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ORIGINAL ARTICLE

A novel starch for the treatment of glycogen storage diseases

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Summary *Objective:* To determine whether a new starch offers better short-term metabolic control than uncooked cornstarch in patients with glycogen storage diseases (GSDs). *Study design:* A short-term double-blind cross-over pilot study comparing uncooked physically modified cornstarch (WMHM20) with uncooked cornstarch in patients with GSD types Ia, Ib and III. Twenty-one patients (ages 3–47, 9 female) were given 2 g/kg cornstarch or WMHM20 mixed in water. Blood glucose, lactate and insulin, and breath hydrogen and $^{13}CO_2$ enrichment were measured, at baseline and after each load. The hourly biochemical evaluations terminated when blood glucose was ≤3.0 mmol/L, when the study period had lasted 10 h or when the patient wished to end the test. The alternative starch was administered under similar trial conditions a median of 10 days later. *Results:* The median starch load duration was 9 h for WMHM20 versus 7 h for cornstarch. Glucose decreased more slowly (p=0.05) and lactate was suppressed faster (p=0.17) for WMHM20 compared with cornstarch. Peak hydrogen excretion was increased (p=0.05) when cornstarch was taken. *Conclusion:* These data indicate longer duration of euglycaemia and better short-term metabolic control in the majority of GSD patients with WMHM20 compared to cornstarch.

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Competing interests: None declared

References to electronic databases: Glycogen storage disease I, OMIM 232200. Glycogen storage disease III, OMIM 232400. Glucose-6-phosphatase, EC 3.1.3.9. Amylo-1,6-glucosidase, EC 3.2.1.33. Oligo-1,4–1,4-glucanotransferase, EC 2.4.1.25

Abbreviations

CNPF	continuous nocturnal pump feed
GSD	glycogen storage disease

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IQ	interquartile range
PDB	Pee Dee Belemnite
UCCS	uncooked cornstarch
WMHM20	Waxy Maize (Heat Modified) 20

Introduction

The glycogen storage diseases (GSDs) comprise a group of rare inherited disorders of glycogen metabolism. GSD I (OMIM 232200) is caused by reduced activity of glucose-6-phosphatase (G6Pase, EC 3.1.3.9); GSD Ia by deficiency of the hydrolytic enzyme; and GSD Ib by deficiency of the endoplasmic reticulum transmembrane glucose 6-phosphate transport protein, G6P translocase. The major metabolic consequence of ineffective function of G6Pase is hypoglycaemia, provoked by relatively short fasts. Secondary metabolic disturbances include hyperlactataemia, hyperuricaemia and hyperlipidaemia (Chen 2001). GSD III (OMIM 232400) is caused by deficiency of glycogen debrancher enzyme (EC 2.4.1.25). Many patients with GSD III are also prone to hypoglycaemic episodes after short fasts, particularly during childhood. Secondary metabolic disturbances include ketosis and hyperlipidaemia.

Maintaining blood glucose concentration in the normal range improves secondary biochemical features as well as clinical parameters. The introduction of continuous nasogastric glucose polymer feeds showed this clearly (Greene et al 1976). The subsequent introduction of uncooked cornstarch (UCCS) into the daily dietary treatment at least matched this improvement (Chen et al 1984, 1993). While the introduction of UCCS has benefited many patients, its use does have problems. For some the duration of normoglycaemia can be less than 4 h, many find the mixture neither palatable nor convenient, and for others there can be symptoms of bloating, flatulence and diarrhoea with large doses (Lee et al 1996). UCCS is only partially utilized and can be associated with malabsorption in GSD I (Bodamer et al 2002). Diarrhoea may also be a feature of GSD I itself or its treatment with cornstarch, and inflammatory bowel disease is a feature of GSD Ib (Sanderson et al 1991; Visser et al 2002).

Apart from sustained normoglycaemia without excessive insulin rise, the features of an ideal starch for treatment of patients with the hepatic GSDs include suppression of secondary biochemical abnormalities, palatability, convenience, few side-effects and maintenance of normal appetite (without excessive weight gain) (Rake et al 2002b; Smit et al 1984). We have looked at many methods of optimizing the efficacy of starch therapy, including delaying gastrointestinal transit time, enhancing digestion of starch and delaying digestion of starch. In a pilot study with one patient, (unpublished data) we found better metabolic control with a physically modified cornstarch, WMHM20 (Glycologic Ltd, Glasgow, UK; international patent WO2005044284).The physical properties of cornstarch and WMHM20 are shown in Table 1. This study was designed to assess whether this benefit was sustained in a larger group of patients. We therefore tested the hypothesis that there is longer duration of normoglycaemia with the short-term use of WMHM20 compared to cornstarch.

