Use of TCD in children with ischaemic stroke

Katarzyna Jarus-Dziedzic[1], Adrianna Wilczek[2], Wojciech Zub[1]

[1] Department of Neurosurgery, Medical University, Wrocław, Poland
[2] Department of Paediatric Neurology, T. Marciniak Specialist's United Hospital

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SUMMARY

Transcranial Doppler Sonography (TCD) is a valuable method of non-invasive measuring of cerebral blood flow. So far, no Polish publications on cerebral blood flow in children with cerebral ischaemia have been issued. One of the reasons is that ischaemic brain strokes are very rare in youngsters. TCD was performed in a group of 21 children at the age of 3, 5 to 18 years (mean age 12 years) with diagnosed cerebral ischaemic stroke (16 cases, including 3 RIND) and TIA (5 cases). In 12 children, TCD examination was performed between 3rd and 30th day after stroke, while in the remaining 9 – 1 to 10 years after that incident. Asymmetry of 30 to 80% in cerebral blood flow velocity between right and left side was observed in 15 children, mainly with decreased cerebral blood flow velocity in the stroke area. Asymmetry in blood flow velocity exceeding 30% was observed in only one child out of 5 children with TIA. In all the patients, CT, MRI and cerebral angiography results revealed a correlation with TCD changes in blood flow velocities.

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INTRODUCTION

In recent years, Transcranial Doppler Sonography (TCD) has become a valuable method of non-invasive assessment of cerebral blood flow in various diseases of the brain1. The method is based on Doppler phenomenon, where ultrasonic wave dispersing on blood cells flowing through blood vessel changes its frequency proportionally to blood flow velocity. The analysis of acoustic signal, the shape of Doppler curve, values of blood flow velocities and indices of vascular resistance allow for indirect evaluation of intracranial vessel diameter.

The data available so far, concerning the use of TCD in paediatric patients are relatively sparse. Considerable dynamics of changes taking place in children during their growth and maturation makes it difficult to establish the range of normal values of blood flow velocity for particular age groups as well as to interpret anomalies detected in TCD. Factors influencing parameters registered in TCD in children include: age, gender, haematocrit value, condition of cardiovascular system, the level of consciousness, position of the head [1,2,3,4,5]. Together with age and body growth children experience changes in cardiac muscle, chest volume, blood, as well as in the architecture, size and morphology of cerebral vessels, which significantly influence cerebral flow and may be reflected in TCD examination [1,5].

According to the latest epidemiological data, stroke incidence ratio in children is 7.91 in 100 thousand children per year [6]. They are most frequent among children aged 3 and less, and in puberty [6,15]. Ischaemic strokes are mainly caused by congenital or acquired heart disease, out of which cyanotic defects account for 25-30% [8,9,10] and by dysrhythmia. The most frequent among genetically determined risk factors are blood clotting disorders. In the majority of cases these are VIII, IIX factor deficits as well as the shortage of C and S protein, antithrombin III (At III) [11,12,13]. Fibrinogen disturbances are less frequent excluding those accompanying disseminated intravascular

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Correspondence address: Katarzyna Jarus-Dziedzic MD, ul. Sonaty 6c/130, 02-744 Warsaw, Poland

coagulopathy (DIC). In 25-30% they are of idiopathic nature [3,14]. Most authors stress that in this group some of the children experienced nasopharyngeal infections, inflammation of cervical lymph nodes, fever of undetermined origin (FUO) or mild trauma of the caput (MTC) a few days or weeks before stroke occurrence [14,15]. Arterial hypertension, diabetes, sclerosis (except for that coexisting with familial hyperlipidaemia) are not significant risk factors of stroke in children [16].

Among other causes, the following should be enumerated: inflammatory and post-traumatic changes of arterial walls as well as fibromuscular dysplasia, Moya-Moya disease and antiphospholipid syndrome [8,17,18].

The aim of the study was to evaluate the usefulness of TCD in ischaemic stroke in children, and particularly to assess the compliance of TCD results with the picture of computerised tomography, magnetic resonance and cerebral angiography.

