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RELATION BETWEEN LIMITED JOINT MOBILITY AND PERIPHERAL NERVE FUNCTION IN DIABETIC CHILDREN*

*Can Fıçıcıoğlu MD***, *Meral Kızıltan MD****, *Ahmet Aydın MD*****
*Perihan Baslo MD******

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In order to assess the relation between limited joint mobility (LJM) and peripheral nerve function in diabetic children, peroneal nerve amplitude and motor conduction velocity as well as sural nerve amplitude and distal latency were measured with a Medelec MSG electromyograph. LJM was examined by observing the hands in the prayer position of 60 unselected diabetic children (average age 11.2 ± 3.1 years; mean duration of diabetes 4.1 ± 3 years) and 31 healthy controls. Of 60 patients, 38.3 percent had limited joint mobility. no influence of sex on expression of LJM was found. Its appearence was influenced by age, duration of diabetes and metabolic control (HbA1c) ($p < 0.001$, $p < 0.001$, $p < 0.001$, respectively). The mean amplitude, nerve conduction velocity and distal latency values in diabetic children with LJM were slower than those in the normal control group (peroneal amplitude $p < 0.01$, peroneal MCV $p < 0.001$, sural amplitude $p < 0.001$, sural distal latency $p < 0.001$). Of four patients with stage IV LJM, three had symptomatic neuropathy diagnosed using the criteria suggested by Dyck. Consequently, LJM identifies a population at risk for development of diabetic neuropathy. Thus, being easy and sensitive, LJM determination may provide both the physician and the patient himself with an important motivation to improve diabetic control in an effort to prevent dibetic neuropathy. *Key words: diabetes, neuropathy, limited joint mobility, childhood.*

Since first reported by Rosenbloom in 1974, limited joint mobility (LJM) has been increasingly recognized as a common manifestation of childhood diabetes, with reported prevalences varying between eight and 43 percent[1-6]. These contractures may involve the hands, feet and larger joints. Thickening of the skin may also be associated with LJM. LJM may precede the onset of clinical complications of IDDM by sufficient time to be utilized as a marker for these complications.

Diabetic neuropathy is a frequent complication of diabetes mellitus. The classical signs of neuropathy are rarely found in children with insulin-dependent diabetes.

* From the Metabolism-Nutrition Unit, Department of Pediatrics, and the Department of Neurology, İstanbul University Cerrahpaşa Faculty of Medicine, İstanbul.

** Pediatrician, İstanbul University Cerrahpaşa Faculty of Medicine.

*** Associate Professor of Neurology, İstanbul University Cerrahpaşa Faculty of Medicine.

**** Professor of Pediatrics, İstanbul University Cerrahpaşa Faculty of Medicine.

***** Professor of Neurology, İstanbul University Cerrahpaşa Faculty of Medicine.

The frequency of electrophysiological abnormalities and peripheral neuropathy has varied widely from nine to 72 percent in different studies reported on diabetic children[7-15].

The aim of this study was to evaluate the relationship between LJM and peripheral neuropathy in diabetic children.

Material and Methods

The study group consisted of 60 insulin-dependent diabetic children from four to 16 years of age (mean ± SD: 11.1 ± 3.1) in whom the duration of diabetes ranged from one to 12 years (mean ± SD: 5.1 ± 3.1), and 31 nondiabetic children from four to 16 years of age (mean ± SD: 10.9 ± 2.8). The diabetic children were treated with two daily injections of human insulin, the dosage of which was adapted according to blood glucose monitoring with dextrostix and a glucometer. No children were treated with isoniazid, and none had a history of drug dependence or rheumatologic disease. None had a family history of hereditary neuropathic disorders.

Serial glycated hemoglobin (HbA1c) values every three months were measured by the colorimetric technique originally described by Fluckiger and Winterhalter[16] with normal concentrations of 6.3 to 7.2 percent.

During routine physical examinations, to in order demonstrate joint mobility, each patient was asked to approximate the palmar surfaces of the interphalangeal joints of both hands with the fingers fanned. Normal extension (approximation) at the interphalangeal joints is usually a minimum of 180°. For definitive diagnosis and staging of LJM, passive extension of the fingers, wrist, and elbow was done.

LJM was classified using Brink-Starkman[1] staging criteria as follows:

Stage 0; no stiffness, no joint abnormalities; Stage I: stiffness of skin only; Stage II: flexion contractures of opposing fifth fingers bilaterally; Stage III: bilateral contractures of more than the fifth fingers; Stage IV: wrist involvement bilaterally; Stage V: other joint involvement.

LJM was assessed by two pediatric diabetologists (each time the same physicians) together at more than one visit in order to confirm the presence of LJM and to stage it correctly. The absence of diabetes was known to the examiners who assessed LJM in the control group.