Table 1 Composition of starches used in study

	Cornstarch	WMHM20
Moisture content	10.9%	11.9%
Amylopectin content	72.8%	99.5%
Total carbohydrate (wet base)	84.6%	84.2%
Resistant starch (Englyst et al 1994)	60.5%	67.7%

Study design

The study was approved by the Joint Ethics Committee of The National Hospital for Neurology and Neurosurgery and Institute of Neurology, London, UK, and the Institute of Child Health/Great Ormond Street Hospital Ethics committee, London, UK. GSD I and III patients were recruited from adult and paediatric tertiary referral metabolic units in London. Written informed consent was taken from all adults above 16 years of age and from a legal guardian of children under 16 years. The diagnosis of GSD I and III was based on a liver biopsy showing reduced activity of the appropriate enzyme, a mutation in the appropriate gene or white blood cell glycogen debrancher enzyme activity indicative of GSD III. All had evidence from their medical history of fasting hypoglycaemia and were taking UCCS.

The study had a randomized double-blind cross-over design. Patients anonymized by reference number were randomly allocated to receive either UCCS (National Starch & Chemical Ltd, Manchester, UK) or WMHM20. Each starch was manufactured using food-grade techniques and packaged in identical containers bearing a reference number. The patient reference numbers and container reference numbers were paired by Glycologic Ltd and the supervising physician was blinded to this pairing. Research participants were asked to re-attend for the second starch load, using the

alternative starch, a median of 10 days (IQ 7–14 days) afterwards. The supervising physician devised a safe personalized fasting period for each patient based on previous cornstarch loads and medical history. Clear instructions were given to the research subject, or their carer, for the participant to have the same diet the day before and fast interval immediately before each starch load.

Methods

Starch load test

Initially, an intravenous cannula was placed in the patient's arm and baseline blood and breath samples were collected. Then, 2 g of the nominated starch per kg body weight (maximum 120 g) was mixed in cold water and ingested. Breath and blood samples were performed hourly after the starch administration. No further intake, apart from drinking water, was allowed. The starch load test ended when the patient had fasted for 10 h, the blood glucose was ≤3.0 mmol/L on the bedside glucose monitor or the patient wished to end the test. When the blood glucose was ≤4.0 mmol/L in children aged 3–16 years, blood tests were performed at 30 min intervals until the test end.

Biochemical data

The blood samples were analysed: bedside whole-blood glucose (Advantage II, Roche diagnostics, Mannheim, Germany); laboratory plasma glucose and lactate (Vitros Fusion 5.1, Ortho-Clinical Diagnostic, High Wycombe, UK); and serum insulin was performed by a solid-phase, two-site chemiluminescent immunometric assay (Immulite 2000, Diagnostic Products Corporation, Los Angeles, CA, USA). The laboratory glucose and lactate samples were collected into lithium fluoride, transported on ice and separated within 30 min of sampling. The insulin samples were collected as a clotted sample and also separated within 30 min. The bedside glucose monitor was used as a screening tool to identify hypoglycaemia (blood glucose ≤3.0 mmol/L) and consequently determine when to end the test. Statistical analyses were performed on laboratory plasma glucose data.

Breath data

Breath hydrogen was measured immediately at the bedside using a portable hydrogen measuring device (Micro H_2, Micro Medical, Rochester, UK), while $^{13}CO_2$ breath samples were collected into a gas sampling system (Micro Medical) and the gas was transferred using a gas-tight syringe to a gas-tight 10 ml vacuum tube (Labco Ltd, High Wycombe, UK). Breath CO_2 was analysed for $^{13}CO_2/^{12}CO_2$ enrichment by gas chromatography on a CP-Poraplot-Q column (Varian Inc., Oxford, UK) followed by isotope ratio mass spectrometry on a Thermo Finnigan Delta-XP (Thermo Finnigan, Bremen, Germany). Sample $^{13}CO_2/^{12}CO_2$ enrichment was standardized against a CO_2 cylinder (5.0 grade, BOC Special Gases, Guildford, UK) calibrated against the international standard Pee Dee Belemnite (PDB) (Iso-Analytical, Sandbach, Cheshire, UK). The WMHM20 and UCCS $^{13}C/^{12}C$ ratios were analysed by elemental analyser isotope ratio mass spectrometry (Iso-Analytical). The enrichments of UCCS, WMHM20 and Maxijul glucose polymer (SHS Ltd, Liverpool, UK) after complete combustion were δ‰=−11.13, −10.75 and −11.32, respectively. UCCS and WMHM20 utilization were calculated from the $^{13}CO_2/^{12}CO_2$ ratios as described previously, substituting the above UCCS and WMHM20 enrichments in the formula (Bodamer et al 2002).

