Carbohydrate and Lipid Metabolism in Relation to Body Composition in Myotonic Dystrophy

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SUMMARY

Body composition and carbohydrate and lipid metabolism were examined in seventeen patients with myotonic dystrophy (MD). Body cell mass and body fat were determined with isotope dilution methods. Adipose tissue fat cell weight was measured and total fat cell number of the body could be estimated. Fasting concentrations of blood glucose, plasma triglyceride, cholesterol, and insulin as well as of glucose and insulin after ingestion of 100 gm. of glucose were also determined.

In comparison with pertinent controls, MD patients showed no difference in body weight, although body composition was markedly altered with decreased body cell mass and increased body fat mass. Patients without physical impairment showed no derangements of metabolism. However, disabled MD patients with pronounced decrease of body cell mass had decreased glucose tolerance and increased levels of fasting plasma insulin and lipids. It was concluded that deranged lipid or carbohydrate metabolism is not a primary characteristic of MD but a phenomenon secondary to muscular impairment and atrophy. Intact muscle function is probably important in regulation of lipid and carbohydrate metabolism. DIABETES 22:238-42, April, 1973.

A high incidence of diabetes mellitus among patients with myotonic dystrophy (MD) has been observed repeatedly.[1-6] Usually, the diabetes is mild and does not require insulin treatment. An excessive insulin response to a glucose load or an insensitivity to exogenous insulin has also been demonstrated. The reason for these abnormalities is not known, although several explanations have been offered.[6-10]

The relationship between, on the one hand, carbohydrate and lipid metabolism and, on the other hand, body composition and physical activity is evident from several observations. Obesity with a high concurrence of diabetes mellitus and elevated insulin production is a striking example.[11,12] Plasma insulin concentration correlates positively with total body fat, particularly the size of the fat cells.[13] This association is, however, broken by acute prolonged physical activity,[14] physical training,[15] or diabetes mellitus.[16] The other extreme of the dependence of carbohydrate and lipid metabolism on body composition is illustrated by athletes, who, with a high muscle mass and little body fat, are able to assimilate glucose very rapidly in spite of low plasma insulin values; they also have low plasma lipids.[17]

A recent study revealed the low muscle mass in MD patients in spite of a normal body weight.[18] The present work was designed to evaluate the influence of physical activity and muscle mass on carbohydrate and lipid metabolism in patients with MD.

CLINICAL MATERIAL

Seventeen patients with different degrees of MD were studied. Myotonic phenomenon in skeletal muscles was clearly apparent as an early manifestation, while muscle atrophy dominated and invalidated the patients in a late stage of the disease. All patients were examined electromyographically and had typical findings.

Before metabolic study, the patients were allocated into three functional groups according to their physical ability. Group 1 comprised nine patients without impairment of physical activity. A forty-year-old man (no. 6 in table 2) was an active athlete. Group 2 included six patients who could no longer perform their usual work but could still handle minor activities in their homes. Group 3 consisted of two disabled women using wheelchairs.

Some characteristics of the patients are given in table 1. Basal metabolic rate was low. Baldness and testicular atrophy was present in two men in group 2. Several of the patients had cardiac arrhythmias including

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TABLE 1

Clinical material

Group	Number of patients	Age (years)	Cataract*	Heredity for MD	Basal metabolic rate†
Women					
1	3	31, 46, 63	2 (1)	2	—2, —33 (4), —10
2	4	51, 58, 52, 53	5	4	—25, —10 (6), —23 (2), —8 (10)
3	2	51, 69	1 (1)	2	—11 (8), +1 (2)
Men					
1	6	40, 34, 32 27, 20,21	2	3	—26, —13, —22 —23, —13, —12
2	2	63, 55	2 (2)	1	—12, —10 (9)

* Numbers within parentheses indicate number of patients with enucleation of the lens.
† Per cent deviation from normal routine standard. Average values of number of determinations given within parentheses.

different types of conduction defects. Some of the patients also had hyperostosis frontalis interna.

A group of randomly selected fifty-year-old women[19] and a group of medical students with an average age of twenty-three years[20] served as controls.

