Biochemical Evidence for the Requirement of Continuous Glucose Therapy in Young Adults with Type 1 Glycogen Storage Disease

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Summary: To determine whether patients with GSD-1 need nocturnal glucose therapy after completing physical growth and development, studies were performed on two consecutive nights. On the first night uncooked cornstarch (UCS) was given at the calculated glucose production rate at 21:00 h and 02:00 h. On the second night UCS was given at 21:00 h but omitted at 02:00 h. Six GSD-1 patients, aged 17.2–20.9 years, previously treated with continuous glucose therapy were studied. Measurements were made of plasma glucose (PG), serum insulin, growth hormone, cortisol, plasma glucagon (n = 4), and blood lactate at 30–60-min intervals. Serum uric acid, cholesterol, and triglycerides were measured at 21:00 h and 07:00 h, and serum FFA at 21:00 h, 02:00 h and 07:00 h on the first night and immediately before treatment for hypoglycaemia on the second night.

For five hours after UCS at 21:00 h, mean PG, serum insulin and blood lactate concentrations were similar on the two nights. With UCS at 02:00 h, mean PG concentrations were ≥ 4.1 mmol/L from 02:00 to 07:00 h. Without UCS at 02:00 h, in all subjects PG concentrations fell to < 2.5 mmol/L after 6.5–8.5 h and mean blood lactate concentration increased to 7.4 ± 3.0 mmol/L. Young adults with GSD-1 developed hypoglycaemia and hyperlactataemia after a relatively brief period without exogenous glucose and, therefore, need to continue nocturnal glucose therapy to prevent fasting hypoglycaemia.

Type 1 glycogen storage disease (GSD-1, McKusick 232200) results from lack of in vivo activity of the hepatic microsomal enzyme glucose-6-phosphatase (EC 3.1.3.9), which catalyses the final step in the production of glucose from glucose 6-phosphate (Burchell 1990). Deficiency of this enzyme, therefore, impairs production of glucose both from glycogenolysis and gluconeogenesis. This results in postprandial hypoglycaemia and increased production of lactic acid, uric acid, and triglyceride (Hers et al 1989). Untreated patients experience severe growth failure and delayed puberty. However, when hypoglycaemia is prevented by providing exogenous glucose at the
basal rate of glucose production throughout the day and night, the biochemical abnormalities are ameliorated and normal growth occurs (Greene et al 1976; Crigler and Folkman 1978; Fernandes et al 1979; Greene et al 1979; Chen et al 1984; Wolfsdorf et al 1990a). Treatment therefore aims to provide a constant supply of glucose at a rate that maintains the blood glucose level above the threshold for activation of glucose counter-regulatory mechanisms (Wolfsdorf et al 1990b).

With increase in age, disorders associated with hypoglycaemia require longer intervals of fasting to induce comparable clinical and metabolic changes. This presumably occurs principally because of major changes in the ratio of brain to body mass. Glucose turnover directly correlates with brain mass (Bier et al 1977); and in adults there is a more favourable relationship between the rate of glucose production and utilization (Aynsley-Green 1982). Two studies that address the issue of providing a continuous source of dietary glucose in adults with GSD-1 came to different conclusions; one suggested that nocturnal feedings may be unnecessary (Greene et al 1981), whereas the other indicated a beneficial effect of 24-hour continuous glucose supplementation (Schwenk 1990).

The purpose of this study, therefore, was to determine whether young adults with GSD-1 whose growth was complete continue to require nocturnal glucose therapy to prevent hypoglycaemia and its attendant metabolic and hormonal consequences.

MATERIALS AND METHODS

Six young adults (3M, 3F), ages 17.2–20.9 years, with biopsy-proven GSD-1 participated in this study. Their adult heights were 150.9–173.5 cm and weights were 55.0–72.6 kg. Subjects had received continuous glucose therapy for periods ranging from 11 to 16.4 years, initially, by continuous overnight intragastric glucose infusion via a gastrostomy and frequent (1–3-hourly) dextrose feedings during the day, and later with intermittent feedings of uncooked cornstarch (UCS) around the clock (Wolfsdorf et al 1990a,b, 1992). All the women had been menstruating regularly for at least two years at the time of this study. All subjects had undergone 24-hour monitoring of serum metabolites and hormones at 6–12-month intervals (6–13 occasions) for six to eight years preceding the current study to demonstrate the ability of UCS feedings to maintain reproducibly the overnight biochemical state (Wolfsdorf et al 1990a,b).

Protocol: These studies were approved by the Clinical Investigation Committee of The Children’s Hospital, Boston, and informed consent was obtained from patients. Subjects were admitted to the Clinical Research Center and an intravenous cannula for repetitive blood sampling was inserted into a forearm vein between 15:00 and 16:00 h and was kept open by a slow infusion of heparinized saline (0.1 U/ml). They followed their usual home dietary regimen until 17:00 h on the day of admission, and were permitted to walk on the ward but not to perform strenuous physical activity. Four subjects were studied on consecutive nights; two had the studies described on nights 1 and 2 on separate admissions to the Clinical Research Center.

On day 1, subjects had supper (a mixed meal that contained 30% of the total daily energy requirement [Food and Nutrition Board and the Subcommittee on the Tenth