Statistics

The gradient of increase of glucose from baseline to peak and gradient of decrease of glucose from peak to the end of each starch load was assessed. Similar gradients were assessed for lactate: baseline to trough lactate and from trough to test end for each load. These paired gradients, for each starch load, were compared using a two-tailed paired *t*-test. Using nonparametric analyses, there was no statistical difference in glucose decline when comparing GSD Ia

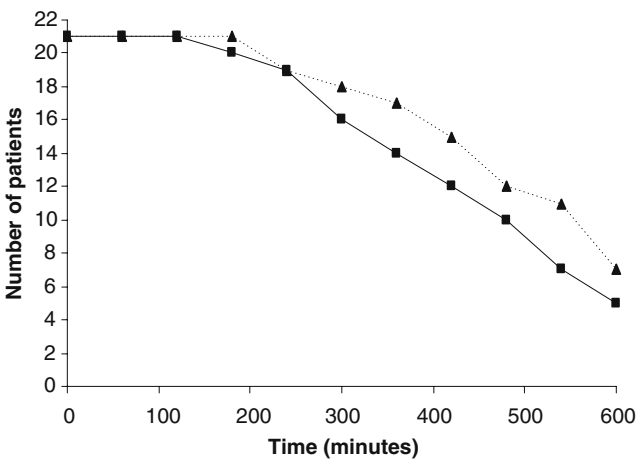
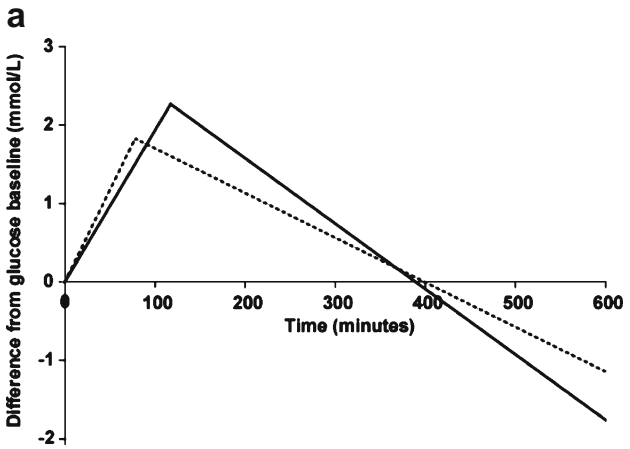


Fig. 1 Test duration for 21 patients with GSD I or III. ···▲···, WMHM20; —■—, UCCS

patients with Ib and GSD Ia with III, but there was a statistical difference between these disorders in the lactate profile. Consequently, glucose data were compared for all patients and also substratified to those with GSD I and GSD Ia only, whereas lactate data were compared for GSD I and GSD Ia only (see Fig. 2). Mean glucose oxidation breath values for each starch load were compared at 60 min intervals using a two-tailed paired *t*-test. However, it was noted using an unpaired two tailed *t*-test that there was a statistical difference (p=0.0035) in the baseline values of $^{13}CO_2$ breath enrichment of those participants who had overnight Maxijul glucose polymer pump feeds prior to the starch loads, with the mean ±1 standard deviation being (−18.4 ± 2.70‰ vs PDB) compared with those taking just UCCS (−21.6 ± 2.97.) Subsequent analysis was therefore performed on those patients who were not managed with continuous nocturnal pump feeds and fasted for 2 h or greater, before the starch load as indicated in Fig. 4. The ^{13}C content of Maxijul by complete combustion was ascertained due to this difference in baseline and is indicated above.



	Baseline to peak	*Peak to trough*
ALL	0.563	**0.0464**
GSD 1	0.394	0.0820
GSD 1A	0.571	0.114

	Baseline to trough	*Trough to peak*
GSD 1	0.173	0.466
GSD 1A	0.381	0.380

Fig. 2 Mean gradient of incline from baseline to peak and decline from peak to test end for glucose (**a**) and from baseline to trough and trough to test end lactate (**b**.)·····, WMHM20; ——, UCCS. Tables indicate *p*-values calculated from paired *t*-tests.

