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NEUROLOGICAL DEFICIT SCALE FOR ASSESSMENT OF ISCHEMIC STROKE IN EARLY CHILDHOOD

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The article discusses the data of an original study on development of a clinical scale for neurological deficits severity assessing in children with arterial ischemic strokes (AIS) under the age of 2 years old (SANDYc). The relevance of SANDYc development is caused by inability to use pedNIHSS scale in children under 2 years of age and limitations of the PSOM using in the acute and subacute IS stages in young children. The study presents clinical features of IS course in 31 children aged up to 2 years old, being treated at children's clinical hospital N5 named after N.F. Filatova from 2005 to 2021. The statistical analysis data are presented, showing statistically significant correlations between the assessment results according to SANDYc and the values obtained according to the PSOM and BMRC scales. Additionally, statistical analysis demonstrated correlation between allelic variants A / C and C / C of the MTHFR A1298C gene (p = 0.044) in the examined children and milder clinical course of AIS as assessed by SANDYc.

Keywords: neurological deficits severity assessment scale, ischemic stroke, children, acute stage, clinical assessment.

Introduction. Despite significant progress in diagnostic and treatment methods improvement, arterial ischemic strokes (AIS) in children remain a potential threat of severe neurological disorders development, in some cases with disabling or fatal outcome.

The variety, and on frequent occasions non-specificity, of clinical manifestations significantly complicate timely diagnosis of AIS, especially in young children, which is partly caused by focal symptoms masking with common, non-focal ones [5, 9]. Fast AIS diagnosis in children gives an opportunity to influence clinical course severity and outcome favorability due to the earlier initiation of pathogenetically oriented treatment. At the same time, the accuracy of neurological deficits severity verification significantly increases when using standardization principle [1, 3, 11] in the form of clinical assessment scales, which allows us to avoid subjectivity factor, as well as reflect dynamics of neurological status deviations with greater sensitivity and specificity.

Supposedly because of the difficulties with young children examination, especially in the acute and subacute AIS stages, a generally accepted scale for neurological deficits assessing in this age group has not been developed yet. The pediatric modification of the US National Institutes of Health Stroke Scale (pedNIHSS) [5] has limitations for use in children under 2 years of age, and Pediatric Stroke Outcome Measure (PSOM) [8] is more intended for use in the recovery stage.

The aim of the present study was to develop a scale for neurological deficits severity assessment in children with cerebrovascular accidents (arterial ischemic strokes) in the age group up to 2 years old.

Materials and methods: from 2005 to 2021 we performed the clinical picture analysis of the acute (first 5 days of stroke) and subacute (up to 21 days from the moment of initial manifestations) stages of AIS in 31 children aged up to 2 years old, being treated at children's clinical hospital N5 named after N.F. Filatova.

The minimum age was 6 months, the maximum one 1 year 11 months. In all age groups male predominance was observed (Table 1).

The diagnosing criterion was acute focal neurological symptoms in the clinical picture, persisted for more than 24 hours. Also a mandatory requirement was the presence of changes corresponding to ischemic stroke (IS) according to neuroimaging data (CT, MRI) [2, 6, 12].

All the examined children underwent a routine somato-neurological examination in dynamics, their life and medical histories were studied.

Clinical assessment of neurological disorders severity was conducted according to the developed scale for neurological deficits assessing in young children (SANDYc). Additionally, clinical verification was performed with the PSOM (Pediatric Stroke Outcome Measure) and the six-point scale for muscle strength assessing of the British Medical Research Council (British Medical Research Council, BMRC) [10].

Molecular genetic testing of blood for polymorphism of thrombophilia genetic markers was performed in 17 children with IS using PCR. Real-time allele-specific PCR and restriction fragment length polymorphism technique (RFLP), with polyacrylamide gel electrophoresis and visualization under UV light, were used.

