Clinical and functional characteristics of the central nervous system in children with type 1 diabetes of Almaty City

Abedimova R.A.

Regional Diagnostic Center of the Republic of Kazakhstan, Almaty City

Summary. The issues of diabetic lesions of the central nervous system (CNS) in children are not well understood. The aim of the study was to investigate the clinical and functional state of the central nervous system in children with type 1 diabetes mellitus (T1 DM) in Almaty. 205 children with T1DM aged 3 to 16 years [91 (44.39%) boys and 114 (55.61%)] girls were followed up. The age of children with T1DM averaged 9.73 ± 3.79 years.The duration of T1 DM in children under study ranged from 6 months to 10 years, on average 2.73 ± 2.58 years. The control group was represented by 101 children without T1DM. The groups were matched by age and gender. Examination of children included: an analysis of the perinatal period, clarification of complaints suggesting the presence of CNS lesion symptoms, clinical neurological examination, electroencephalography (EEG). The majority (79.5%) of surveyed children with T1 DM showed signs of CNS lesion, in the form of complaints and cerebrasthenic and cerebral nature, multilocular neurological symptoms and nonspecific EEG changes.
Keywords: type 1 diabetes, children, central nervous system, electroencephalography

Diabetes mellitus (DM) presents one of prevalent diseases of contemporaneity because it is observed all-around ubiquitous frequency disease incidences [1]. Verdict of WHO adjudication committee concluded DM is been taken non-infectious epidemic proportions. Nowadays it should be noted tendency towards type 1 diabetes mellitus (DM1) frequency that increased among children population. It is known DM1 course in children are distinguished with frequent decompensation that, first of all, leading to more frequent complications of diabetes - diabetic neuropathy, encephalopathy, retinopathy, nephropathy, etc. [2].

The nervous system issues in adults by are good cleared in the literature [3], however, but the information about the diabetic central nervous system damage in children is not enough. Therefore, the aim of our study was clinical and functional condition of the CNS in children with type 1 of Almaty.

Materials and methods

205 children with T1DM aged 3 to 16 years [91 (44.39%) boys and 114 (55.61%)] girls were followed up. The age of children with T1DM averaged 9.73 ± 3.79 years. The duration of T1 DM in children under study ranged from 6 months to 10 years, on average 2.73 ± 2.58 years (Table. 1).

The largest share fell to the children with disease duration from 1 to 5 years (Table2).

In accordance with the IDF recommendations [4], the patients were divided into 3 groups depending on the DM1 degree compensation: in the first group were included 49 children (mean age 9.13 + 3.24 years) into levels of glycated haemoglobin (HbA_{1c}) from 6.5 to 7.4 mmol/l, in the second - 55 children (mean age 9.49 + 4.42 years) into HbA_{1c} levels from 7.5 to 9 mmol/l, in the third - 101 children (mean age 10.07 + 3.57 years) whose HbA_{1c} level exceeded 9 mmol/l (Table 3).

The control group was represented by 101 children without T1DM. The groups were matched by age and gender.

From the examination were excluded children who had in their anamnesis the craniocerebral injuries, neuroinfections and other organic lesions of the encephalon.

All the DM1 children have been carefully examined by a pediatric neurologist. Examination of children included: an analysis of the perinatal period, clarification of complaints suggesting the presence of CNS lesion symptoms, clinical neurological

Table 1. Distribution of children with DM by age and sex

Age	**boys**		**girls**		**altogether**	
	abs	*%*	*abs*	*%*	abs	%
3-5 years	17	8.29	20	9.75	37	18.05
6-8 years	16	7.80	23	11.22	39	19.02
9-11 years	22	10.73	26	12.68	48	23.41
12-14 years	32	15.61	38	18.54	70	34.15
15-18 years	4	1.95	7	3.41	11	5.37
altogether	91	44.39	114	55.61	205	

Table2. Distribution of children by sex and duration disease

Sex	**Duration of disease**							
	till 1 year		**1-5 years**		**over 5 years**		**altogether**	
	abs	*%*	*abs*	*%*	*abs*	*%*	*abs*	*%*
boys	42	20.49	38	18.53	11	5.36	91	44.39
girls	41	20.79	49	23.90	24	11.71	114	55.61
altogether	83	40.49	87	42.44	35	17.07	205	

Table3. Distribution of children by level HbA_{1c}

	Level HbA_{1c}, in blood, mmol/l					
	boys		girls		altogether	
	abs	*%*	*abs*	*%*	*abs*	*%*
6.5-7.4	20	9.75	29	14.15	49	23.90
7.5-9	23	11.22	32	15.61	55	26.83
more than 9	48	23.41	53	25.85	101	49.27

examination, electroencephalography (EEG). The condition of the cranial nerves (CN), motor, autonomic, and coordination systems were assessed by neurologic examination.

