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Effects of cornstarch treatment in very young children with type I glycogen storage disease

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Abstract. Three children aged 1–2 years with glycogenosis type I were treated with 2 g/kg bodyweight oral cornstarch per meal (4–5 times a day) for a period up to 16 months. In comparison to the previous dietary regimen (day and nocturnal feedings every 3 h) the cornstarch diet stabilised serum glucose profiles and dramatically improved secondary hyperlipoproteinaemia. Mean total triglycerides decreased up to one half, consistent with a fall of very low density lipoprotein-triglycerides up to two thirds. Metabolic acidosis and hyperuricaemia did not occur and normal growth rates (0.7–1 cm/month) were achieved. We conclude that the cornstarch regimen even in the age group up to 2 years can be considered as an efficient alternative in the treatment of glycogenosis type I patients with less frequent feedings and without nocturnal infusion.

Key words: Glycogen storage disease type I – Dietary management – Uncooked cornstarch

Introduction

In type I glycogen storage disease (GSD-I) the inherited absence [9] or deficiency [1] of glucose-6-phosphatase [5] leads to accumulation of glycogen in kidneys, intestine and especially in the liver. The functional absence of this microsomal enzyme rapidly leads to hypoglycaemia even after brief periods of fasting.

Secondary effects of deficient endogenous glucose production include severe metabolic acidosis due to abundant lactate production from glucose-6-phosphate, hyperuricaemia and extreme hyperlipidaemia. Goal of therapy is the prevention of hypoglycaemic episodes by means of a constant delivery of exogenous glucose thereby correcting most of the metabolic abnormalities. To achieve this, infants and younger children are currently treated with frequent daytime feedings and nocturnal intragastric infusions [2, 3, 6, 8] while elder children and adults can be treated very effectively by intermittent feeding of uncooked cornstarch [3, 15, 16]. Children younger than 2–4 years of age were thought not to respond satisfactorily to the starch regimen, eventually due to low pancreatic amylase activity within this age group [3, 11, 13].

In this paper we report on the beneficial effects of long-term administration of oral cornstarch in children with GSD-I aged 12–27 months.

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Abbreviations: GSD-I = Glycogen storage disease type I; VLDL = very low density lipoprotein

Patients and methods

Three children (two girls aged 12 and 27 months, one boy aged 18 months) with hepatic glucose-6-phosphatase-deficiency were studied. Prior to the study the boy and the elder girl were on a dietary regimen with additive maltodextrin [17] at a dose of 5–5.3 g/kg body weight per day at 3 h intervals for a period of 17.5 and 10.5 months, respectively. In the 10-month-old girl the cornstarch regimen was established immediately after diagnosis. The children were admitted to the metabolic ward of the University Children's Hospital and informed consent was obtained from all parents.

In order to assess the individual response, oral carbohydrate tolerance tests were performed on the 2nd day of hospitalization 2.5–3 h after the last meal (Figs. 1, 2). Uncooked cornstarch (Maizena GmbH, Heilbronn, FRG) suspensions (2 g/kg body weight) were prepared in water (weight to volume-ratio 1:2). Blood samples for measurement of glucose were obtained at regular in intervals; if the serum glucose level was below 45 mg/dl the test was terminated by administration of intravenous dextrose. A normoglycaemic state was assumed when serum glucose remained at the level of 70 mg/dl and above. According to the results of the carbohydrate tolerance tests the intervals between the meals were determined (4.8 and 6 h, respectively) and the starch feedings were continued to obtain a 24 h serum glucose profile. Finally, the starch feedings were added to the usual diet and carbohydrate tolerance tests were performed again (Fig. 2). For 2 additional days, serum glucose levels were obtained prior to each meal in the individual child. After discharge, the children were seen as outpatients every 4–6 weeks for general assessment, blood sampling and dietary advice. Blood samples including blood gas analysis were drawn exactly at the end of the feeding intervals in order to detect possible change sin starch digestion.