Statistical analysis. Statistical processing of the obtained data was carried out using the programs "Statistica 12.0" (StatSoft, USA), Microsoft Excel-2010 with nonparametric criteria. For each group, a number of statistical parameters were calculated: symptom incidence rate and incidence error, mean value, standard deviation, median, 95% confidence interval for the median. Because of the abnormal distribution the Spearman's rank correlation test was used. To standardize the statistical assessments results the critical values for all studied parameters were defined at the significance level ($p < 0.05$), common for biomedical research.

Results and discussion. The clinical picture analysis enabled definition of 8 main groups of neurological manifestations (indicators) of AIS course in children under 2 years of age.

The groups of common non-focal cerebral symptoms and epileptic disorders were entirely new, not found in the PSOM and pedNIHSS scales when assessing

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neurological deficits in children. The list of groups of clinical manifestations in children with ischemic stroke is given in Table 2.

In all children AIS occurred in carotid artery territory with more frequent involvement of the left internal carotid artery (ICA) (19 children, 61.3%), less often – the right ICA (12 children, 38.7%). Lenticulostriate branches of the middle cerebral artery were mainly affected (29 children, 93.5%), two children had cerebral infarct in anterior choroidal artery territory (6.5%). Ischemic injury area included the internal capsule (25 children, 80.6%), the caudate nucleus (19 children, 61.3%), the lenticular nucleus (19 children, 61.3%), the thalamus (18 children, 58%), and the centrum semiovale (1 child, 3.2%). In all children the clinical picture was presented by motor symptoms in the form of central hemiparesis, in 24 cases combined with facial central palsy (77.4%). The assessment of muscle strength using the BMRC scale in the acute stage of stroke was performed in 26 children, because of the difficulties with its use in infants. The average paresis degree in the upper limb was 2.2 ± 1.05, in the lower limb – 2.5 ± 1.3 points. All children underwent the assessment of neurological deficits severity according to the PSOM scale, the average score was 1.24 ± 0.6, with a minimum score of 0.5, a maximum of -3.0 points.

Based on the clinical picture analysis, a scale for neurological deficit assessing in young children with stroke (SANDYc) was developed. The gradation of parameters changes was carried out in accordance with previously developed criteria [3, 4, 11, 13].

For each group of symptoms neurological disorders severity was assessed from 0 points – absence, to 4 points – the most severe neurological manifestations. When choosing the parameters, assessability of every specific clinical sign in the acute and subacute AIS stages in children of the younger age group was considered. Regression (loss of previously acquired skills) was assessed in the following subgroups: speech skills, fine motor skills and self-care skills. Epileptic disorders included clinical and electrophysiological characteristics. The detailed description of the assessment parameters is presented in Table 3.

The criteria for assessment of regression severity of acquired speech skills, fine motor skills, and social interaction and self-care skills for different age groups will be presented in separate publication due to the large amount of material.

Using the developed scale, we assessed neurological status of 31 examined children with AIS in the acute and subacute stages. The average value of neurological deficit indicator in points was 10.8 ± 3.4, with boundary values of 6 and 18. The interquartile range extends from 8 to 13 points. The distribution and graphical display of the values ranges are shown in Figures 1 and 2.

For additional assessment of neurological disorders severity the PSOM scale was used in all children of the study group (Fig. 3).

The statistical analysis was performed with nonparametric methods because of a lack of normal distribution of the data obtained and the study group size. The Spearman's rank correlation test revealed statistically significant direct relationships between the values of SANDYc and PSOM ($r = 0.45$, $p = 0.0103$, with a threshold value of < 0.05). Also, statistically significant inverse correlations were found between the SANDYc and the BMRC indicators in the subacute AIS stage, for the upper limb $r = -0.634$, $p = 0.0005$, for the lower limb $r = -0.630$, $p = 0.0006$. Negative correlation coefficients are explained by multidirectionality of the scales (maximum deficit severity according to the BMRC scale is 0, and according to SANDYc – -43 points).

