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Clinical and functional features of diabetic polyneuropathy in children

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Introduction

Diabetes mellitus (DM) is one of the leading medical-social problems of the modern medicine. The incidence rate growth of insulin-dependent diabetes mellitus (IDDM), or type 1 diabetes mellitus (type 1 DM), is observed worldwide. In 2000 in St. Petersburg the prevalence rate of DM in children (0–14 years) was 91.5 per 100 000, twice as high as in 1985. Also the incidence rate changed from 5.7 per 100 000 children in 1985 to 14.6 in 2000 [2]. Nervous system disorders are the most frequent complication of DM which negatively affects quality of life, causes disability, growth of mortality rate, and large economic losses [10, 11]. Neurological complications may be observed in patients with both type 1 DM, and type 2 DM [8, 9].

The aim of this investigation is to study clinical characteristics, neurophysiological picture and dynamics of these indices in children with diabetic polyneuropathy during the basal-bolus insulin therapy and adjuvant treatment.

Materials and methods

During 2005–2009 in St. Petersburg Child Diabetes Centre 102 children were observed aged 7– 17 (mean age 14.1 years), among them 45 girls (44%) and 57 boys (56%) with type 1 DM complicated by diabetic polyneuropathy. Disease duration ranged from 3 to 16 years (mean 8.6).

The group for examination and dynamic monitoring consisted of 39 patients chosen from these 102 children. Disease duration ranged from 3 to 15 years (mean 7.8). The mean age in this group was 14 years old.

The observed children were divided into 2 groups: 45 patients (44.1%) got only basal-bolus insulin therapy with glycaemic control, the rest 57 children (55.9%) – additionally the preparation of thioctic acid (Thioctacid, VIATRIS GmbH & Co KG, Germany) up to 6 months (mean 4.8 months).

The degree of diabetic polyneuropathy was estimated according to the classification of American Academy of Neurology and American Diabetes Association in San-Antonio [7]: thus, 69 children (67.6%) had peripheral diffuse polyneuropathy, 33 patients (32.4%) – subclinical stage. Severity of polyneuropathy was estimated with international neurological questionnaires: Neurological Symptoms Score (NSS), Neuropathy Disability Score (NDS).

Along with routine somatic and neurological assessment [5] a monofilament (weight 10 g, Semmes-Weinstein) was used to define touch sensibility, and a graduated tuning-fork Rydel-Seiffer, vibration frequency 128 hz, – to define vibratory sensibility, also an apparatus Bio-Thesiometer was used for this aim (PVD Bio-Thesiometer, USA). Pain and tactile hyperesthesia as one of the main criteria of diabetic polyneuropathy diagnostics was estimated in our investigation also according to the rules of palm and nines that are usually used in surgery to estimate burns area [3].

Neurophysiological investigation was fulfilled with an apparatus Neuro–MVP (Russia) according to the standard method of stimulating electromyography [1].

The results were processed with the standard programme STATISTICA V.6.0 for Windows (StatSoft, Inc., 2001) with Student's criterion, Whitney–Mann, Phi2*2, Spearman. LSD TEST variance analysis was made, and also discriminant function analysis – to test validity of the classification. The critical confidence level of statistical hypothesis (p) was taken equal to 0.05 [4, 6].

Results

The family history showed that 37 children (36.3%) had close relatives with diabetes mellitus, the rest 65 families (63.7%) denied this disease. Among families with burdened familial history in 25 cases (67.6%) the relatives had type 2 diabetes mellitus, 9 (24.3%) – type 1 DM, in 3 families (8.1%) both type 1 DM and type 2 DM were observed.

In the present investigation glycated hemoglobin (HbA1c) was taken as the main criterion of glycaemic control. Eleven children (10.8%) had HbA1c below 7% (compensation), 42 children (41.2%) – 7–9% (sub-compensation), and 49 patients (48%) were with HbA1c greater than 9%.

During primary inspection 28 children (27.4%) presented problems connected with DM.