METHODS

Body composition was determined by isotope dilution methods.[21-23] Fat cell diameter was determined by a microscopic method[24] in a specimen of adipose tissue obtained by percutaneous needle biopsy[25] in the gluteal region in the men and in the femoral region in the women. The fat cell size from these areas has been demonstrated to be representative of major subcutaneous adipose tissue depots at the age and sex in question.[19] Total fat cell number was estimated by dividing body fat by an average fat cell weight, determined from the diameter measurements and calculations according to Goldrick,[26] assuming a density of the fat cell triglyceride of 0.915.[27]

After overnight fasting, the concentrations of blood glucose[28] and heparin plasma immunoreactive insulin,[29] triglyceride,[30] and cholesterol[31] were determined. Classification of lipoprotein abnormalities was performed by paper electrophoresis described by Lees and Hatch.[32] After administration of 100 gm. of glucose orally, blood glucose and plasma insulin were determined at thirty-minute intervals up to two hours after ingestion. Student's *t* test was utilized for comparisons between patients and controls.

RESULTS

Table 2 shows the results of the investigations. A direct comparison between the MD patients without and those with physical impairment (group 1 versus groups 2 and 3) showed decreased body cell mass, increased body fat, decreased glucose tolerance, and elevated plasma lipids in the latter groups. The comparison was not considered entirely pertinent, however, because most of the patients in group 1 were considerably younger than the others.

Group 1 which consisted mainly of men not older than forty years, was compared with a group of controls made up of young men. These MD patients with no physical impairment were shorter and had lower body cell mass and higher body fat than the controls but were not different with regard to body weight or the metabolic variables. Groups 2 and 3, consisting mainly of middle-aged women, was compared with a control group of middle-aged women. These disabled MD patients had marked decrease in body cell mass. However, body weight was not decreased, due to an increase in body fat. Glucose tolerance was decreased, and fasting plasma insulin and lipids were elevated.

There were no significant correlations between plasma insulin values on the one hand and body fat or fat cell size or number on the other.

DISCUSSION

The metabolic data revealed a higher frequency of abnormalities in MD patients who were physically disabled. Statistical analyses showed that the MD patients without physical impairment were shorter and had a lower body cell mass and an increase in body fat than pertinent controls. The difference in age between patients and controls might well have contributed to the increased body fat,[20] and the difference in height probably contributed to the lower body cell mass in the MD group.[23] No significant changes were found in the metabolic variables. With physical disability, however, several aberrations were found in both lipid and carbohydrate metabolism in association with more pronounced

TABLE 2
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Results of determinations in patients with myotonic dystrophy

Patient no.	Sex	Age (yr.)	Length (cm.)	Body weight (kg.)	Body cell mass (kg.)	Body fat (kg.)	Fat cell weight (μg.)	Fat cell number ($\times 10^{10}$)
1	M	20	162	42	14.1	3.9	—	—
2	M	21	178	77	29.5	19.7	0.45	4.4
3	M	27	175	72	26.0	18.8	0.41	4.6
4	M	32	168	62	29.5	19.7	0.23	8.6
5	M	33	164	58	25.0	9.8	0.20	4.9
6	M	40	181	69	26.9	12.5	0.42	3.0
7	M	55	174	70	18.5	16.6	0.83	2.0
8	M	63	181	75	21.7	18.8	0.30	6.3
9	F	31	165	55	19.0	11.1	0.52	2.1
10	F	46	163	48	11.3	11.9	0.51	2.3
11	F	63	161	67	14.7	23.8	0.72	3.3
12	F	51	150	60	14.2	22.0	0.62	3.5
13	F	51	164	53	10.6	14.1	0.70	2.0
14	F	52	164	78	14.2	39.3	1.04	3.8
15	F	53	164	85	17.4	32.7	0.76	4.3
16	F	58	162	61	12.8	24.2	0.58	4.2
17	F	69	172	64	10.2	26.5	0.39	6.8
Group 1 (n:9)		35±4	169±3	61±4	22±2	15±2	0.43±0.06	4.2±0.7
Control men (n:12)		22-24	184±1	69±2	30±1	10±1	0.44±0.03	3.1±0.2
		—	$p<0.001$	n.s.	$p<0.01$	$p<0.05$	n.s.	n.s.
Groups 2 and 3 (n:8)		57±2	166±3	68±4	15±1	24±3	0.65±0.08	4.1±0.6
Control women (n:23)		50	166±1	70±3	27±1	19±1	0.62±0.03	3.3±0.2
		—	n.s.	n.s.	$p<0.001$	$p<0.05$	n.s.	n.s.