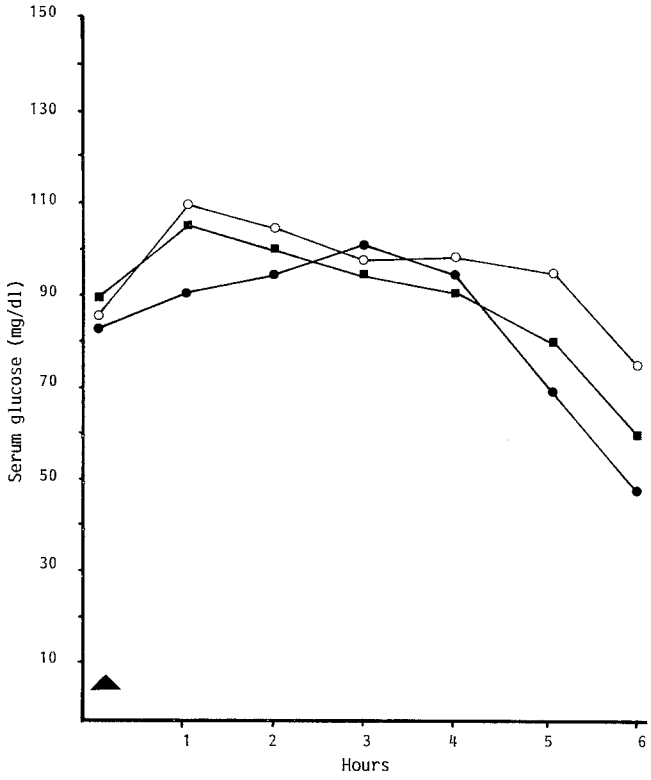

Fig. 1. Blood glucose profile after administration of 2 g/kg BW cornstarch (▲). ○, male, 18 months; ■, female, 12 months; ●, female, 27 months

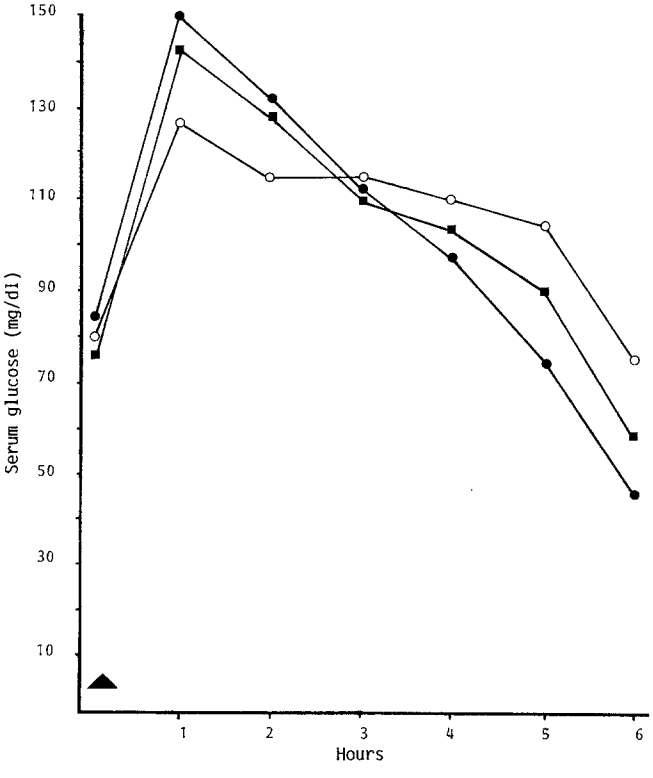

Fig. 2. Blood glucose profile after administration of 2 g/kg BW cornstarch added to a meal (▲). Symbols as for Fig. 1

Laboratory methods

Lipoproteins were fractionated by ultracentrifugation and polyanion precipitation according to LRC (Lipid Research Clinics)-methods and cholesterol and triglycerides estimated by enzymatic methods. All other routine laboratory parameters were determined by a fully automated analyser.

Diet

The diet was individually prepared for each child and in general consisted of (expressed as % of total daily energy intake): 60–70% carbohydrates, 10%–15% protein (skimmed milk, vegetables, lean meat) and 25%–35% fat (mainly as polyunsaturates, corn oil, margarine). (Special attention was drawn to the temperature of the cornstarch preparation supplied in order to prevent hydrolysis of the starch granules. Foods high in lactose, sucrose and fructose were avoided as far as possible.)