18 children stated cramps in calf muscles and feet during night sleep, in the morning and at night, 10 children complained of fatigability in feet and paresthesia in feet and calves during exercises. In neurological state of the examined children no changes of cranial innervation are fixed. Muscle tone and muscle strength are up to the standards. While studying deep reflexes we noted knee-jerk and Achilles tendon reflexes decline in 11 children (10.8%), 1 child (0.9%) had no Achilles tendon reflex. Pain hyperesthesia of lower extremities was noted in 65 patients (63.7%), 21 children (20.6%) had changes in upper and lower extremities sensibility.

When vibratory sensibility was tested the values varied within standards: 8 – in 13 children (12.8%), 7 – in 86 (84.3%), 6 – in 3 (2.9%). In test with Bio-Thesiometer the values were normal: 0.09 μ – in 2 (1.9%), 0.16 μ – in 19 (18.7%), 0.25 μ – in 66 (64.7%), 0.36 μ – in 15 children (14.7%) without significant asymmetry. Scores of neuropathy severity on the scale NDS were as follows: expressed – 0.9%; moderately expressed – 60.8%; on the scale NSS: severe – 3%, expressed – 2%, moderate – 19%. Types of peripheral nerves lesion according to electroneuromyographic data are presented in the picture 1.

In the group for dynamic monitoring 18 children (46.1%) got basal-bolus insulin therapy with glycaemic control, 21 child (53.9%) additionally got the preparation of thioctic acid, treatment course lasted up to 6 months (mean 4.8). Four children in this group had glycated hemoglobin below 7%; 19 children – 7–9%; 16 children – greater than 9%.

As for neurological status, during dynamic monitoring no cranial nerves, muscle strength or muscle tone changes were observed. Only 2 children (5.1%) showed knee-jerk and Achilles reflexes decline.

When vibratory sensibility was tested the values varied within standards: 8 – in 25 children (64.1%), 7 – in 13 (33.4%), 6 – in 1 (2.5%). In test with Bio-Thesiometer the values were also normal: 0.16 μ – in 10 children (25.7%), 0.25 μ – in 24 (61.6%), 0.36 μ – in 1 (2.5%), 0.49 μ – in 4 (10.2%). The values of vibratory sensibility were symmetrical. Scores of neuropathy severity on the scale NDS were as follows: expressed – in 3% of cases, moderately expressed – in 23%; NSS: moderate – in 5.2% of cases.

Neurophysiological data of the examined group is presented in the picture 2.

The statistic analysis results demonstrated that integrated values in children of the main group who got basal-bolus therapy were lower than in children who got thioctacid (4.67 ± 2.84; 6.3 ± 3.27; $p = 0.008$). Nerve Conduction Velocity of sensory fibers of the peroneal nerve in the

main group was significantly higher than in the group of adjuvant treatment (49.7 ± 5.4; 43.7 ± 15.8; p = 0.02).

Values of Galvanic-skin reflex of footstep in the main group were also lower than in the group of dynamic monitoring (2.06 ± 0.33; 2.2 ± 0.34; p = 0.03). In the latter group NDS scores in children who got basal-bolus therapy were lower than in children who got additional preparation (1.5 ± 2.4; 4.2 ± 4.06; p = 0.02). Results of Spearman correlation demonstrated that child's age correlated with integrated scores NDS of polyneuropathy severity (r = 0.3, p = 0.002), and several symptoms of sensibility disorders: hyperalgesia area (r = 0.25, p = 0.01), touch sensibility disorders in foot (r = 0.2, p = 0.02). The duration of diabetes mellitus affected self-estimation of polyneuropathy severity at night on the scale NSS (r = 0.2, p = 0.02), growth of ulnar nerve M-responses amplitude (r = 0,2, p = 0,03) and decrease of Nerve Conduction Velocity of afferent fibers of the peroneal nerve (r = -0.2, p = 0.04). Dynamic monitoring showed that additional therapy correlated with absence or decline of knee-joint and Achilles reflexes (r = 0.4, p = 0.008), and higher scores on the sub-scales NDS и NSS (complaints' period and symptoms) (r = 0.3, p = 0.04).