Additional statistical analysis made it possible to find an inverse correlation between neurological deficit severity according to SANDYc and the MTH-

Table 1

Age and gender distribution of children with IS under the age of 2 years, total number, n = 31

	Age group		
	6-12 months	1-1.5 years	1,5-2 years
Male	7 (22.6)	7 (22.6)	4 (12.9)
Female	6 (19.4)	4 (12.9)	3 (9.7)
Total number	13 (41.9)	11 (35.5)	7 (22.6)

Table 2

Группы клинических проявлений (показателей) у детей с ОНМК по ишемическому типу в возрасте до 2 лет

Indicators	Number of children with deviations, n (%)
Consciousness level (CL)	1 (3.2)
Common non-focal cerebral symptoms (CNFC)	18 (58.0)
Visible active movements limitation (VAML)	31 (100)
Movement disorders prevalence (after 60 weeks postmenstrual age) (MDP)	31 (100)
Hyperkinesis (H)	13 (2.0)
Cranial nerves (including facial palsy due to central lesions) (CN)	24 (77.4)
Skills regression (degree) (SR) (change in skills acquired before stroke is assessed)	20 (64.5)
Epileptic disorders (in the acute and subacute stages) (E) NB! Repeated paroxysms without epileptiform changes, managed with AET (antiepileptic treatment) during 7 days – 2 points	2 (6.45)
Ataxia (A) Not evaluated in paretic limbs with predominance of movement disorders. In case of hyperkinetic disorders dominance in the examined limb(s), ataxia is also not assessed	0

Table 3

Parameters of neurological deficits assessment in children with stroke according to SANDYc

Indicator	Assessment	Points	Description	Primary source of modification
1	2	3	4	5
CL	Normal	0	Wakefulness, normal arousal response, normal quantity and quality of motor responses	J.J. Volpe, 2008
	Slight stupor	1	Sleepy appearance, arousal response diminished (slight), quantity of motor responses diminished (slight), quality – at high level	
	Moderate stupor	2	Child asleep, arousal response diminished (moderate), quantity of motor responses diminished (moderate), quality – at high level	
	Deep stupor	3	Child asleep, arousal response absent, quantity of motor responses diminished (marked), quality – at high level	
	Coma	4	Child asleep, arousal response absent, quantity of motor responses diminished (marked), or absent, quality – at low level	
CS	No	0		
	One of the symptoms: short-lived headache less than 30 minutes (or its signs), nausea, lack of appetite, general weakness (lack of energy), drowsiness, restlessness	1		
	Single vomiting episode, or presence of two symptoms, headache for more than 30 minutes	2		
	Two vomiting episodes, presence of three or more symptoms, combination of a symptom with a headache lasting more than 30 minutes	3		
	Repeated episodes of vomiting, presence of other symptoms	4		
VAML	No limitations	0	*** assessment is carried out in the limb with the most severe motor deficit** **Mild:** minor active movements limitation, notable to a great extent because of reduced active movements range – compared to the opposite side, or muscle strength in pre-stroke period. Able to hold the limb poised in the air for more than 5 seconds, to stand up, to stand unsupported. **Moderate:** significant active movements limitation, able to hold the limb poised in the air up to 5 seconds (moving against gravity), poor grip strength, short unsupported standing (less than 5 seconds). **Severe:** low-amplitude limb movements, not able to grasp and hold a toy, to stand unsupported. Minimal movements, no power to act against gravity. **Plegia:** complete absence of motor activity in the limb.	Medical Research Council (Great Britain), 1976
	Mild paresis	1		
	Moderate paresis	2		
	Severe paresis	3		
	Plegia	4		