MATERIAL AND METHODS

A sudden occurrence of transient or permanent neurological defects, confirmed by clinical investigation at admission to hospital was the basic criterion of inclusion into the study group. CT and/or MRI were performed in all the cases, which allowed to exclude haemorrhagic, post-traumatic or neoplastic lesions. The children were also subjected to cerebral angiography and/or angiomagnetic resonance imaging (angio MRI). The time in which these investigations were performed was determined by their availability, but in the majority of cases, these examinations were carried out during the first two weeks after the occurrence of clinical symptoms of ischaemic stroke.

In selected cases, the examinations of circulatory system (ultrasonography of the heart, 24-hour ECG) and coagulation system (AT III, C, S proteins, cardiolipin antibodies) were also performed.

During TCD, pulsed-wave transducer 2 MHz and TCD 2000 S/N unit manufactured by EME was used. The examination was performed in the Department of Neurosurgery, Medical University in Wrocław. Blood flow was registered bilaterally in the following cerebral arteries: middle (MCA), anterior (ACA), posterior (PCA), as well as in vertebral arteries (VA) and basal artery (BA) with the use of standard ultrasonic windows. TCD investigation was supplemented with the measurement of blood flow velocity in common, internal, external carotid arteries, as well as with Doppler Ophthalmic Test (DOT). Blood flow velocity in intracranial vessels was supplemented with haemodynamic test with the compression of internal carotid artery.

Due to large differences in age between examined children, the comparison of mean velocity values for particular arteries was not performed. The following were taken into account in the interpretation of TCD results: asymmetry of blood flow velocity and location of disturbed blood flow in TCD. We compared the values of mean flow velocity (MFV) for particular arteries registered on one side with the values registered on the opposite side. Asymmetry was given as a percentage, while the asymmetry not greater than 20% was considered a border-value of physiological norm.

RESULTS

Study group consisted of 21 children (8 girls, 13 boys) aged 3.5-18 years (mean age 12 years) treated in the Department of Paediatric Neurology of T. Marciniak Specialist's United Hospital in Wrocław, due to the diagnosis of ischaemic stroke – 16 children (including 3 RIND cases) or the incident of transient ischaemic attack (TIA) – 5 children (Table 1 and 2).

In order to confirm the diagnosis, CT of the head was performed in 15 children and MRI – in 17 children. In 5 cases, angiography of the arteries in question was done, and 15 children were subjected to angio MRI.

The following were accepted as the basis of ischaemic lesions in two cases: obliteration of internal carotid artery coexisting with Moya-Moya syndrome in one case and stenosis of left internal carotid artery in the other child. In 7 cases, stroke was most probably of cardiogenic nature: fibrosis of mitral valve cusp, incompetence of mitral, tricuspid valves, post-inflammatory lesions in aortic, mitral valves, atrial fibrillation. In one case, stroke followed disseminated intravascular coagulopathy (DIC). Furthermore, the following disorders were observed: familial hyperlipidaemia (1), hyperprothrombinaemia (1) and inflammatory background in the course of colitis ulcerosa and Herpes virus infection in two cases. In five children, the occurrence of stroke was preceded by: physical exercise, pneumonia, skin graft, open fracture of lower leg, which may be considered risk factors. The cause of the disease was not established in 4 cases.

Table 1. Characteristics of patients with ischaemic stroke (n=16). *HP-haemiparesis, FP-focal paresis