The amplitude and conduction velocity of the motor fibers of the peroneal nerve in both lower extremities, and the sensory amplitude and distal latency of the sural nerve were measured in the patients and healthy children by the same observer using a Medelec (MSG) electromyograph.

Complete neurologic examination and electromyographic measurements were performed on all children by a neurologist who was not aware of the presence or absence of LJM. Muscle strength was evaluated according to the principles

suggested by the Medical Research Council[17]. Tendon reflexes were evaluated in the biceps brachii, triceps brachii, brachioradialis, quadriceps and gastrocnemius soleus muscles. Sensory deficit was evaluated at three different points from distal to proximal on each extremity. Cotton wool was used to assess touch-pressure. Disposable pins and a 25 cm long, 28 Hz tuning fork were used for pain and vibratory sensation, respectively. Joint position was tested by manually displacing the great toe or finger.

The findings of the neurologic examination were scored as to neurological symptoms and neurological disability. The criteria for the diagnosis and staging of diabetic neuropathy were as follows[15,17]:

Stage 0-no neuropathy.

Stage Ia-early subclinical (asymptomatic) neuropathy: abnormality of amplitude or nerve conduction (more than 3 SD below the mean for normals) or distal latency (more than 3 SD above the mean for normals) of one or more attributes in two or more nerves and not due to a disease other than IDDM or to faulty electrode placement or low nerve temperature.

Stage Ib-subclinical (asymptomatic) neuropathy: abnormalities of both peripheral nerve test and neurologic examination (abnormality of one or more of muscle strength, tendon reflexes or sensation, judged to be due to diabetic neuropathy).

Stage II-symptomatic neuropathy: two or more abnormalities of nerve conduction, neurologic examination or neuropathic symptoms. Neuropathic symptoms present but of lesser severity than in Stage III.

Stage III- disabling neuropathy: two or more abnormalities of peripheral nerve test, neurologic examination or neuropathic symptoms. Disabling neuropathic symptoms present.

Statistical methods: Statistical analyses were performed using Chi-square test, Fisher's exact test, Kruskal-Wallis analysis of variance, Mann-Whitney U-test, and the stepwise regression procedure.

Results

Of 60 patients, 38.3 percent (n: 23) had limited joint mobility. Two subjects (8.6%) had stage I, 11 subjects (47.8%) had stage II, four subjects (17.3%) had stage III and six subjects (26%) had stage IV involvement of their interphalangeal joints. The presence of contractures was significantly related to mean longitudinal HbA1c (coefficient of variation for HbA1c value was 12.1%), duration of diabetes and age ($p < 0.001$, $p < 0.001$, $p < 0.001$, respectively). We did not find LJM in the nondiabetic control group (Table I). The peroneal motor conduction velocity (MCV) was the most significant correlate with LJM, followed by HbA1c, neuropathy

(symptomatic + asymptomatic) and duration of diabetes, which were next in importance as determined by step-wise regression analysis (Peroneal MCV: r^2: 0.77, F: 19.3, $p < 0.001$; HbA1c: r^2: 0.49, F: 11.7, $0.001 < p < 0.01$; neuropathy: r^2: 0.47, F: 11.5, $0.001 < p < 0.01$; duration of diabetes: r^2: 0.43, F: 11.1, $0.001 < p < 0.01$).

Table I: Duration of Diabetes, HbA1c Values and Age (Mean ± SD) in Diabetic Children with and without LJM and in Normal Controls

	Diabetic children with LJM (n: 23)	Diabetic children without LJM (n: 37)	Non diabetic children (n: 31)	Significance		
Duration of diabetes	7.3 ± 2.05	2.1 ± 1.6		$p < 0.001$*		
HbA1c	14.3 ± 1.6	9.5 ± 1.3	6.1 ± 0.4	$p < 0.001$*	$p < 0.001$**	$p < 0.001$***
Age	13.5 ± 2.3	9.9 ± 2.8	10.9 ± 2.8	$p < 0.001$*	$p < 0.001$**	$p > 0.05$***

* Significance between diabetic children with and without LJM.
** Significance between diabetic children with LJM and controls.
*** Significance between diabetic children without LJM and controls.

