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GASTRIC EMPTYING TIME IN CHILDREN WITH PROGRESSIVE MUSCULAR DYSTROPHY*

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Gastric emptying was evaluated in 11 male children (mean age 8.2 ± 3.2 years) with progressive muscular dystrophy to detect gastrointestinal smooth muscle involvement. No patient had gastrointestinal symptoms. Gastric emptying studies were performed by using 500 μCi of technetium 99m sulfur colloid bound to a scrambled egg, and scintigraphic measurements were taken continuously for 60 to 90 minutes. The gastric emptying studies were compared with those of eight male children (mean age 8.2 ± 2.8 years) without gastrointestinal or muscular disorders. The mean percentage of retention of gastric isotope was significantly greater in the study group than in the control group. These data suggest that dysfunction of the smooth muscle of the upper gastrointestinal tract is detectable in children with progressive muscular dystrophy, even when gastrointestinal symptoms are absent. *Key words: progressive muscular dystrophy, smooth muscle, gastric emptying.*

The X-linked recessive or progressive type of muscular dystrophy is one of the most common forms of the muscular dystrophies. The disorder is caharacterized by: a) onset in early childhood; b) symmetrical involvement of the pelvic girdle musculature first and of the shoulder girdles later; c) enlargement of the calves (pseudohypertrophy); and d) rapid progression that usually leads to the inability to walk before age 12 or 16, and to death in the second or third decade of life. Patients with Duchenne muscular dystrophy have a dystrophin deficiency, whereas patients with Becker muscular dystrophy have abnormal dystrophin[1]. Immunologic evidence of dystrophin has also been reported in smooth muscle, heart and brain[2,3]. Several autopsy reports in muscular dystrophy patients comment on the presence of typical dystrophic changes in visceral muscle[4-7]. Visceral smooth muscle involvement of the gastrointestinal tract may be prominent in the muscular dystrophies and may give rise to clinical manifestations or may be asymptomatic for some time[7]. We believe that smooth as well as skeletal muscle is affected in progressive muscular dystrophy. Therefore, the purpose of this study was to demonstrate whether the smooth muscle of the stomach is functionally impaired in progressive muscular dystrophy with radionuclide gastric-emptying studies.

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Material and Methods

The study population consisted of 11 male children with progressive muscular dystrophy. No patient had joint contractures or clinical evidence of muscle wasting from birth. The mean age of the patients was 8.2 ± 3.2 years (range 5-13 years). The control group consisted of eight boys without gastrointestinal or muscle disorders. The mean age was 8.2 ± 2.8 years (range 6-12 years). The clinical characteristics of the study group are described in Table I.

Table I: Clinical Characteristics of Patients with Progressive Muscular Dystrophy

Patient no.	Age (months)	Clinical stage	Serum CK (N 27-221 U/L)	Muscle ultrasound	Muscle biopsy	Electromyography
1	56	Mild	13.800	PMD	PMD	Myopathic
2	108	Severe	5.860	PMD	PMD	Myopathic
3	146	Severe	6.024	–	PMD	Myopathic
4	156	Severe	5.218	–	PMD	Myopathic
5	63	Mild	16.500	PMD	PMD	Myopathic
6	66	Moderate	18.000	–	PMD	Myopathic
7	60	Moderate	6.480	PMD	PMD	Myopathic
8	72	Mild	8.600	PMD	PMD	Myopathic
9	87	Moderate	40.000	PMD	PMD	Myopathic
10	132	Severe	9.140	–	PMD	Myopathic
11	13	Severe	4.410	PMD	PMD	Myopathic

CK : Creatine kinase.
PMD : Progressive muscular dystrophy.
Mild : walks and clims stairs without assistance.
Moderate : walks unassisted but cannot rise from chair or climb stairs.
Severe : walks in long leg braces but requires assistance for balance.

The diagnoses in this study were established on the basis of the clinical examination, family history and laboratory investigations. All children were examined by a pediatric cardiologist, and telecardiographic and electrocardiographic studies were done. In all 11 patients, needle electromyography was performed according to the standard procedure. Muscle biopsies were performed under local or general anesthesia. For the histologic studies, the biopsy specimens were stained with hematoxylin-eosin.

None of the patients in the study group had gastrointestinal symptoms. The control subjects were ultimately found to have no gastrointestinal motility or muscle disorders. In all cases, informed written consent for participation in this study was obtained from the parents.

