Normal Blood Flow Velocities of Basal Cerebral Arteries Decrease with Advancing Age: A Transcranial Doppler Sonography Study

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Transcranial Doppler sonography (TCD) is a non-invasive diagnostic tool enabling evaluation of blood flow characteristics of basal intracerebral vessels via thin calvarian regions. Several factors may affect the normal values of cerebral hemodynamic parameters, and standard reference values for each laboratory are needed for precise interpretation of the results. The aims of this study were to determine normal values of flow velocities of basal cerebral arteries of our TCD laboratory, and to study the influence of age and gender on normal values. We studied 63 healthy volunteers (30 male and 33 females; age range, 5 - 69 years old) with TCD with a 2-MHz transcranial probe. The subjects were divided into 7 age groups: 5-10 years, 11-20 years, 21-30 years, 31-40 years, 41-50 years, 51-60 years and > 60 years. Mean velocity (V mean), peak systolic velocity (PSV), and end-diastolic velocities (EDV) were determined in middle, anterior and posterior cerebral arteries. No significant gender difference was found. However, there was a decrease in blood flow velocities in all vessels with advancing age, which was significant when subjects older than 40 years and ≦ 40 years old were compared. V mean, PSV and EDV values were highest in the age group of 5 - 10 years old and lowest in volunteers older than the age of 60 ($p <$ 0.05). As a conclusion, flow velocities in basal cerebral arteries range widely and are significantly age-related. Age matching of TCD data is a requirement for clinically relevant conclusions. ——— transcranial Doppler sonography; basal; cerebral arteries; normal values; healthy subjects.
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Doppler ultrasound instruments, named after Christian Andreas Doppler, detect shifts in frequency of sound waves reflected from moving objects. In human body such objects are mainly erythrocytes. Doppler ultrasound is used to determine the speed and direction of flow in blood vessels. Up to discovery of transcranial Doppler sonography (TCD) by Aaslid et al. (1982), the skull was considered as an impenetrable barrier for ultrasounds. To enable sufficient transmission of ultrasound through the skull, they used a low frequency transducer; a 2-MHz probe. Subsequently, this noninvasive tool was used as an alternative method to invasive procedures such as arteriography and venography.

TCD is the only noninvasive, practical and

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painless method that enables the accurate assessment of intracranial arteries, adding physiologic information to the anatomic images (Lupetin et al. 1995a; Sharma et al. 2007). With this technique, it is possible to evaluate the flow characteristics of intracranial arteries, to detect embolus, vasospasm or vasomotor autoreactivity (White and Venkatesh 2006). It may also be used as a supportive test for the diagnosis of brain death (Monteiro et al. 2006).

The acoustic windows ordinarily used in TCD examinations are the regions where the cranial bone is relatively thin. The temporal bone is the thinnest portion of the skull and transtemporal window permits the insonation of ipsilateral middle cerebral artery (MCA), anterior cerebral artery (ACA) and posterior cerebral artery (PCA).

TCD technology has evolved considerably, leading to new clinical and research applications. In order to achieve any informative insonation of vessels and respectful interpretation of findings, data of normal flow characteristics of distinct vessels are necessary (Ringelstein et al. 1990). However, in contrast to other ultrasound modalities, such as carotid duplex, TCD velocity values may be prone to a greater variation. Diagnostic accuracy is substantially improved if individual TCD laboratories generate their own normal values and standards (Tong and Albers 1999).

The available studies using this technique have tended to provide disparate results with regard to changes in blood flow velocities with age and gender (Aaslid et al. 1982; Brouwers et al. 1990; Ringelstein et al. 1990; Liboni et al. 2006). We aimed in this study to determine normal values of flow velocities of basal cerebral arteries of our TCD laboratory, and to study the influence of age and gender on normal values.

Material and Methods

Subjects

Healthy volunteers (n = 63) without a prior medical history of cardiac, neurological, or cerebrovascular disease were enrolled into this study. The subjects in the study included students, members of the hospital staff, and their relatives. Subjects with atherosclerotic plaque or stenosis at the site of measurement examined by Doppler and duplex sonography were excluded. The study protocol was in accordance with the Helsinki declaration of human rights, and was approved by the local Ethics Committee and all volunteers gave written informed consent to participate in the study.

TCD recordings

The examinations were performed in a room with a comfortable temperature after a rest of at least 15 min in the supine position. A 2-MHz probe of a multigated transcranial pulsed Doppler system (Multidop X_4 DWL, Sipplinghen, Germany) was used. M1 segment of the MCA, A1 segment of ACA, the first (P1) and second (P2) segments of the PCA were examined via transtemporal window. M1 segment of MCA was found by moving the probe slowly at depths of 45 to 55 mm. Blood flow was toward the transducer. A1 segment of ACA was insonated by tracking the MCA signal and increasing the depth setting up to 55 - 70 mm of depth. The flow in the origin of ACA was away from the transducer. PCA was insonated by returning to the internal carotid artery bifurcation and then rotating the transducer posteriorly and inferiorly, with the depth setting of 65 - 70 mm. The flow was toward the transducer in the P1 segment of PCA and was away from the transducer in P2.