NO	Clinical symptoms	Location on lesion in CT	Location of lesion in MRI	Angio-MRI	Angiography	TCD
1.WE	Left-side HP, consciousness disorders	Right frontal-parietal-temporal region	Right frontal-parietal-temporal region	Obliteration of right ICA	Not performed	No flow in right ICA, decreased flow in right MCA, reverted flow in right ACA, increased flow in right PCA, DOT positive on the right side
2.KM	1993 diplopia, cerebellar syndrome, hypoacusia, right-side HP	No perfomed	1993 left cerebellar hemisphere, 1995-left cerebellar hemisphere	Not performed	1993 vertebral artery-normal	Decreased flow in left AV by 30% when compared to right AV
3.MG	1985 left-side HP, FP of left VII nerve	1985 right internal capsule 0.7 cm	Not performed	Not performed	1985 normal	1985 UDP without features of stenosis greater than 75% 1995 acceleration in right MCA
4.JJ	1989 loss of consciousness motor aphasia right-side HP	1989 left temporalparietal region	Not performed	Not performed	1989 stenosis of left MCA and ICA	1995-accelerated flow in left ICA, low flow in left MCA, increased flow in left PCA
5.MS	Right-side HP focal epileptic attacks	Left internal capsule 1 cm diameter	Left internal capsule	Normal	Not performed	Decreased flow in left MCA by approx. 40% when compared to right MCA
6.PŁ	Loss of consciousness motor aphasia right-side HP bradycardia	Normal	Not performed	Normal	Not performed	Lower flow: left MCA by approx. 45%, left ACA by approx. 50% when compared to right side
7.MB	Loss of consciousness left-side HP	Right frontal region 3.5x4.0 cm	Not performed	Normal	Not performed	Decreased flow in left MCA by approx. 30% when compared to right MCA
8.PA	Left-side HP, FP of right VII nerve	Right temporal region	Right temporal parietal region	Normal	Not performed	Lower flow in MCAr by 30% when compared to left MCA segmental acceleration of flow in right ICA
9.BB	Vision disturbances	Right temporal region	Right temporal-parietal region	Normal	Not performed	Insufficient circulation through ACoA
10.SJ	Features of alternating syndrome	Left parietal region 1.7x1.4 cm	Not performed	Not performed	Not performed	Lower flow in left ACA by 65% when compared to right one
11.KJ	Vision disturbances, aphasia, HP and FP of right VII nerve	Normal	Not performed	Not performed	Not performed	Lower flow in left ACA by 40% and left AV by approx. 20% when compared to the right one
12.MP	Consciousness disorders, motor aphasia, convulsions of left extremities, left-side HP, alexia, disgraphia	1st day: left brain hemisphere, 5th day: evolution of ischaemic area	Not performed	Not performed	DSA normal	Segmental narrowing of left MCA by approx. 70-80%, widening of spectrum, turbulences
13.KZ	An hour convulsion state tetraparesis	* both temporal lobes * in 4 month antrophy of both hemispheres of temporal lobes	Not performed	Normal in 3 month	Not performed	Low flow in AV, symmetrically increased in MCA and in ACA bilaterally
14.AD	Generalised convulsions, right-side HP, aphasia	Normal	Not performed	3 yers later slight stenosis of left ICA	Not performed	Flow: increased in ICA I by 40%, lower in left MCA by 35% lower in left PCA by 45%
15.SD	Defects in the field of vision	Not perfomed	Left parietal lobe	Normal	Not performed	Lower flow in left PCA by 45%
16.PP	Right-side HP	Not perfomed	Left temporal-parietal area	Normal	Not performed	Lower flow in left ICA by 45%

Table 2. Characteristics of patients with transient ischaemic attacks (n=5).

NO	Clinical symptoms	Location on lesion in CT	Location of lesion in MRI	Angio-MRI	Angiography	TCD
1.WW	Vision disturbances, paresthesia of right half of the face	Normal	Normal	Normal	Not performed	Lower flow in MCAl by 25% and Avl by approx. 2% when compared to the right one no record in left PCA
2.OS	Vision disturbances, aphasia, right-side HP, FP of right VII nerve	Not performed	Normal	Normal	Not performed	Turbulent flow in right ICA
3.KP	Vision disturbances, motor aphasia right-side HP	Normal in 1 st 24 hours	Normal in 1 st 24 hours	Normal	Not performed	Lower flow *left ICA by 35% *left MCA by 45%
4.EG	Loss of consciousness right-side HP	Normal in 1 st, 2 nd 24 hours	Normal in 3 rd month	Not performed	Not performed	Lower flow *left ACA by 30% *left ICA by 35%
5.WP	Loss of consciousness right-side HP	Not performed	Not performed	Normal	Not performed	Lower flow *left ICA by 25%

Table 3. TCD result in patients with ischaemic stroke n=16.