EEG was performed on 32-channel "Nicolet" encephalograph (USA). The dome-shaped electrodes were put by the international system 10-20 Jasper, were used mono- and bipolar circuit erection diagrams. During recording routine EEG were performed functional tests: arousal reactions, rhythmic photostimulation and hyperventilation for 3 minutes. Basic rhythm of EEG was analyzed - alpha rhythm, its frequency responses, regularity, spatial distribution, the index of representation and also alpha rhythm reaction on the functional load.

Infant children (3-3.5 years) were examined in asleep state; at the same time were analyzed stages and physiological transits of sleep.

During EEG results interpreting, international classification of EEG conclusion by Luders (2000), also age peculiarities [5].

Results and Discussion

Perinatal period analysis of children with T1DM had showed that in 102 (49.7%) patients' mothers were observed physiological pregnancy and childbirth course, the remaining 103 (50.3%) ones had one or other pathology of pregnancy and childbirth: asiderotic anemia, termination of pregnancy threat, nephropathy, gestosis, accelerated, prolonged labor, a large fetus weight, mild and moderate degree of asphyxia. The mean weight children at birth of the main group compounded 3263,41 ± 30,71g, mean value by Apgar score 7,29 ± 0,04 points.

Statistically reliable difference between the control group and children with T1DM were not observed: pathologic pregnancy and childbirth in the control group were observed in 49 (48.5%) of mothers ($p > 0.5$). The average birth weight of children in the control group - 3275,57 ± 34,68 g value by Apgar scale - 7,41 ± 0,05 points.

Psychomotor children development of main and control group in their tender years had no statistically significant differences: the majority of children (91.2%) of the main group before 1 year old were developed appropriately by age, only 8.8% were observed a slight delay of psychomotor development that expressed in latter independent walk and appearance of speech. In the control group data was properly totaled 86.1% and 13.9% ($p > 0.5$).

Questioning of patients with T1DM was exposed complaints cerebroasthetic and cerebral nature: headaches are occurred in 52.7% (108), fatigability – in 58.5% (120) meteodependence – in 47.3% (97), transport intolerance – in 32.2% (66), emotional lability in 91.7% (188), sleep disorders - in 38,5% (79). In 15.1% (31) children with long-lasting T1DM, were noted affective disorders in the form of hysteroid reactions, character changes, dysphoria, aggressiveness, in 1.46% (3) were observed convulsive attacks.

It should be noted that the foregoing complaints were observed only in 13.6% (28) children before T1DM disease, the incidence is increased for sure after the development of the disease ($p < 0.05$). Similar complaints have been observed in children regardless of the T1DM duration.

The control group children are also noted: headaches - in 36.6% (37), fatigability – in 44.5% (45), transport intolerance - in 30.6% (31), emotional lability - in 56.4% (57). Revealed complaints were reliably more frequent in the main group ($p < 0.05$).

Neurological examination revealed disseminated neurological micro symptoms from the side of CN, motor and coordination fields/spheres in 46.3% (95) of T1DM children and 42.5% (43) children in the control group were not observed serious neurological symptoms in both groups. During CNN condition examination was exposed micro symptoms from the side of facial nerve in the form of flatness nasolabial fold, mild facial asymmetry in 19.0% (39) patients of the main and in 14.8% (15) children of the control group; from the side of oculomotor nerves in the form of hidden convergent or divergent strabismus - in 17.5% (36) and in 12.8% (13) children respectively. An examination of the motor sphere in children with T1DM and in healthy children were observed decrease in muscular tonus in 46.3% (95) and in 42.5% (43), tendinous anisoreflexia – in 42.4% (87) and in 40.5 % (41), moderate coordination disorders in the form of static ataxia in Romberg posture, unsatisfactory finger-nose test in 32.6% (67) and in 28.7% (29) respectively.

Thus, a significant statistical difference was not observed between the children of both groups in the neurological status ($p > 0.5$).

On the ground of complaints, medical history and examination data children with T1DM were established clinical neurological syndromes: asthenoneurotic - in 47.3% (97), vegetovascular dystonia syndrome - in 36.5% (75), psychopathic - in 15.1% (31). In the control group asthenoneurotic syndrome was occured in 42.5% , vegetovascular dystonia syndrome - in 34.6% (35) ($p > 0.05$), psychopathic syndrome was not observed in the control group ($p < 0.001$).