Peak systolic velocity (PSV), end-diastolic velocity (EDV), and mean velocity (V mean) were measured in both right and left arms of the basal cerebral arteries. PSV was defined as the maximum velocity achieved during systole. EDV was defined as the lowest flow velocity measured at the end of a cardiac cycle. V mean was based on the continuous measurement of the peak velocity envelope over the entire cardiac cycle. These three flow velocities were calculated and displayed automatically on the TCD instrument. The range of normal reference values was determined in respect to gender and seven age groups as: 5-10 years, 11-20 years, 21-30 years, 31-40 years, 41-50 years, 51-60 years and > 60 years. Age dependency was evaluated in two groups; subjects ≦ 40 years old and subjects > 40 years old.

Statistical analysis

Mann-Whitney's U-and Kruskal-Wallis test methods were used for the comparison of the values according to gender, and age groups. Statistical significance was defined as a p value of less than 0.05. All statistical analyses were performed using SPSS version 10.0 (SPSS Inc., Chicago, IL, USA).

Results

The characteristics of the subjects are seen in Table 1. There were 30 male in the age range of 5 to 69 years old (mean ± s.d., 32.3 ± 18.5 years), and 33 female subjects in the age range of 6 to 69 years old (mean ± s.d., 31.9 ± 17.1 years). The largest age group was the one between 21 and 30 (total 12 subjects), and we evaluated 5 subjects older than 60 years old.

All of the arteries were successfully insonated. The mean and standard deviation of the measured values are presented in Table 2. There was no significant difference between the measure-

Table 1. Characteristics of the subjects.

	Age groups (yrs)						
	5 - 10	11 - 20	21 - 30	31 - 40	41 - 50	51 - 60	> 60
Gender							
Male (n = 30)	5	5	6	3	5	3	3
Female (n = 33)	5	5	6	7	4	4	2
Mean age ± s.d.	8.3 ± 1.9	18.3 ± 0.8	24.8 ± 0.9	33.4 ± 2.4	44.7 ± 3.2	53.8 ± 3.2	65.4 ± 4.0

s.d., standard deviation.

Table 2. Flow velocities of basal cerebral arteries. Values are means ± s.d.

	Age groups (yrs)							p*
	5 - 10	11 - 20	21 - 30	31 - 40	41 - 50	51 - 60	> 60	
MCA								
V mean	75.7 ± 8.7	63.6 ± 12.1	57.4 ± 8.7	57.9 ± 11.2	65.9 ± 14.5	51.3 ± 12.7	46.9 ± 5.7	< 0.05
PSV	112.3 ± 11.7	99.2 ± 17.0	94.0 ± 22.2	84.3 ± 19.7	96.4 ± 22.3	77.8 ± 12.8	75.0 ± 12.0	< 0.05
EDV	55.7 ± 8.4	44.4 ± 10.9	38.4 ± 9.0	38.2 ± 8.0	46.9 ± 10.2	35.7 ± 9.6	30.4 ± 8.7	< 0.05
ACA								
V mean	65.4 ± 9.9	42.9 ± 7.1	43.6 ± 9.2	41.2 ± 9.4	43.0 ± 9.2	39.3 ± 11.4	37.7 ± 6.5	< 0.05
PSV	102.1 ± 13.7	76.1 ± 13.9	64.4 ± 10.9	65.8 ± 10.2	64.4 ± 11.0	60.0 ± 9.5	59.8 ± 10.8	< 0.05
EDV	46.7 ± 9.6	26.6 ± 9.3	27.4 ± 6.4	24.2 ± 7.6	29.5 ± 10.7	27.8 ± 11.3	27.8 ± 5.2	< 0.05
PCA (P1)								
V mean	47.4 ± 6.6	33.9 ± 9.5	33.1 ± 5.3	37.7 ± 11.9	35.9 ± 9.5	32.2 ± 8.3	31.6 ± 8.1	< 0.05
PSV	69.2 ± 11.5	62.5 ± 10.3	52.4 ± 7.5	58.9 ± 18.2	54.1 ± 11.9	45.7 ± 13.4	44.4 ± 11.5	< 0.05
EDV	37.2 ± 5.5	20.6 ± 6.7	19.1 ± 5.0	20.2 ± 9.7	19.8 ± 7.9	22.8 ± 6.5	21.4 ± 7.2	< 0.05
PCA (P2)								
V mean	45.3 ± 4.6	38.3 ± 12.1	34.9 ± 9.6	36.7 ± 9.3	30.9 ± 6.0	28.7 ± 4.0	29.3 ± 4.3	< 0.05
PSV	73.1 ± 8.0	65.6 ± 22.1	54.9 ± 17.8	58.1 ± 12.8	49.8 ± 9.7	48.5 ± 7.0	49.4 ± 6.5	< 0.05
EDV	32.1 ± 4.6	23.1 ± 9.7	19.4 ± 7.8	22.6 ± 6.6	18.1 ± 5.6	14.5 ± 2.2	15.4 ± 0.9	< 0.05

*p *values* show comparison of velocity values between age groups of ≦ 40 years and > 40 years.

