orthostatic hypotension and that duplex ultrasonography may be a helpful tool to evaluate the effect of drugs used for controlling these symptoms.

Key Words • cerebral blood flow • hypotension • laser-Doppler flowmetry • ultrasonics

It is well documented that patients with pandysautonomia,1 Shy-Drager syndrome,2 and Parkinson’s disease as well as familial amyloidotic polyneuropathy (FAP) type I.4,5 show systemic autonomic dysfunction, such as orthostatic hypotension (OH), diarrhea, pupil disorders, bladder or rectal disturbances, and abnormal patterns of sweating. Among various complaints reflecting autonomic dysfunction, OH is one of the most serious because patients’ daily life is restricted by dizziness or syncope accompanying OH. Moreover, these symptoms may become life-threatening because OH often causes transient loss of consciousness due to cerebral ischemia, and a resulting sudden fall may lead to brain injury or bone fracture. However, significant decrease in blood pressure after standing or changing postures does not always induce syncope. Some patients with OH may have certain compensatory mechanisms for preventing such an attack during OH.5 Thus, it is very important to identify a useful examination to analyze dizziness or syncope during OH and to treat these symptoms to provide life support to these patients.

Recently, several methods for measuring cerebral blood flow (CBF), such as the 133Xe inhalation method, single-photon emission computed tomography, positron emission tomography, and transcranial Doppler ultrasonography (TCD), have been developed.6-9 Duplex ultrasonography is one of the most useful tools to detect the carotid and vertebral blood flows noninvasively and quantitatively.10 Compared with TCD, duplex ultrasonography is more useful in identifying the vessels and in correcting the angle at which the probe is inserted.11

To elucidate the effect of OH on CBF in patients with severe OH and the correlation between dizziness or syncope and OH, we examined blood flow velocities (BFVs) of both common carotid arteries (CCAs) and vertebral arteries (VAs) of 12 patients (6 patients with FAP, 3 with Shy-Drager syndrome, 2 with pandysautonomia, and 1 with senile OH) by duplex ultrasonography during OH. Simultaneously, peripheral blood flow was also measured by laser-Doppler flowmetry (LDF). Moreover, to treat dizziness or syncope during OH, a low dose of norepinephrine was administered by intravenous infusion to 2 patients with dizziness during OH.

Subjects and Methods

Subjects

We examined 6 patients with FAP (4 men and 2 women aged 31 to 43 years; average, 36.7±4.6 years), 3 with Shy-Drager syndrome (3 men aged 63 to 73 years; average, 69.3±5.5 years), 2 with pandysautonomia (2 women aged 37 and 38 years), and 1 with senile OH (a woman aged 61 years) for the measurement of BFVs and peripheral blood flow. All the patients had been referred to Kumamoto University School of Medicine and had taken no drugs for at least 24 hours before the examinations. FAP patients were diagnosed by protein chemistry and genetic investigations in addition to clinical findings.12 Other patients included in these studies had a definite diagnosis based on clinical findings. As a control, 5 healthy volunteers (3 men and 2 women aged 26 to 40 years; average, 30.2±6.0 years) were also studied. All the healthy volun-
volunteers had no abnormal physical or neurological findings. The study was in agreement with the guidelines of the ethics committee at our institution. The nature and aims of the study were explained to all the subjects, who gave their consent.

**Measurement of Cervical Blood Flow Velocities by Duplex Ultrasonography**

The equipment used was a commercially available Aloka SSD-680 apparatus (Aloka Co, Ltd). The duplex probe consisted of a 7.5-MHz imaging transducer and a 15-MHz pulsed-Doppler transducer.

BFVs were measured with subjects in both a supine and a 70° upright position by using a tilting table for comparison between positions. The patient's head was turned away from the side being scanned, the neck was extended, and the transducer was placed on the neck using the anterior oblique approach. On longitudinal scans, the sample volume (1 mm) was set in the CCA and VA, which were displayed as linearly as possible. Particular care was taken to keep the incident angle between the CCA or VA and the beam at less than 60°. During the examinations, systemic blood pressure was also monitored.

