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Limited joint mobility in diabetic children: a risk factor of diabetic complications?

L Madácsy, M Peja, K Korompay, B Biró

Second Department of Paediatrics and Department of Ophthalmology, Postgraduate Medical School, and Hospital for Pulmonology, Miskolc, Hungary

Limited joint mobility (LJM) was detected in 24 of 55 children with type I diabetes. Among children with longer duration of diabetes (5 years) 15 of 25 had LJM. Ten of these 15 also had preclinical diabetic retinopathy. LJM, impaired respiratory function and early retinopathy together were detected in 8 patients. Three children had early retinopathy without LJM but two of them also had impaired respiratory function. The findings were not related to the degree of metabolic control. These results confirm the great importance of connective tissue changes in childhood diabetes with respect to the early development of diabetic microvascular disease.

It has been shown that diabetes mellitus is accompanied by widespread biochemical, morphologic and functional abnormalities of collagen and elastin [3, 11, 15]. Previously we reported impaired respiratory function in diabetic children, probably due to an abnormal elastic behaviour of the lung [12], and diminished vital capacity has been observed in a diabetic boy suffering from joint contractures [1]. Recently it has been suggested [14] that limited joint mobility affecting mainly the proximal interphalangeal joints of the hands indicates an increased risk for early development of microvascular complications in childhood diabetics. Earlier, we found a significantly higher prevalence of early retinopathy in diabetic children with limited joint mobility than in patients without joint limitation [9]. Simultaneously, an increased prevalence (36.5%) of joint limitation was observed in patients with type I diabetes who had a significantly higher incidence of retinopathy than patients with normal joint mobility [7].

The aim of the present study was to investigate the association of limited joint mobility, impaired respiratory function and preclinical diabetic retinopathy in childhood type I diabetes mellitus.

Patients and Methods

Fifty five insulin-dependent children and adolescents were evaluated whose diabetes had become clinically apparent before the age of 14 years. Their age ranged from 5 to 18 years (mean 13.3 $\pm$ 5.1), the duration of diabetes ranged from 1 to 10 years (mean 4.5 $\pm$ 2.6). They had no history of previous lung disease or atopy and none of them smoked cigarettes. All patients were free from manifest proteinuria.

To demonstrate limited joint mobility, the patient attempts to approximate tightly the palmar surface of the inter-

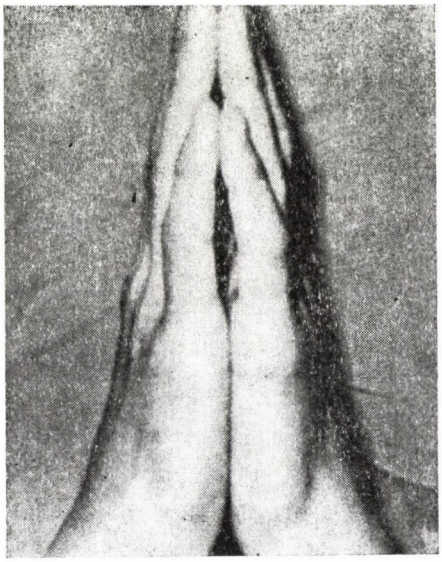

FIG. 1. Limited joint mobility in a diabetic child stage II

phalangeal joints of both hands (Fig 1). Joint contractures were classified in three stages according to Grgic et al [6] as follows. Stage I: unable to make contact with some portion of one finger of each hand; Stage II: unable to make contact with two or more fingers of each hand; Stage III: joint limitation of all fingers of each hand, plus in some larger joints (wrist or elbow).

Respiratory function data of all but five subjects were measured with the patient seated in a constant volume whole body plethysmograph (Fenyves-Gut, Basle). All lung volumes were quoted at BTPS (Body Temperature Pressure Saturated) conditions. Predicted values were taken from Polgár [13].

Fluorescein angiography was performed in patients having had diabetes for more than 5 years. Signs of preclinical retinal microangiopathy were evaluated according to Brooser [2].