MCA, middle cerebral artery; ACA, anterior cerebral artery; PCA, posterior cerebral artery; P1, the first segment of PCA; P2, the second segment of PCA; V mean, mean velocity; PSV, peak systolic velocity; EDV, end - diastolic velocity.

ments of right and left arms of the arteries (p = 0.3). Therefore, averaged values from both hemispheres were used in further analysis.

No differences were observed between female and male subjects for the blood flow velocities in all arteries and in all age groups. However, we found a decrease in all velocities of the basal cerebral arteries with advancing age, which was pronounced in subjects who were more than 40 years old ($p < 0.05$). V mean value of MCA of the subjects ≦ 40 years old and subjects > 40 years old were 63.65 ± 10.2 cm/sec and 54.7 ± 11 cm/sec, respectively ($p < 0.05$). V mean values of ACA, PCA (P1) and PCA (P2) of the subjects ≦ 40 years old were 47.2 ± 10.17 cm/sec, 37.93 ± 5.94 cm/sec, and 38.5 ± 4.27 cm/sec, respectively. On the other hand, subjects older than 40 years old had V mean values of 40.54 ± 3.58 cm/sec, 33.73 ± 2.62 cm/sec and 29.82 ± 2.65 cm/sec in ACA, PCA (P1) and PCA (P2), respectively ($p < 0.05$).

V mean, PSV and EDV values were highest in the group involving subjects 5 to 10 years old and lowest in volunteers older than the age of 60. When age groups of 5 - 10 years and older than 60 years were compared, V mean, PSV and EDV values of MCA decreased approximately 39%, 34% and 46%, respectively. The values of measured velocities reduced approximately 40% for ACA and 38% for PCA between the age groups of 5 - 10 years and > 60 years ($p = 0.01$).

Discussion

The present study was designed to establish normal reference values of different age and sex groups for the V mean, PSV and EDV of the basal cerebral arteries, as determined with TCD in healthy subjects. The standard TCD ultrasonographic examination is a noninvasive and highly reproducible measure for obtaining information about the flow velocities of the intracranial vessels. Transcranial Doppler examinations can be performed on any subject at bedside, whether ambulatory or comatose, who is able to remain stationary in the supine position.

The effectiveness of TCD in clinical use has been documented in a wide range of diseases like subarachnoid hemorrhage and vasospasm, arterial stenosis and occlusion, head injury, brain death, and arteriovenous malformations (Lupetin et al. 1995b). However, as several factors like age, gender, hematocrit, partial pressure of carbon dioxide, partial pressure of oxygen, cardiac output, blood viscosity, turbulence, cerebral metabolism, and degree of brain activation may affect the normal reference values of cerebral hemodynamic parameters (Tong and Albers 1999), standard reference values are needed for precise interpretation of the results. This background is needed to develop criteria for the diagnosis of pathologic conditions. An appreciation of the degree of variability in TCD measurements may minimize false positive and false negative diagnosis.

The influence of age on cerebral blood flow parameters is a well-known phenomenon (Naritomi et al. 1979; Melamed et al. 1980). The decline in cerebral blood flow with advancing age may be associated with certain changes in cerebrovascular hemodynamics such as decreased metabolic demands, higher hematocrit and lower partial pressure of carbon dioxide levels (Melamed et al. 1980), vessel-size changes (Kusunoki et al. 1999), and lower cardiac output (Safar 1990). Several investigations demonstrated the importance of age on the TCD velocities (Arnolds and von Reutern 1986; Brouwers et al. 1990). Arnolds and von Reutern (1986) found a 20% decrease in Doppler shift of MCA from a mean age of 17 to 67 years. Grolimund and Seiler examined 535 patients who had a history of a previous neurological event, but with normal neurological examination, and found that MCA, ACA and PCA velocities decreased by an average of 0.51%, 0.5% and 0.37% per year, respectively (Grolimund and Seiler 1988). Similar with these studies, we also found a wide range of reference velocity values in all vessels of different age groups. Statistical analysis of our data showed that pediatric subjects have the highest flow velocities and flow velocities start significantly to decrease particularly above the age of 40 years.

Sex of subject is another factor that may affect the velocity measurements by TCD. In some of the studies it was shown that women have higher flow velocities than men (Arnolds and von Reutern 1986; Brouwers et al. 1990), and this finding was attributed to the lower hematocrit in women. Shamma and colleagues (1992) suggested that hormonal status, especially estrogen levels, appeared to contribute in some way to the reactivity and state of tone in the cerebral microcirculation of women. However, like Ringelstein et al. (1990), we did not find a gender effect on TCD values.

In conclusion, flow velocities in basal cerebral arteries range widely. They are significantly age dependent and decrease with advancing age. Normalized velocity data for distinct age groups are a prerequisite for differentiating normal and pathological flow conditions.

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