Means ± S.E.M.

changes in body composition. The dependence of the metabolic abnormalities on physical impairment and the lack of metabolic disturbances in patients with full physical activity indicate, contrary to the suggestion of Walsh et al.,[33] that MD as such is not associated with disturbances in lipid and carbohydrate metabolism. Rather, these aberrations are probably secondary to the inactivity and muscular atrophy of later stages of MD. Collis and Engel[5] found that about one-third of patients with different muscle wasting diseases have abnormal glucose tolerance. This finding supports the suggestion that decreased glucose tolerance in our subjects was a consequence of muscular atrophy and inactivity.

Whether the increase of body fat in the MD patients was due to an increase of fat cell size or number was not determined; increases in one of these two factors were seen in individual patients, but the average values were not significantly elevated.

In the disabled MD patients, plasma triglyceride was frequently abnormally high. With elevation of prebetalipoprotein concentration (lipoprotein electrophoresis types II + prebeta and IV), the body fat increase was often followed by large adipose tissue fat cells (patient nos. 7, 12, 13, 14, and 15) as previously described.[34] Glucose tolerance was decreased and fasting plasma insulin elevated. Thus, in this group metabolic characteristics of the same type as those found either in endogenous hypertriglyceridemia[35] or maturity onset diabetes mellitus were frequent.

Significant correlations between adipose tissue variables, particularly fat cell size, reported previously in men[19] and in patients with endogenous hypertriglyceridemia,[34] were not found in the present patients. This is probably due to the fact that diabetes mellitus, present in the MD group, disturbs these relationships.[16]

Huff and Lebovitz[36] and Gorden et al.[37] recently described a marked hypersensitivity of the insulin producing mechanism in patients with MD. This was also found in only a few patients in the present work. The presence of patients with clinical diabetes mellitus in the present group of patients might explain the apparent discrepancy in results.

As discussed above, it seems unlikely that MD as such is associated with disturbances in carbohydrate and lipid metabolism. The development of endogenous hypertriglyceridemia and maturity onset diabetes mellitus in

TABLE 2
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Results of determinations in patients with myotonic dystrophy

Patient no.	Fasting glucose (mg./100 ml.)	Sum of glucose values during glucose tolerance test (mg./100 ml.)	Fasting insulin (μU./ml.)	Sum of insulin values during glucose tolerance test (μU./ml.)	Tri-glyceride (mg./100 ml.)	Cholesterol (mg./100 ml.)	Lipoprotein electro-phoresis type	Group
1	—	—	—	—	42	225	N	1
2	92	607	27	817	152	220	N	1
3	71	533	8	267	258	374	II + pre-β	1
4	77	374	1	68	50	220	N	1
5	54	395	1	184	108	220	N	1
6	68	281	0	157	193	234	N	1(+)
7	80	896	15	328	272	267	IV	2
8	78	917	10	367	201	281	IV	2
9	68	403	0	280	84	248	N	1
10	62	340	4	126	65	192	N	1
11	56	411	0	198	112	281	N	1
12	74	562	7	266	138	309	IV	2
13	—	—	7	—	244	346	II + pre-β	3
14	76	600	14	—	200	351	II + pre-β	2
15	75	1,000	22	—	232	271	IV	2
16	62	313	9	218	132	346	II	2
17	72	743	2	113	139	248	N	3
Group 1 (n:9)	69±4	418±37	5±3	262±83	118±24	246±18		
Control men (n:12)	67±2	391±20	11±2	200±21	73±7	205±8		
	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.		
Groups 2 and 3 (n:8)	74±2	718±92	11±2	258±44	195±19	302±15		
Control women (n:23)	71±2	434±12	5±1	223±34	80±6	251±10		
	n.s.	$p<0.02$	$p<0.01$	n.s.	$p<0.001$	$p<0.02$		

Means ± S.E.M.

these patients is probably a consequence of inactivity and muscle atrophy. Physically well trained middle-aged men, on the other hand, have been found to have high glucose tolerance, which is maintained in spite of very low plasma insulin values. They also have low plasma lipid values and a small body fat mass with small fat cells but probably an increased mass of active muscle tissue.[17] These two extremes of chronic muscle inactivity and chronic high muscular activity demonstrate the importance of muscle mass and activity in regulation of lipid and carbohydrate metabolism.

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