The obtained data processed with variance analysis by LSD TEST showed that in both sub-groups of the main group decrease of NDS scores was observed. There was no significant difference on the scale NDS between children who got basal-bolus insulin therapy and the ones who got the preparation of thioctic acid (p = 0.57).

Taking into account the results of dynamic examination of children with diabetic polyneuropathy, we offer to arrange clinical units of polyneuropathy in the following way. The present scheme is based on the patients' complaints, use of international scales NSS and NDS, rules of palm and nines to define area of hyperesthesia as one of the first symptoms of diabetic polyneuropathy, values of glycated hemoglobin affecting diabetes mellitus course.

Diagnostics scheme of diabetic polyneuropathy severity level in children

Mild: no complaints; NSS 0; NDS 6 scores; tactile hyperesthesia 1% (ankle and hand base); pain hyperesthesia 1% (ankle and hand base); glycated hemoglobin greater than 7–9% .

Moderate: complaints are possible; NSS 3–4 scores; NDS 7–8 scores; tactile hyperesthesia 1% (ankle and hand base); pain hyperesthesia 8% (mid-calf); glycated hemoglobin greater than 9%.

Severe: complaints of cramps, pain in feet; NSS 5–6 scores; NDS 8 and more scores; tactile hyperesthesia 8% (mid-calf), 9% (knee-joint); pain tactile hyperesthesia 8% (mid-calf), 9% (knee-joint); glycated hemoglobin greater than 9%.

To test validity of the present scheme we used discriminant function analysis with computation of linear discriminant function (LDF). The following results were got: in main group diagnosis accuracy was 88.1% average, for mild level – 98.1%, moderate – 81.8%, severe – 64.3%.

Viewing the results of discriminant function analysis we can state that the suggested scheme is highly informative. The most significant symptoms are NDS and NSS scores, and also values of tactile and pain hyperesthesia which are defined with the rules of palm and nines.

Conclusions

The present investigation demonstrates that clinical symptoms of diabetic polyneuropathy develop in children with type I diabetes mellitus when the disease duration exceeds 3 years. Polyneuropathy presents itself as disorders of upper and lower extremities peripheral nerves with prevalence in distal parts of lower extremities. EMG shows disturbances of peripheral nerves electrogenesis, decrease of nerve conduction velocity, amplitude and distal latencies of M-responses and F-waves in motor, sensory and autonomic nerve fibers. Correlation of clinical and electroneuromyographic data allows to define prevalence and severity of difficult to be identified sensory disorders in children with diabetic polyneuropathy. Variance analysis of clinical data and neurophysiological examination allowed to develop the differential diagnostics scheme of neuropathic disturbances according to severity level.

Under dispensary observation with adequate basal-bolus insulin therapy and strict glycaemic control mild forms of diabetic polyneuropathy prevail, and symptoms of autonomous neuropathy are absent.