The degree of metabolic control was estimated by repeated measurements by the Boehringer test of haemoglobin A_1c in each individual.

Student's t test was used for statistical analysis.

RESULTS

Limited joint mobility was detected in 24 patients; 15 were classified as stage I, 9 as stage II. Clinical data of patients with normal joint and with limited joint mobility are shown in Table I. Duration of diabetes and the mean insulin dose differed significantly between the two groups ($p < 0.01$ and $p < 0.05$, respectively). The latter finding would be expected in view of the longer duration of diabetes. No statistical differences were apparent between the two groups in age at diagnosis, in sex distribution and in the level of metabolic control.

The increased frequency of joint limitation with longer duration of diabetes is also shown in Fig 2. The shortest duration of the disease in any patient with joint limitation was just over one year. Most of the chil-

TABLE I

Clinical data of diabetic patients

	Patients with normal joints (n = 31)	Patients with limited joint mobility (n = 24)	Significance
Age at onset of diabetes, years	8.9 ± 1.8	9.3 ± 2.0	N.S.
Duration of diabetes, years	2.9 ± 1.7	6.5 ± 1.9	$p < 0.01$
Hb A_1, per cent	10.8 ± 1.4	11.3 ± 2.1	N.S.
Daily insulin dose, units/kg/day	0.87 ± 0.1	1.12 ± 0.2	$p < 0.05$

Results are mean ± SD

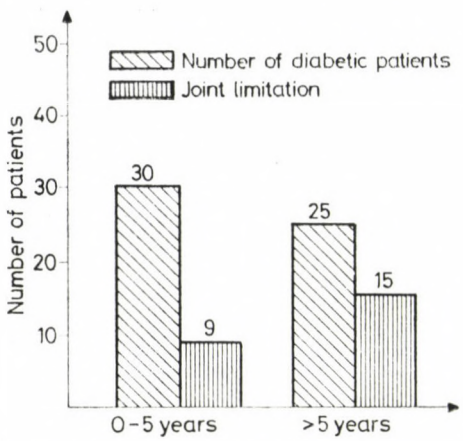

FIG. 2. Frequency of joint limitation according to duration of diabetes. Number of patients is indicated above the columns

dren were unaware of any abnormality of their hands and so it was not possible to evaluate exactly when the joint limitation had started. The 30 patients with a duration of less than 5 years included 9 patients with joint limitation; the 25 patients with a duration of more than 5 years included 15 with joint limitation.

The frequency of preclinical retinal microangiopathy in patients who had diabetes for more than 5 years is shown in Fig 3. Among the 10 children without joint limitation, 3 had microvascular abnormalities, while among 15 children with limited joint mobility, 8 had preclinical retinal changes.

Pulmonary function data in diabetic children with and in those without joint limitation are shown in Table II. All values except for the data of airway resistance are expressed as per cent predicted, as determined by the subject's height and age. There were significant differences between the two groups in total lung capacity (TLC), in airway resistance (Raw), and in peak expiratory flow measured at 50% of forced vital capacity (PEF50%). TLC and PEF50%

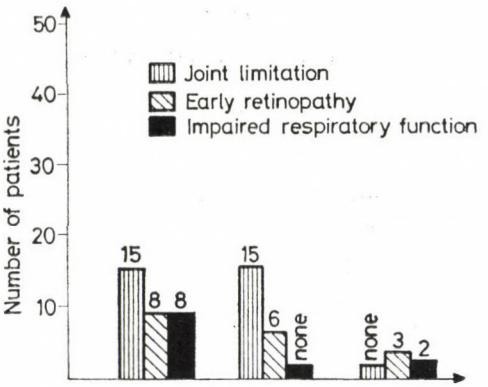

FIG. 3. Frequency of early retinopathy and impaired respiratory function, according to presence of joint limitation in patients with diabetes for more than 5 years. Number of patients is indicated above the columns

TABLE II

Comparison of pulmonary function data in diabetic patients with joint limitation and those without it (values are mean ± SD)