NO	Gender	Age	Time interval from stroke	Asymmetry %	Location of lesions in TCD
1.WE	F	15	3 months	30%-MCA 20%-PCA	no flow in right ICA, reverted flow in right ACA
2.KM	F	8/11	3 years	30%-AV	AV left
3.MG	M	3/14	10 years	35%-MCA	MCA right
4.JJ	M	13/18	5 years	35%-ICA 25%-MCA 30%-PCA	ICA left MCA left PCA left
5.MS	F	10	17 days	40%-MCA	MCA left
6.PŁ	M	15	7 days	45%-MCA 50%-ACA	MCA left ACA left
7.MB	F	13	4 days	30%-MCA	MCA left
8.PA	F	13	1 years	30%-MCA 45%-ICA	MCA left ICA left
9.BB	M	12	10 days	—	ACoA
10.SJ	M	3.5	3.5 years	65%-MCA	MCA left
11.KJ	F	15	7 days	40%-ACA 20%-AV	ACA left AV left
12.MP	M	11	7days	80%-MCA	MCA left
13.KZ	M	1.2/3	1.5 years	—	low flow in AV
14.AD	M	3/6	3 years	40%-ICA 35%-MCA 45%-PCA	ICA left MCA left PCA left
15.SD	F	9/10	1 years	45%-PCA	PCA left
16.PP	M	8	8 days	45%-ICA	ICA left

Table 4. TCD result in children with transient ischaemic attacks (TIA) n=5.

NO	Gender	Age	Time interval from stroke	Asymmetry %	Location of lesions in TCD
1.WW	M	14	10 days	25%-MCA 20%-AV	MCA left AV left
2.OS	M	15	15 days	none	turbulent flow in right ICA
3.KP	M	16	3 days	35%-ICA 45%-MCA	ICA left MCA left
4.EG	F	12/15	2 years	25%-ACA 20%-ICA	ACA left ICA left
5.WP	M	13	4 days	25%-ICA	ICA left

TCD examination was performed: in 11 children 30 days after stroke, and in the remaining cases: 1, 3, 5, 10 years after stroke.

Asymmetry

TCD performed in 21 children revealed that in 19 cases asymmetry in blood flow exceeded 20%, including 9 children with asymmetry in one artery, 7 children with asymmetry in two arteries, 2 children with asymmetry in 3 arteries and 1 child with asymmetry in four arteries. In the majority of cases, asymmetry concerned blood flow in middle cerebral arteries (MCA) – 12 cases (asymmetry 25-80%), in anterior cerebral arteries (ACA) – 3 cases (asymmetry 25-50%), in internal carotid arteries (ICA) – 7 cases (asymmetry 20-45%), in vertebral arteries (VA) – 3 cases (asymmetry 20-35%) and in posterior cerebral arteries (PCA) – 4 cases (asymmetry 20-45%). (Table 3 and 4).

Among 16 children with ischaemic stroke, in 14 patients flow asymmetry between the sides was greater than 30%, in the remaining two children the following were observed: circulatory failure through anterior communicating artery in one case, while in the other – bilaterally lower blood flow in vertebral arteries. Among 5 children with TIA, asymmetry of blood flow velocity exceeding 30% was observed in one child, while in 3 cases asymmetry ranged between 20% and 30%.

Normal values of blood flow in examined vessels were recorded only in two cases, including one child with TIA and one – with ischaemic stroke.

TCD allowed to detect obliteration of internal carotid artery in one child with collateral circulation through right posterior cerebral artery, anterior communicating artery and right ocular artery (from external carotid artery). The diagnosis was subsequently confirmed in angiography of carotid arteries. On the basis of TCD investigation, the stenosis of internal carotid artery (ICA) was diagnosed in 4 children. It was characterised by: segmental acceleration of blood flow, decrease in blood flow in middle cerebral artery (MCA) and anterior cerebral artery (ACA) as well as slightly increased blood flow in posterior cerebral artery (PCA) on the same side (in 2 cases), which was confirmed by angiography in one child only.