Normal EEG pattern was significantly less observed in the main group in 20.5% (42) of children with T1DM and in 56.4% (57) of children in the control group, in the remaining children of main in 79.5% (163) and in 43.6 % of the control group were recorded various changes of functional activity of brain ($p < 0.05$).\

Children with T1DM with normal EEG pattern had the average frequency of alpha rhythm 9.73 + 0.15 Hz, the average amplitude - 53,69 ± 3,16 mV, the average index - 57,61 ± 1,90%. Alpha rhythm of children with normal EEG pattern was characterized by correct zonal distribution, in other words was registrated in parietooccipital parts. Alpha rhythm was regular and appropriated by age. In all children with normal EEG pattern were observed adequate reactions of activity on functional loads. In the control group, the main activity was characterized by following factors: average frequency - 9,91 ± 0,18 Hz, the average amplitude - 55,87 ± 4,12 mV, the average index - 58,52 ± 1,85%.

Non-specific changes in the form of main rhythm regularity with heightened index of theta-and delta-oscillations in the background recording, the zonal distribution of the alpha rhythm, mismatching the age peculiarities, were observed in 53.6% (110) of children of the main group and in 28.7% (29) – in control. The average alpha rhythm distribution of children with T1DM was equaled 7,98 ± 0, S Hz, the average amplitude - 61,96 ± 2,37 mV, the average index - 29,19 ± 0,59%. Correct zonal distribution of main activity in children with rhythm regularity disturbance was observed in 51.8% (57) of children, in the remaining 48.2% (53) – zonal boundary displacement was observed. Reactions of the main activity on the functional loads were adequate. In the control group the observable parameters quantity were following: the average frequency of alpha rhythm - 8,05 ± 0,21 Hz, the average amplitude - 60.28 + 1.87 mV, the average index - 30,12 ± 0,74%.

The main activeness slowdown of first-degree background recording was observed in 23.4% (48) of children with T1DM and in 12.9% (13) of children in the control group. The average frequency of alpha rhythm with main activeness slowdown of background recording in children with T1DM was compounded 6,43 ± 0,20 Hz, the average amplitude 78,5 ± 4,74 mV, the average index - 20,2 ± 0,85%. Zonal boundary displacement was observed in 62.5% (30), the correct spatial alpha rhythm distribution - in 37.5% (18) children. Reactions on functional loads were nonhomogeneous. Thus, the activation reaction was adequate in all children, but in 2.4% (5) children with T1DM were recorded epileptiform activity (EA) in rhythmic photostimulation and hyperventilation as complexes of sharp-slow wave that carried generalized character. In the control group mentioned indicators were: average frequency of alpha rhythm - 6,75 ± 0,32 Hz, amplitude - 81,3 ± 1,54 mV, EA - in 1.9% (2) of children ($p > 0.05$). It should be noted that three of the five children (60.0%) with T1DM and registered EA were marked epileptic seizures in the type of generalized tonic-clonic seizure (GTCS), which were one-fold and were observed in ketoacidotic coma except one child whose seizures are noted in hypoglycemia. The remaining 40.0% (2) of children epileptic seizures were not observed.

Thus, in children with T1DM revealed neurological symptomatology, confirmed by instrumental survey techniques. Asthenic and cerebral nature complaints and EEG changes were observed significantly more frequently in children of the main group. It should be noted that such complaints and EEG changes were exposed in children with T1DM, which mothers' past history had physiological pregnancy and childbirth course. Occurrence of disseminated neurological symptoms and its absence of significant differences between groups can be explained as the result of feto-maternal disease or childbirth of examined observed children' mothers. It is known that perinatal pathology leads to hypoxemic ischemic encephalopathy, which is expressed by occurrence of residually organic insufficiency and exposed by disseminated neurological symptoms. Complaints pointing to the involvement of the CNS and EEG changes were significantly more likely observed concluding in children with T1DM than in children without DM1. Let us suppose the occurrence of CNS lesions of diabetic genesis in physiological pregnancy and childbirth course in past history, and also mixed (residually diabetic) genesis - in occurrence of unfavorable perinatal history. At the present time, there are studies proving diabetic CNS lesions with type 2 diabetes mellitus in the literature [6,7]. By our opinion, toxic action of

chronic hyperglycemia products on the brain of the child can not be excluded.

Conclusions.

1. Children with type 1 diabetes mellitus are observed clinical signs of the central nervous system lesions.
2. Children with T1DM signs of central nervous system lesions are significantly more frequently occured than in children without diabetes.
3. The majority (79.5%) of children with T1DM are found electrobiological activity changes in the brain.

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