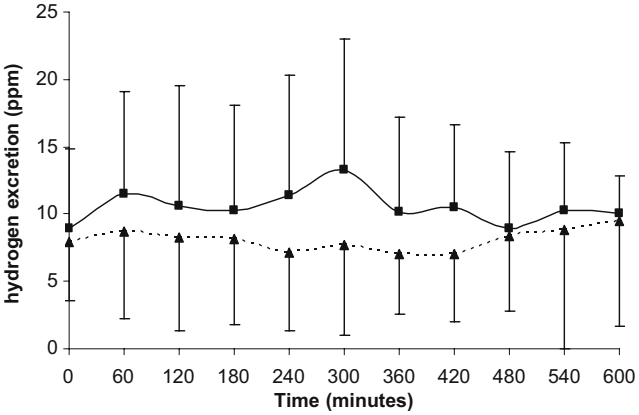


Fig. 3 Mean hydrogen excretion for patients taking WMHM20 or cornstarch (errors bars of one standard deviation). ···▲···, WMHM20; —■—, UCCS

The mean hourly hydrogen excretion for each starch was compared during using a two tailed paired *t*-test as indicated in Fig. 3. The area under the graph for each profile was also calculated; the mean area for each cohort and comparison by paired *t*-tests is indicated in Table 2. However, the area under the curve may not be entirely representative of hydrogen excretion as shorter trials have less area than longer trials with similar excretion. Consequently, the mean hydrogen excretion per starch load is also indicated in Table 2.

Table 2 Mean area under the breath hydrogen curve and mean hydrogen excretion per patient for starch-load duration for subjects with GSD Ia and Ib able to perform breath tests (n=16) and GSD Ia (n=11.) Comparison by paired *t*-test

	Cornstarch	WMHM20	*p*-Value
Mean area under curve (ppm×min)			
GSD Ia and Ib	5220	3930	0.178
GSD Ia	4740	3940	0.434
Mean hydrogen excretion (ppm)			
GSD Ia and Ib	11.3	8.11	0.0635
GSD Ia	11.2	8.74	0.163

For the 6 children in our study who were 14 years and under who were able to perform breath tests adequately, the mean hydrogen excretion (±SD) for the duration of the studies was 3.8 ppm (±2.6) for WMHM20 and 3.5 ppm (±2.1) for UCCS. For the 12 patients who were 15 years and over, these values were 9.8 ppm (±6.1) for WHMH20 and 13.4 ppm (±6.8) for UCCS. In addition, there was statistical significance difference ($p<0.00001$) using a two-tailed unpaired *t*-test comparing the mean hourly excretion between the two age ranges for each starch.

Results

Patient demographics and test duration data are shown in Table 3. If the patient ended the test with a laboratory glucose ≤3.0 mmol/L, the duration of normoglycaemia is indicated by the last glucose>3.0 mmol/L, usually 1 h (occasionally 30 min) previous to the low value. Median test duration for WMHM20 was 9 h (IQ 6.0–10.0) and for UCCS was 7 h (IQ 5.0–9.0). Comparative test duration is indicated in Fig. 1. The patients ended the tests for various reasons: for WMHM20, six had genuine hypoglycaemia, two patients ended their trial because the bedside glucose monitor under-read the laboratory glucose, six terminated for personal reasons unrelated to hypoglycaemia and seven lasted the full test duration of 10 h. For UCCS, nine patients ended the test with genuine hypoglycaemia, four because the bedside glucose monitor under-read the laboratory glucose, three for personal reasons unrelated to hypoglycaemia and five patients lasted for the full test duration of 10 h. Patients as a whole had a longer period of euglycaemia using WMHM20, but 8/21 from the WMHM20 group and 7/21 from the UCCS group terminated the study prematurely. There was no significant difference in the mean area under the curve for the glucose profiles ($p=0.47$). However, the area under the curve does not necessarily represent the primary outcome of duration of normoglycaemia, as discussed later. Consequently, the gradients for each glucose and lactate profile from baseline to peak values and from peak to trough were taken as described above. There was no statistical difference for the gradient of increase in glucose, but WMHM20 had a slower glucose decline than cornstarch ($p=0.05$), in the whole cohort. There were no statistical differences in the lactate profile but the mean lactate tended to decrease faster in all GSD I patients ($p=0.17$) for WMHM20 compared with UCCS.