Continuation of the table 3

1	2		3	4	5
MDP	No		0		
	Monoparesis		1		
	Para-/hemiparesis		2		
	Threeparesis		3		
	Tetraparesis		4		
H	No		0		A.A. Skoromets et al., 2012
	Dystonia / Hyperkinesis in one limb, or one muscle group (discrete, short-term)		1		
	Dystonia / Hyperkinesis in several limbs, or muscle groups (intermittent)		2		
	Dystonia / Hyperkinesis in several muscle groups, or limbs, regular		3		
	Prolonged generalized hyperkinesis (including transition from focal forms), choreo-/athetosis		4		
CN	Normal		0		A.A. Skoromets et al., 2012
	1 nerve damage		1		
	2 nerves damage		2		
	Multiple nerves paresis (incl. Bulbar palsy)		3		
SR	Speech	Norm	0		
		Mild	1		
		Moderate	2		
		Severe	3		
		Mutism	4		
	Fine motor skills	Norm	0		
		Mild	1		
		Moderate	2		
		Severe	3		
		Complete loss	4		
	Self-care skills (if acquired before), social interaction	Norm	0		
		Mild	1		
		Moderate	2		
		Severe	3		
		Complete loss	4		
Э	No		0		
	Single epileptic seizure		1		
	Repeated epileptic seizures without epileptiform changes on EEG / single convulsive seizure with persistent epileptiform changes on EEG		2		
	Recurrent seizures with epileptiform changes on EEG, need for basic AET		3		
	Status epilepticus		4		

End of table 3

1	2	3	4	5
A	Mild	1	**Points are scored if one of the signs is present:** minimal tremor when trying to reach an object (toy), slight unsteadiness (up to 5 seconds) in standing and (or) sitting position	
	Moderate	2	Moderate intention tremor when trying to reach a toy, and (or) occasional failed attempts to grasp a toy leading to final successful grasping. Moderate unsteadiness in standing and (or) sitting position (more than 5 seconds, still able to keep balance unsupported)	
	Severe	3	Severe intention tremor, able to grasp an object only with help. Unsupported standing and sitting for less than 5 seconds	
	Complete lack of movements coordination, voluntary movements present	4	Lack of movements coordination, complete loss of balance in standing and sitting positions	
Total		Max = 43		

Note. Criteria for assessing the severity of regression of acquired speech skills, fine motor skills, social interaction and self-service for different age groups will be presented in a separate publication due to the large volume of material.

FR A1298C gene mutation (p = 0.044), allelic variants A / C and C / C. The obtained results may suggest milder clinical course of AIS in children of the younger age group with the MTHFR A1298C polymorphism.

Conclusions. The practical significance of SANDYc lies in the possibility to quantify and ensure objectivity of neurological symptoms severity in children under 2 years of age in the acute and subacute stages of AIS. The obtained strong statistical correlations between the neurological deficit sum scores according to SANDYc and the indicators of generally accepted scales (the PSOM, the 6-point BMRC scale) suggest diagnostic significance of SANDYc for neurological deficit assessment in young children with AIS. The use of additional, previously not applied for comprehensive assessment, parameters, such as common non-focal cerebral symptoms and epileptic disorders, expands diagnostic capabilities of the scale in neurological deficit sum score calculating, and also makes it more accurate and personalized for each individual case of AIS. In case of common non-focal cerebral symptoms severity prevalence over focal ones SANDYc shows higher scores of neurological deficit compared to the PSOM, thus, makes it possible to more accurately assess the clinical picture of AIS acute stage in young children.

Taking into account the small sample of patients in the present study, SANDYc testing in a larger group of children will make possible assessing of its widespread use in various types of stroke, which is already available in multicenter studies. It may prove to be promising to use the scale in children up to 3 years of age, that is include an additional number of children with IS into the comparison group.

Scoring of neurological deficit would enable more accurate dynamic observation of children with IS, use of the results in research work, and continuity of assessment at various stages of medical care. SANDYc practical application in other types of stroke, including hemorrhagic strokes, requires separate study, and verification with existing scales.

The correlation between milder course of IS in children of the younger age group and the MTHFR A1298C gene mutation requires additional research.

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