Patients	Age, years	Duration of diabetes, years	VC per cent pred.	TLC per cent pred.	Raw, cm H_2O lit/sec	PEF per cent pred.	PEF 50 per cent pred.
With joint limitation (n = 24)	16.1 ±1.2	6.4 ±0.8	92 ±4	88 ±4	3.1 ±0.2	95 ±5	90 ±3
			N.S.	$P < 0.05$	$P < 0.01$	N.S.	$P < 0.05$
Without joint limitation (n = 26)	11.4 ±0.9	3.1 ±0.6	99 ±5	100.5 ±3	2.0 ±0.1	102 ±8	112 ±7

VC = vital capacity
TLC = total lung capacity
Raw = airway resistance
PEF = peak expiratory flow
$PEF_{50\%}$ = peak expiratory flow measured at 50% of forced vital capacity
per cent pred. = per cent predicted value

were significantly lower ($p < 0.05$), Raw was significantly higher ($p < 0.01$) in patients with limited joint mobility.

The frequency of retinal microangiopathy and altered respiratory function according to the presence of joint limitation in subjects with diabetes of more than 5 years duration is shown in Fig 3. Limited joint mobility was detected in 60% of these patients. Preclinical retinal microangiopathy, disturbances in respiratory function, and joint limitation together have been shown in 32% of patients. Three children had retinal microangiopathy without joint limitation but two of them also had impaired pulmonary function.

Discussion

Limited joint mobility, mainly involving the small joints of the hand, is a common manifestation of childhood onset type I diabetes [6]. Its prevalence varied from 8.4 to 36% in different diabetic population [6, 7, 14]. We found an even higher prevalence (43%) in our study [9].

Although the exact aetiology of limited joint mobility in diabetes is unknown, increased cross-link formation with accumulation of inflexible collagen has been demonstrated in induced diabetes in animals [4]. It is always difficult to extrapolate from animal studies to human disease but it does appear that collagen structure and biosynthesis are abnormal, particularly in the skin of human diabetics [5].

Recently, Lyons and Kennedy [8] investigated the glycosylation of skin collagen from diabetic patients with and without limited joint mobility. Although their results do not support the hypothesis that non-enzymatic glycosylation of collagen would play an important part in the development of joint limitation in diabetes, the possibility that subsequent degradation of the ketoamine link may play a role remains to be investigated [8].

Abnormalities in lung elastic behaviour due to the widespread elastin and collagen abnormalities in diabetes have been shown in 11 young men suffering from type 1 diabetes [16], and earlier we observed impaired pulmonary function in diabetic children [12]. In our present study significant differences were found in three parameters of pulmonary function between patients with joint limitation and those without it, i.e. total lung capacity, airway resistance and peak expiratory flow measured at 50% of forced vital capacity. Although such abnormalities in lung elastic behaviour are, in some respects, similar to those that occur during normal aging [17], their presence in childhood without lung disease is extremely rare, and it seems that the observed changes are due to alterations in tissue elasticity. The relation between limited joint mobility and the early development of microvascular complications in type I diabetes has been postulated by Rosenbloom et al [14] and has been confirmed by other reports [7, 9]. These findings suggest that the alterations of periarticular connective tissue are related to changes occurring in the microvasculature [14]. Retinopathy is a sequel of diabetes mellitus that causes significant morbidity in the form of visual loss, however, describing the association of retinopathy with the degree of metabolic control, the age of onset and duration, and genetic factors, have been contradictory [10].

Therefore, detection of limited joint mobility in diabetic children would appear to identify patients who are exceptionally at risk for the development of diabetic retinopathy.

In conclusion, our data support the concept that limited joint mobility is another chronic complication of diabetes developing prior to retinopathy,

nephropathy and neuropathy [8]. On the other hand, abnormalities in lung elastic behaviour could also be an evidence of connective tissue changes in diabetes.

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L Madácsy MD
Pf 188
3501 Miskolc, Hungary