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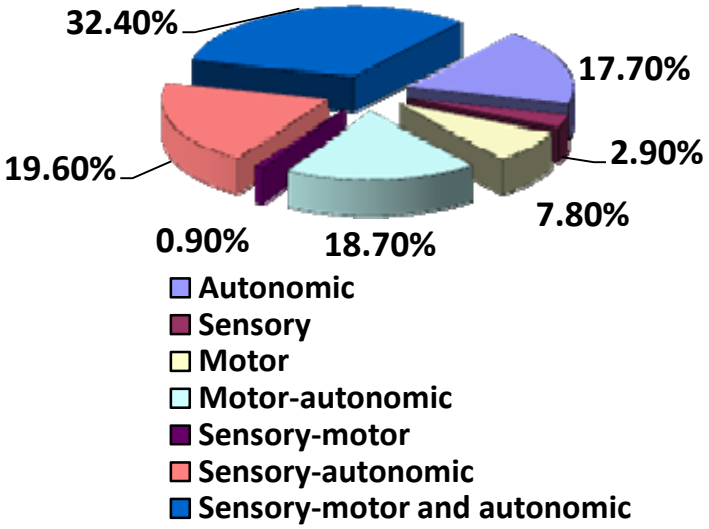
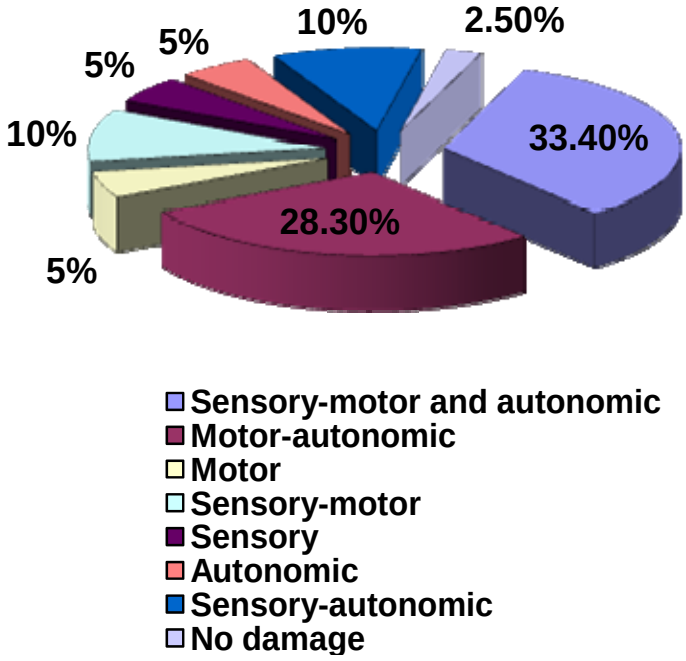
Summary

In St. Petersburg Child Diabetes Centre 102 children aged 7–17 with type 1 DM complicated by diabetic polyneuropathy were observed by means of the routine neurological assessment, standard neuropathic scales (NDS, NSS), EMG and Nerve Conduction Velocity. The investigation demonstrated that the clinical symptoms of neuropathy developed in 3 years after the DM had been diagnosed. Polyneuropathy presents itself as disorders of upper and lower extremities peripheral nerves, with prevalence in distal parts of lower extremities. EMG showed decrease of nerve conduction velocity, amplitudes and distal latencies of M-responses and F-waves in motor, sensory and autonomic nerve fibers. Variance analysis allowed to develop the differential diagnostics scheme of neuropathic disturbances according to severity level.

Key words: children, type I diabetes mellitus, polyneuropathy, functional disturbances.



Picture 1. Types of peripheral nerves lesion according to electroneuromyographic data in the main group



Picture 2. Types of peripheral nerves lesion according to electroneuromyographic data in the examined group

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Neonatal Hypoglycemia as the Factor in the Development of Neurologic Impairments in Infants.

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Key words: hypoglycemia, newborns, neurodevelopment.

Damaging effect of hypoglycemia on the brain is caused by formation of substances adversely influencing on cerebral tissue metabolism in the oxidation process.) Hypoglycemia syndrome can be of various clinical presentation, and in certain cases of asymptomatic course. In the presence of clinical semiology more often mild and moderately severe hypoglycemia is shown in the form of hyperexcitability syndrome, and profound one – distress syndrome.

Ключевые слова: гипогликемия, новорожденные, неврологическое развитие.

Выявлено, что гипогликемический синдром может иметь различную клиническую картину, а в некоторых случаях имеет бессимптомное течение. При наличии клинической симптоматики чаще всего легкая и среднетяжелая гипогликемия проявляется в виде синдрома гипервозбудимости, а тяжелая – синдрома угнетения.

The nervous system affection in cases of glucose homeostasis in an organism has been studied thoroughly for the last years [12, 14, 15, 16, 19].

Glucose is the basic, and typically the unique substratum of power exchange in brain. If it stops supplying the brain, endogenetic resources can provide its normal metabolism only within 10-15 minutes [5, 8].

Damaging effect of hypoglycemia on the brain is caused by formation of substances adversely influencing on cerebral tissue metabolism in the oxidation process. Besides, glucose,