In one case we observed a clear disproportion between circulation in the anterior part of Willis circle and its posterior part with low blood flow values in vertebral arteries, which might be the evidence of their hypoplasia. In two children, decreased blood flow velocity in vertebral arteries (one or two) coexisted with abnormal flow in the remaining arteries.

Cerebral angiography, magnetic resonance angiography (MRA) and TCD

Intracranial artery angiography performed in 5 children revealed anomalies in two cases: in the first of them – obliteration of internal carotid artery (ICA) with a fine network of collateral circulation vessels of the Moya-Moya syndrome type, and in the second – stenosis of internal carotid artery (ICA) and middle cerebral artery (MCA) on the left side, which corresponded to TCD result. In one child, angiography of right carotid artery performed in 1985 (a few weeks after stroke) did not visualise any vascular lesions, while 10 years later TCD revealed changes of the kind of right MCA segmental stenosis. The child with impaired blood flow in left vertebral artery (VA) and ischaemic lesion in left cerebellar hemisphere visualised in CT demonstrated normal results of vertebral artery angiography. In one case, digital subtraction angiography (DSA) did not confirm segmental MCA stenosis diagnosed in TCD with extensive ischaemic zone in frontal-parietal-temporal region found in CT.

Magnetic resonance angiography (MRA) was performed in 15 out of 21 children; including 5 cases

with the symptoms of TIA and 10 cases with ischaemic stroke. None of the patients with TIA symptoms revealed vascular anomalies. Among 10 children with ischaemic stroke, only two manifested the following lesions: narrowing of internal carotid artery (ICA), and obliteration of internal carotid artery (ICA) with coexistent Moya-Moya syndrome. In these two cases, TCD confirmed lesions found in MRA. Furthermore, we registered blood flow asymmetry greater than 20% in 10 children, including 9 cases with ischaemic stroke and one with TIA. In 5 children, including 4 patients with TIA and one with ischaemic stroke, no pathology was detected either in TCD or in MRA investigations.

Computerised tomography, magnetic resonance and TCD

CT of the head was performed in 17 out of 21 children at various time intervals from the onset of clinical symptoms. In CT, ischaemic focus was present in 11 children with ischaemic stroke. CT performed in 3 children during the first 24 hours after stroke did not reveal ischaemic foci; they were visible only in repeated investigation 5 to 21 days later. Normal results of CT investigation were observed in 4 children with the symptoms of TIA. CT revealed ischaemic foci with respect to the vascularisation of middle cerebral artery (MCA) in 7 patients. TCD was performed in 15 children 3 days to 3 months after the first CT investigation, and in the remaining 6 children 1-15 years later. In all the cases, the location of ischaemic area in CT corresponded to the abnormal blood flow within the artery supplying blood to this area. In the case of extensive ischaemic lesions in CT, disturbed blood flow in a given vessel was more pronounced.

MRI performed in 12 children after ischaemic stroke experienced in the past revealed the presence of ischaemic foci in all of them. MRI picture was normal in 5 children with the symptoms of TIA. Location of changes in MRI corresponded to ischaemic areas observed during CT and to the disturbances in blood flow recorded during TCD.

On the basis of clinical picture as well as CT, MRI, MRA, angiography and TCD ischaemic stroke was diagnosed in 16 children, including 3 cases of RIND and 5 cases of TIA. Among 16 children with clinical symptoms of ischaemic stroke, 14 had blood flow asymmetry greater than 30% detected in TCD. Two children demonstrated insufficient circulation through anterior communicating artery and low values of blood flow velocity through both vertebral arteries, respectively. Among 5 children with TIA, only one patient manifested asymmetry of blood flow greater than 30%.

DISCUSSION

TCD may be used in children in order to diagnose internal hydrocephalus, increased intracranial pressure and vasospasm following subarachnoid haemorrhage and cranial-cerebral injuries, as well as for the detection of vascular malformations (e. g. arteriovenous haemangioma), Moya-Moya syndrome, functional disorders of cerebral circulation (e. g. erectile syndrome), brain death, and finally for the diagnosis of intravascular embolisms, narrowing or obliteration of intracranial vessels and vascular hypoplasia. Some authors also report the existence of significant lesions in TCD in the course of mental illnesses, cerebro-spinal meningitis, encephalitis, severe metabolic disorders with brain oedema, neoplastic diseases, in epilepsy and ventricular bleeding [1,4,10,19,20,21,23]. Many authors raise the issue of TCD usefulness in the diagnosis of hypoxic ischaemic encephalopathy – HIE in newborns [14,22].