Results

The results of the carbohydrate tolerance tests are shown in Figs. 1 and 2. Oral cornstarch at a dose of 2 g/kg body weight resulted in constant serum glucose levels for more than 5 h in all children, the boy repeatedly had serum glucose levels above 75 mg/dl after 6 h. In contrast to the maltodextrin regimen the cornstarch load was able to maintain stable serum glucose levels between 65 and 115 mg/dl even during the following 24 h when feeding intervals were 4.8–6 h. When cornstarch was given prior to a meal, postprandial glucose levels were higher than those after a starch meal alone, nevertheless the duration of the normoglycaemic period was unchanged in all patients. Based on the results of the individual carbohydrate tolerance tests the feeding intervals were arranged to be 4.8 h in the girls and 6 h in the boy. Treated as outpatients serum glucose levels were surprisingly constant over the observation period. Mean serum uric acid levels were in the normal range and similar to those under the 3 h feeding regimen, while a marked fall of uric acid compared to baseline levels could be achieved (Tables 1–3). The most striking changes, however were observed with

Table 1. Laboratory data of 3 patients with GSD-1 prior to dietary intervention

	Patient 1 (female)	Patient 2 (male)	Patient 3 (female)
Age on diagnosis GSD-1 (months)	5.5	7.5	10
Fasting glucose (mg/dl)	6–20	18–23	22–34
Uric acid (mg/dl)	10	9.8	4.7
SGOT U/l	38	290	37
SGPT U/l	26	287	46
Gamma-GT U/l	30	161	40
Total cholesterol (mg/dl)	694	401	259
Triglycerides (mg/dl)	3320	2700	2390
VLDL-chol (mg/dl)	572	175	148
VLDL-TG (mg/dl)	2800	2100	1960
HDL-chol (mg/dl)	10	15	18
LDL-chol (mg/dl)	58	200	133

Table 2. Effects of maltodextrin-supplementation in two patients with type-1 glycogen storage disease

	Patient 1 (female)	Patient 2 (male)
Age (months)	9.5	7.5
Feeding interval (hours)	3	3
Duration of therapy (months)	17.5	10.5
Dose (g/kg/d)	5	5.3
No. of samples	13	9
($\bar{x}$ ± SD) mg/dl		
Glucose[a]	104 ± 40.7 (27–215)	93 ± 38 (46–195)
Uric acid	5.9 ± 3	5.0 ± 2.5
Total cholesterol	318 ± 85	226 ±57
Total triglycerides	1697 ± 766	709 ± 447
VLDL-C	160 ± 87	44 ± 47
VLDL-TG	1240 ± 564	453 ± 211
HDL-C	13 ± 7	23 ± 15
LDL-C	139 ± 42	153 ± 47
Linear growth (cm/month)	0.5	0.9

[a] Indicates $\bar{x}$ ± SD and range of glucose values 3 h after maltodextrine-supplementation

LDL = low density lipoprotein; HDL = high density lipoprotein; VLDL = very low density lipoprotein

Table 3. Effects of cornstarch supplementation in type-1-glycogen storage disease

	Patient 1 (female)	Patient 2 (male)	Patient 3 (female)
Age (months)	27	18	12
Duration of therapy (months)	15	16	12
Dose (g/kg/d)	10	8	10
Feeding interval (hours)	4.8	6	4.8
Numbers of feedings/d	5	4	5
No. of samples	10	12	14
mg/dl ($\bar{x}$ ± SD)			
Glucose[a]	86.1 ± 33 (36–154)	77.1 ± 14 (54–106)	70 ± 25 (36–118)
Uric Acid	5.7 ± 1.5	6.0 ± 1.2	3.0 ± 0.9
GOT U/l	21 ± 3	149 ± 37	17 ± 3
GPT U/l	21 ± 4	181 ± 45	14 ± 4
Gamma-GT U/l	24 ± 4	122 ± 57	23 ± 7
Total cholesterol	184 ± 35	225 ± 67	164 ± 43
Total triglycerides	883 ± 205	547 ± 189	337 ± 117
VLDL-C	48 ± 29	39 ± 20	22 ± 10
VLDL-TG	436 ± 212	277 ± 118	167 ± 74
HDL-C	14 ± 5	18 ± 7	30 ± 4
LDL-C	111 ± 21	161 ± 57	106 ± 31
Linear growth (cm/month)	0.7	0.8	1.0