Gastric emptying studies were performed with a modification of methods reported elsewhere[6, 8]. A test meal consisting of an omelet sandwich (one egg, two slices of bread) labeled with 500 μCi of technetium 99m (^{99m}Tc) sulfur colloid with 100 ml of water was ingested after a fast of at least four hours. Continuous scintigraphic measurements were then taken for 60 to 90 minutes with a gamma camera (General

Electric Starcom 3200) positioned over the supine subject's abdomen. Time zero was defined as the time of meal completion.

After correction for decay of ^{99m}Tc and patient movement, gastric emptying was quantitatively expressed as a percentage $CT_t/CT_0 \times 100$ where C_t was the count rate of ^{99m}Tc at any time in the stomach and CT_0 was the initial count rate of ^{99m}Tc in the stomach).

Statistical methods: Data were reported as mean ± SD. Mean values across patient groups were compared using the Mann-Whitney H test. A p value of less than 0.05 was required for statistical significance.

Results

The clinical characteristics in patients with progressive muscular dystrophy are reported in Table I. No serious problems were uncovered by cardiologic examination. The clinical stage of disease was defined according to Rose and Walton[9].

The percentage of retention of solids at 60 minutes was significantly greater ($p < 0.05$) in patients with progressive muscular dystrophy (81 ± 7%; range 70-91%) than in control subjects (58 ± 7%; range 47 69%). The minimal degree of gastric retention at 60 minutes was 70 percent in the study group. However, the maximal degree of gastric retention at 60 minutes was 69 percent in the control group. No patient in the study group had gastric retention results at 60 minutes in the control range. The percentage of solids at 90 minutes in patients with progressive muscular dystrophy and control subjects was also significantly different ($p < 0.05$). The gastric retention rate of the study group was 61 ± 11 percent (range 46-76%), and in the control group was 36 ± 10 percent (range 20-46%, Table II, Fig. 1).

Table II: Gastric Retention Rate in the Study and Control Groups

	Study group		Control group	
Patient no.	60 min %	90 min %	60 min %	90 min %
1	80	57	47	20
2	73	57	59	42
3	82	52	69	43
4	70	53	57	41
5	91	77	56	23
6	88	75	49	21
7	75	55	62	46
8	89	76	61	38
9	79	64	–	–
10	81	46	–	–
11	81	57	–	–
Mean:	80.8 ± 6.6*	61.2 ± 11.2*	57.5 ± 7.0*	36.2 ± 10.0*

* $p < 0.05$.