In the case of slight and considerable stenosis of arterial vessels, TCD reveals segmental acceleration of blood flow velocity. In large and critical stenoses, blood flow velocity decreases, and in the case of vascular obliteration – there is a complete blockade of blood flow1. In our material, segmental acceleration of blood flow velocity was observed in the majority of children with stroke. Complete blockade of blood flow in internal carotid artery was recorded in one child with total obliteration of this artery. According to many authors, disturbed blood flow in TCD correlates to large extent with ischaemic lesions visualised during computerised tomography (CT) or magnetic resonance imaging (MRI), which correspond to the arterial vascularisation area with abnormal blood flow [1,20,21].

In our material, the location of ischaemic foci in CT and/or MRI corresponded to the lesions in respective arteries registered in TCD. TCD result was in agreement with CT and/or MRI, independently of the time that elapsed from stroke onset. In one case, even ten years later TCD confirmed previous diagnosis of stroke with respect to the vascularisation of left internal carotid artery. Hence, our findings correspond to those reported in literature [1,24]. Kogutt et al. (1994) proved that in the case of children with sickle cell anaemia, TCD is a

reliable and unfailing method which allows to record blood flow disturbances in a vessel supplying blood to the area of ischaemic stroke. TCD proved 94% sensitivity and 30% specificity in this group of patients, when compared to MRI as well as to angio-MRI – 91% sensitivity and 22% specificity, respectively [20].

TCD effectiveness in the diagnosis of narrowing of the main stem of internal carotid artery and middle cerebral artery greater than 60% is estimated at 96% and more [1,2,24]. It is much more difficult to formulate a final assessment of the lesions recorded in anterior cerebral artery and posterior cerebral artery, because these vessels often demonstrate considerable asymmetry of blood flow velocity between the sides as well as anatomical anomalies, even in non-pathological conditions. Therefore, impaired signal received from PCA and ACA does not allow to establish conclusive diagnosis [2,20].

Another issue in the clinical approach to ischaemic stroke are transient ischaemic attacks (TIA), which were usually free from impaired blood flow in intracranial vessels visualised in TCD as well as from any other anomalies in the picture of CT, MRI and MRA. In children with steroid-resistant nephrotic syndrome, chronic renal failure, repeated TIA symptoms leading in time to disseminated vascular lesions were observed. There exists a group of children with risk factors of ischaemic stroke, in whom TCD is a good, non-invasive way to monitor the lumen of intracranial vessels. Soper described a case of a 2-year-old child with diagnosed Wilms syndrome, in whom multifocal ischaemic lesions of the brain related to segmental stenosis of cerebral vessels were observed on the basis of MRI, MRA and TCD [15]. In children, certain role is played by hypoplastic vascular lesions, in which thrombi and embolisms may develop with coexisting risk factors.

The diagnosis of ischaemic stroke in CT during the first few hours after its clinical symptoms is extremely difficult or even impossible in many cases. Therefore, TCD has raised great interest and hopes as it might be useful in the detection of vascular lesions as early as a few minutes after closure of a given vessel.

Finally, it should be pointed out that the method also has its drawbacks. TCD is greatly dependent on the experience of the performer as well as on the co-operation on the part of the patient. Specificity and sensitivity of this method may be enhanced by its more frequent use in children.

CONCLUSIONS

1. TCD allows for a non-invasive evaluation of intracranial vessels in children with ischaemic stroke.
2. Ischaemic foci in ischaemic strokes detected during CT and/or MRI corresponded to the lesions in respective arteries observed during TCD.
3. The results of TCD corresponded to those found in CT and/or MRI, irrespectively of the time that elapsed after the onset of clinical symptoms.
4. In the cases with TIA symptoms, no significant anomalies in blood flow in intracranial arteries were observed.

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