**Measurement of Peripheral Blood Flow**

Peripheral blood flow was measured with LDF (Model ALF 2100, Advance) by attaching the LDF probe to the pulp of the second finger. After the patient was tilted up to the 70° upright position, changes in the blood flow were measured. Because responses partially depended on finger temperature, the room was maintained at 25°C.

**Treatment of Dizziness or Syncope During Orthostatic Hypotension by the Administration of Norepinephrine**

Norepinephrine (2.5 μg/min) was intravenously infused for 10 minutes, and the changes in the BFV of both the CCA and VA were measured in a 38-year-old male FAP patient and a 72-year-old male Shy-Drager syndrome patient.

**Results**

**Measurement of Blood Flow Velocity at the 70° Upright Position**

Changes in BFV after the patient was tilted to the 70° upright position were measured using duplex ultrasonography. As indicated in Fig 1, bottom, the patients showing dizziness or syncope in the upright position exhibited characteristic reverse flow at the end-diastolic phase on the Doppler flow image (patients 1, 2, 3, 9, and 11; Table) when compared with those in the resting position (Fig 1, top). No such flows were seen in the control subjects. This pattern was recognized in both CCA and VA studies. In contrast, despite severe OH, reverse flow was not recognized in any patients who did not show dizziness or syncope in the upright position. The occurrence of dizziness or syncope was perfectly consistent with the presence of reverse flow as displayed by duplex ultrasonography (Table).

**Changes in Peripheral Blood Flow at the 70° Upright Position**

To evaluate the changes in peripheral blood flow after patients with OH were placed in the 70° upright position, we measured the peripheral blood flow in the second fingertip in patients with severe autonomic dysfunction and in control subjects. Although rapid blood compensation after transient decrease in blood flow was obtained in the control subjects, no such recovery of blood supply was recognized within several minutes in the patients with OH (Fig 2). However, no apparent difference was recognized between patients with and without symptoms.

**Treatment of Dizziness or Syncope During Orthostatic Hypotension by Intravenous Infusion of Norepinephrine**

To treat dizziness or syncope during OH, 2.5 μg/min norepinephrine was administered by intravenous infusion for 10 minutes, and the changes in BFV in a 38-year-old male FAP patient (patient 3) and a 72-year-old male Shy-Drager syndrome patient (patient 9) were measured. Reverse flow at duplex ultrasonography and dizziness or syncope during severe OH were effectively treated during norepinephrine infusion, while manifest OH was still observed even during these treatments ([0 and 10 minutes after infusion, respectively] mean blood pressure: patient 3, 126 mm Hg—66 mm Hg; patient 9, 160 mm Hg—50 mm Hg; diastolic blood pressure: patient 3, 96 mm Hg—52 mm Hg; patient 9, 132 mm Hg—41 mm Hg) (Figs 3 and 4).

**Discussion**

In this study, dizziness or syncope was not observed when reverse flow was not detected by duplex ultrasonography in all patients with clinical symptoms. BFV in the CCA does not directly reflect CBF. However, Newell et al14 showed that relative changes in middle cerebral artery velocity measured by TCD accurately
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Summary of Relation of Symptom to Reverse Flow

<table>
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<tr>
<th>Case</th>
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<th>Age, Sex</th>
<th>Change in Diastolic BP After Tilting to 70°, mm Hg*</th>
<th>Diastolic BP, mm Hgt</th>
<th>Symptoms</th>
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BP indicates blood pressure; FAP, familial amyloidotic polyneuropathy; S-D synd, Shy-Drager syndrome; Pandysaut, pandysautonomia; and OH, orthostatic hypotension.

*Maximum decreased values of the diastolic BP after tilting.
†Increased or decreased BP after tilting. In patients 3, 8, and 9, blood flow velocities were measured twice and in patient 11, three times.

reflect relative changes in internal carotid artery flow measured by electromagnetic flowmeter during dynamic autoregulation testing in humans. As in this phenomenon, some significant change in the cerebral blood supply may be induced by standing in patients with severe OH.