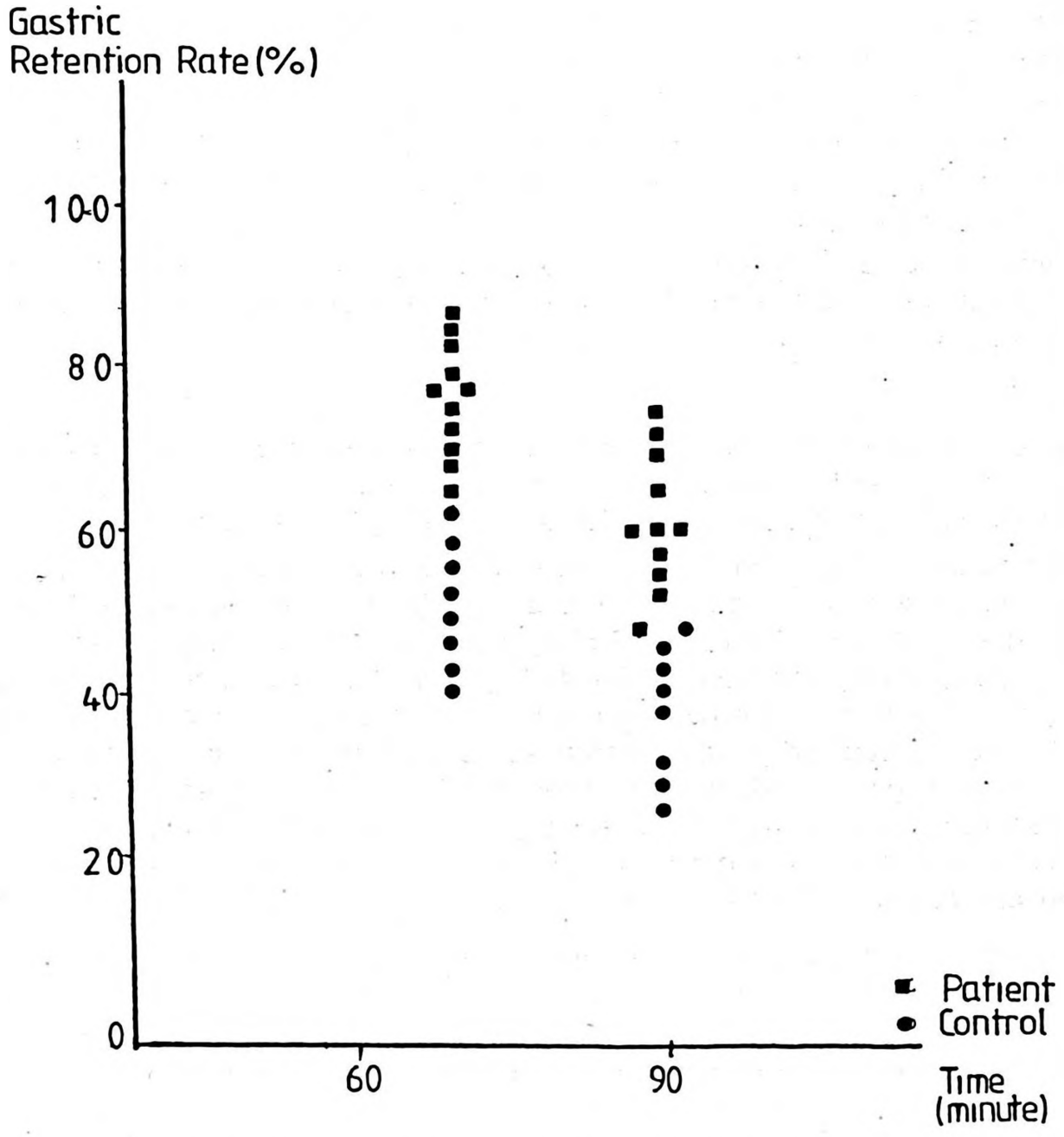

Fig. 1: Gastric Retention in the Study and Control Groups.

Discussion

In the published studies on progressive muscular dystrophy, the pathological and clinical involvement of smooth muscle in the gastrointestinal tract has received little attention[8]. The earliest report of smooth-muscle loss and of its replacement by adipose and connective tissue in the stomach is attributed to Bunting[10]. Later, autopsy descriptions of Duchenne's dystrophy by Bevans[4], Huvos and Pruzunski[5] noted fatty infiltration and smooth-muscle degeneration in the muscular layers of the stomach and intestine. Nevertheless, the prevalence of pathologic

gastrointestinal involvement remains unknown, and a clinical correlation with gastrointestinal symptoms has been infrequently documented[11-13].

The results of this study indicate that many children with progressive muscular dystrophy have gastric motor dysfunction. All of the patients in the present study had delayed gastric emptying. These findings confirm previous observations in adults with various muscular dystrophies[7].

Our subjects had motor dysfunction of the stomach, in which only smooth muscle is present. The delayed gastric emptying is most likely caused by weakness of diseased smooth muscle. The smooth muscle abnormalities were similar to those found in dystrophic skeletal muscle in patients with progressive muscular dystrophy[2, 3, 8, 12].

Progressive muscular dystrophy is a disorder characterized by severe, progressive muscle wasting. Mapping of the gene responsible for these disorders to a specific region of the x-chromosome marked the first step in a series of discoveries leading to the cloning of the gene and identification of its protein product, dystrophin. This protein is localized in the surface membrane of normal muscle fibers. Dystrophin was clearly localized in the smooth muscle layers in the lungs, stomach, digestive organs and ureter but was absent or reduced in the smooth muscles of patients with progressive muscular dystrophy[2, 3, 13]. These results suggested a possible systemic dysfunction of smooth muscle layers due to deficiency of dystrophin in progressive muscular dystrophy[3].

Gastrointestinal involvement in patients with progressive muscular dystrophy may cause a feeling of fullness or bloating, or may even prove to be fatal as a result of pseudo-obstruction syndrome[14, 15]. Gastrointestinal symptoms may dominate the clinical picture, but in most cases motility disorders in patients with progressive muscular dystrophy cause no serious problems[7]. Our findings suggest that gastrointestinal motor abnormalities in our patients were not related to the age of the subjects or the clinical stage of the disease.

We believe that smooth muscle disorders in progressive muscular dystrophy may be more common than is generally appreciated. Early demonstration of gastrointestinal motor dysfunction may lead to earlier treatment (e.g., with prokinetic drugs).

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