[a] Indicates $\bar{x}$ ± SD and range of glucose measured at the Paediatric Outpatients Department 4.8 and 6 h after a cornstarch meal

regard to serum lipids and lipoproteins. Mean serum cholesterol decreased up to 50% compared to baseline levels, total triglycerides up to 60%. In one patient total triglycerides fell from 2300 to mean levels of 330 mg/dl, consistent with an 11 fold reduction in the very low density lipoprotein (VLDL) fraction. Mean low density lipoprotein-cholesterol slightly increased. Diarrhoea and flatulance, well-known side-effects during ingestion of large amounts of starches did not occur during the study period.

Growth rate

When the diagnosis of GSD-I was established, all children were below the 3rd percentile according to the growth curves of Tanner and Whitehouse; the bodyweight ranged between the 25th and 50th percentile at the start and end of the observation period.

During cornstarch supplementation all children showed normal or slightly accelerated growth with two of them attaining the area between 3rd and 10th percentile. The linear growth rate varied between 0.7–1.0 cm/month.

Discussion

During 12–16 months under the cornstarch regimen normoglycaemic serum glucose profiles for 4.8–6 h could be observed in three young children, one at the age of 1 year. Maintenance of stable blood glucose profiles is the therapeutic goal in treatment of GSD-I patients [2, 3, 6, 8, 9, 18] for most of the metabolic abnormalities can be reversed [4]. Chen et al. [3] were the first to demonstrate that by means of intermittent intake of uncooked cornstarch serum glucose levels higher than 70 mg/dl in adults could be achieved while an 8-month old infant failed to respond. This unresponsiveness was interpreted to be due to the low pancreatic amylase activity within this age group [10, 11].

Sidbury et al. [14] reported a patient aged 8 months treated with oral cornstarch without adding pancreatic enzymes and normoglycaemia was established in two infants with dumping syndrome after a starch meal [7]. In contrast to the findings of other authors [3, 13] in all our patients aged 12–27 months normoglycaemic blood glucose profiles similar to these of older GSD-I patients could be achieved, even without adding pancreatic enzymes. The observation that the feeding intervals could be extended indicates that intestinal starch hydrolysis was sufficient during the study period. Pancreatic amylase activity is low in the newborn period and reaches adult levels at the age of 2–4 years, but can be stimulated by feeding oral starches [10, 11].

The supplementation of partially hydrolysed cornstarch (maltodextrin) might be responsible for the improved starch hydrolysis in our patients.

The hyperlipidaemia in GSD-I predominantly expresses as excessive hypertriglyceridaemia and is thought to be the result of both an increase of production and impaired clearance from the circulation due to greatly reduced activity of lipoprotein lipase as well [12]. Thus,

secondary hyperlipidaemia can be dramatically improved by maintenance of constant serum glucose levels. This is confirmed by the observation of Burr, who reported a decrease of triglyceride levels in seven patients from 3600 to 1800 mg/dl after 5 years of nocturnal intragastric feeding [2]. In our patients serum triglyceride levels were between 340 and 880 mg/dl, consistent with a marked fall in the VLDL fraction indicating better metabolic control even when compared to the maltodextrin diet.

The linear growth rate is considered a reliable parameter for the effectiveness of a therapeutic regimen in GSD-I patients [8]. Chen observed catch-up growth in three patients during the period of nocturnal infusion and normal or slightly accelerated growth rates under cornstarch administration [3]. In our study the elder girl showed an increased growth rate under cornstarch compared to the frequent feeding regimen, but failed to reach the 3rd percentile, while the other children crossed the 3rd percentile during the cornstarch diet. Our data suggest that even in infants with GSD-I oral application of uncooked cornstarch may be an alternative to gastric drip feeding and frequent daytime feedings. The results emphasise that even in infants, feeding intervals up to 6 h are possible. It should be stated that long-term treatment with cornstarch leads to marked reductions of excessive hyperlipoproteinemia, normal growth rates and stable blood glucose profiles, even when the feeding intervals are extended.

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