We have sometimes encountered patients with severe autonomic dysfunction who showed no dizziness or syncope despite severe OH. In healthy subjects, several compensatory mechanisms for preventing cerebral ischemia may be operating after standing up or changing postures.5 It is well known that humans have self-protecting systems such as reflex arteriolar or venous constriction, reflex acceleration of heart rate, increased plasma catecholamines, activation of renin-angiotensin-aldosterone system, release of arginine vasopressin, decreased cerebral vascular resistance, augmentation of respiration, and increased striated muscle tone. However, in patients showing OH, such reactions may be lacking. In fact, as indicated in Fig 2B, vasoconstrictive response was severely impaired in patients with OH, and as the result of this phenomenon, blood stasis in the peripheral vessels may occur. Unfortunately, we could not find a difference between patients with and without clinical symptoms. We suppose that cardiac output

![Graph showing changes in peripheral blood flow after the subject was tilted up to a 70° upright position.](http://stroke.ahajournals.org/Downloadedfrom)
FIG 3. Duplex ultrasonography of patient 3 (38-year-old man with familial amyloidotic polyneuropathy) shows effects of treatment of syncope during orthostatic hypotension by norepinephrine administration. Top, Before administration of norepinephrine, reverse-flow pattern (arrows) was recognized 2 minutes after the patient was tilted up to a 70° upright position. Bottom, After drip infusion of 2.5 μg/min norepinephrine for 5 minutes, this pattern had totally disappeared. The incident angle of 60° was indicated as the angle between the vertical line of white dots (Doppler beam) and the vessel in the left of the figures. *Common carotid artery.

might decrease because of the stasis of the systemic-peripheral veins in patients showing dizziness or syncope during OH.

Serra et al\textsuperscript{15} reported that an abnormal Doppler pattern was recognized in a pregnant woman during OH by using TCD. However, no systematic analyses were performed for identifying the mechanism of this specific phenomenon. We have demonstrated in this study the interaction between CCA, VA, and peripheral blood flows by using duplex ultrasonography and LDF (Figs 1 and 2) and presented the importance of reverse flow as a ultrasonographic marker of the clinical symptoms.

Grubb et al\textsuperscript{16} reported that patients with vasovagal syncope did not show any reverse flow by TCD. However, no information about duplex ultrasonography was available in that report. Our article may be the first to describe the detection of end-diastolic reverse flow in patients with severe OH by duplex ultrasonography.

Hassler et al\textsuperscript{17} presented the finding of the same reverse flow detected by TCD in the middle cerebral artery of patients with raised intracranial pressure after clinical brain death. They demonstrated in this report that, when intracranial pressure reached the same level as the diastolic arterial pressure, the diastolic part of the flow velocity spectrum started to disappear. Moreover, when intracranial pressure rose to the levels between systolic and diastolic blood pressure, the diastolic blood flow was observed in the reverse direction. Hassler et al explained that cerebral perfusion pressure is determined by the difference between systemic arterial blood pressure and intracranial pressure and that diastolic backflow occurs when the cerebral perfusion pressure becomes negative at some point during diastole.\textsuperscript{17} In the same way as in this phenomenon, in those patients showing dizziness or syncope while tilted to a 70° upright position with decreasing diastolic blood pressure, intracranial pressure level might be between the systolic and diastolic blood pressure levels. For this reason, blood pressures are expressed by diastolic values (Table).

From these results, we propose that end-diastolic reverse flow is a useful indicator in detecting symptomatic OH because dizziness or syncope may not be predicted by the evaluation of cardiac autonomic examinations, such as cardiographic R-R interval. Some patients start to show dizziness and syncope as the initial symptom of stroke, and patients with stroke sometimes exhibit OH during the course of the illness. The data given in this article may provide important information for treating stroke patients with autonomic dysfunction.

References


Detection of reverse flow by duplex ultrasonography in orthostatic hypotension.
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