No influence of sex on expression for LJM was found (p: 0.97, chi-square test). Of 23 diabetic children with LJM, 13 (56.5%) had either clinical or subclinical neuropathy. Diabetic neuropathy was significantly more common in diabetic children with LJM (p: 0.0000149, Fisher's exact test). The mean amplitude, nerve conduction velocity and distal latency values in diabetic children with LJM were slower than in the normal control group (common peroneal amplitude $p < 0.01$, peroneal MCV $p < 0.001$, sural amplitude $p < 0.001$, sural distal latency $p < 0.001$) and in the diabetic group without LJM (peroneal amplitude $p > 0.05$, peroneal MCV $p < 0.001$, sural amplitude $p < 0.001$, sural distal latency $p < 0.001$) (Table II). Of six patients with stage IV LJM, three had symptomatic neuropathy diagnosed using the criteria suggested by Dyck[17]. Three other patients had both abnormal peripheral somatic electrophysiologic nerve test results in two or more nerves and pathologic findings in the neurologic examination (asymptomatic neuropathy). Three of the patients with stage IV LJM had retinopathy and one had nephropathy. The duration of diabetes and the values of HbA1c as the degree of metabolic control of patients with stage IV LJM were significantly greater than those of patients with less severe LJM ($p < 0.001$, $p < 0.001$, respectively). One of the four diabetic children with stage III LJM had asymptomatic neuropathy. Three of the 11 patients with stage II LJM had asymptomatic neuropathy. Three other patients with stage II LJM had only abnormal electrophysiological test results in one or more attributes of two or more nerves, and were diagnosed as having early subclinical neuropathy. Subclinical neuropathy was diagnosed in only two patients without LJM. The frequency of both clinical and subclinical neuropathy was 25 percent.

Table II: Electrophysiologic Measurements (Mean ± SD) in Diabetic Children with and without LJM and Control Group

	Diabetic children with LJM (n: 23)	Diabetic children without LJM (n: 37)	Non diabetic children (n: 31)	Significance		
Common peroneal CMAP* (milivolts)	2.9 ± 1.9	3.1 ± 1.6	4.5 ± 2.5	$p > 0.05^{**}$	$p < 0.001^{***}$	$p < 0.001^{****}$
Common peroneal MCV* (m/s)	39.7 ± 6.9	48.5 ± 9.2	49.4 ± 6.9	$p < 0.001^{**}$	$p < 0.001^{***}$	$p > 0.05^{****}$
Sural SNAP* (microvolts)	11 ± 6.3	17.4 ± 5.9	17.4 ± 6.9	$p < 0.001^{**}$	$p < 0.001^{***}$	$p > 0.05^{****}$
Sural distal latency (m/s)	4.8 ± 1.04	3.7 ± 0.9	3.4 ± 0.7	$p < 0.001^{**}$	$p < 0.001^{***}$	$p > 0.05^{****}$

*CMAP: Compound muscle action potential amplitude.
MCV : Motor conduction velocity.
SNAP : Sensory nerve action potential amplitude.

* Significance between diabetics with and without LJM.
** Significance between diabetics with LJM and controls.
*** Significance between diabetics without LJM and controls.

Discussion

LJM is a common complication of IDDM and is seen more frequently in diabetic children than in the normal population[1-6]. A simple screening test to find LJM is to ask the patient to press the palms of the hands together as if in prayer. Patients with LJM are unable to oppose the palmar surfaces together. The exact pathogenesis of LJM is not clear, but it is thought to be due to connective tissue glycosylation in children and adults with diabetes mellitus; these patients are more likely to develop complications associated with diabetes because their microvascular systems and intracellular structures undergo glycosylation in a similar fashion[18, 19]. It is often overlooked because it causes little disability and is therefore thought to be of little clinical importance.

Our data suggest an association of LJM with diabetic neuropathy in children with IDDM. LJM was noted in 23 (38.3%) of the 60 children with IDDM. The presence of LJM was significantly associated with longitudinal HbA1c values and with the duration of diabetes. Of 23 diabetic children with LJM, 13 (56.5%) had either clinical or subclinical neuropathy. Three of the patients with stage IV LJM had both clinical neuropathy and retinopathy, and one of them had nephropathy. Ten patients with stage I, II or III LJM had no other diabetic complications except subclinical neuropathy. Our results suggest that the more severe the LJM, the more likely that diabetic complications will be diagnosed.

The relationship between LJM, diabetic renal and retinal complications is well known[5, 18, 20, 21]. The relative risk of nephropathy and retinopathy if a patient has LJM is reported as 6:1 and 4:1, respectively[1]. Although the prevalence of microvascular complications has been reported in most studies on LJM, the prevalence of neuropathy has been stated in few of them[22, 23]. Brink et al.[1] reported the relative risk for diabetic neuropathy in the presence of LJM as 4:1. Jung et al.[23] described 23 adult diabetics with LJM who also had evidence of neuropathy. Starkmann et al.[21] reported a significant association of LJM and neuropathy in patients less than 40 years of age. We could not compare our results with those of others because there has been no similar study in diabetic children. LJM may be used as a marker to identify diabetic patients who are at risk for the development of diabetic neuropathy. Thus, LJM determination may provide the physician and the patient himself with an important motivation to improve diabetic control in an effort to prevent diabetic complications, including diabetic neuropathy. Further studies are necessary in order to delineate the links between the pathogenetic mechanisms of LJM and peripheral neuropathy in diabetes.

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