Table 3 Diagnosis, pre-test management, trial duration and conditions for trial termination for both WMHM20 and cornstarch

Age(years)	Sex(M/F)	GSD diagnosis	Pre-load fast (h)	Nocturnal regimen	WMHM20 (h)	T*	Cornstarch (h)	T*
3	F	Ia	<0.5	CNPF	3	h	3	h
4	F	Ia	<0.5	CNPF	4	h	4	h
5	M	Ia	<0.5	CNPF	3	h	4	h
5	M	Ia	<0.5	CNPF	7	u	4	u
7	M	Ia	<0.5	CNPF	9	p	6	u
12	M	Ia	1	CNPF	9	p	7	p*
21	M	Ia	2	CNPF	10	m	10	m
22	F	Ia	4	UCCS	10	m	9	h
22	M	Ia	1	CNPF	6	h	5	u
23	F	Ia	2	UCCS	6	h	8	h
33	M	Ia	2	UCCS	10	m	6	h
34	M	Ia	10	UCCS	10	m	10	m
47	M	Ia	12	UCCS	7	p	10	m
13	M	Ib	1	CNPF	9	p	9	$p^{\#}$
14	F	Ib	5.5	UCCS	10	m	8	h
15	F	Ib	3	UCCS	9	p	10	m
24	M	Ib	4	UCCS	10	m	7	u
35	M	Ib	2	UCCS	8	h^{+}	10	m
38	F	Ib	12	UCCS	10	m	5	h^{+}
3	F	III	<0.5	CNPF	5.5	u	2	h
12	M	III	0.5	CNPF	7	p	8	p

CNPF, continuous nocturnal pump feed; UCCS, uncooked cornstarch taken overnight.
T*: *Conditions for test end*—h=hypoglycaemia (glucose<3.0 mmol/L) confirmed on laboratory glucose; u=under-reading: bedside glucose (<3.0 mmol/L), resulting in test end, laboratory glucose>3.0 mmol/L; p=personal reasons unrelated to hypoglycaemia at test end; p*=patient had profound headache and lethargy at test end; $p^{\#}$ =patient had profound diarrhoea at test end; h^{+} =patient's baseline preparation different for each test load against advice; m=maximum test duration=10 h.

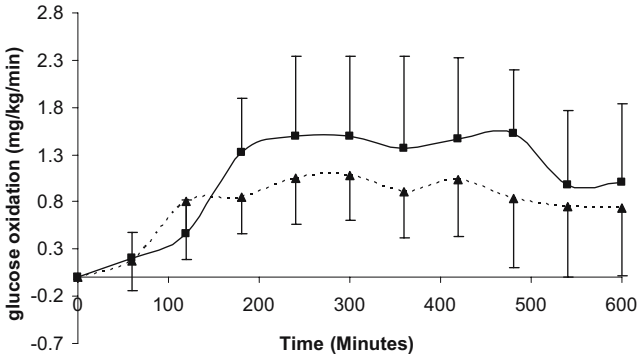


Fig. 4 Mean calculated glucose oxidation of 10 patients who had fasted for ≥2 h prior to starch load (errors bars of one standard deviation). ···▲···, WMHM20; —■—, UCCS

The mean gradients for each sector are demonstrated in Fig. 2 to illustrate how the difference applies to the glucose and lactate profiles.

There were no statistical differences noted in the insulin profile. The mean peak (±1 SD) insulin for UCCS was 15.9 IU/L (±12.3) and for WMHM20 was 13.7 IU/L (±12.2). On average, peak insulin was reached in 1 h for UCCS and in 2 h for WMHM20.

There was no statistically significant increase in utilization of UCCS compared to WMHM20 in the 10 patients who did not take overnight glucose polymer (Fig. 4). The mean hydrogen breath data are shown in Fig. 3. There was a statistically significant difference at 300 min (p=0.05), indicating greater colonic fermentation and potentially malabsorption of UCCS compared to WMHM20.

Discussion

This study compared the short-term metabolic profile of 'traditional' cornstarch and a novel physically modified cornstarch and demonstrates preliminary evidence of a more favourable outcome with the latter. We demonstrate a longer duration of action, slower decrease in glucose, more rapid suppression of lactate and less relative colonic fermentation of the novel starch compared to UCCS.

Since the identification of glucose-6-phosphatase by Cori and Cori in 1952, several strategies for ameliorating metabolic disturbances in patients with GSDs have been attempted. Portocaval shunts in the 1960s aimed to reduce hepatic first-pass metabolism of dietary glucose (Starzl et al 1965.) The use of parenteral nutrition appeared a more effective strategy (Folkman et al 1972). This was simplified further by the introduction of continuous nocturnal enteral feeds in conjunction with frequent daytime meals (Greene et al 1976; Wolfsdorf and Crigler 1999). The latter strategy demonstrated very clear improvement in growth and overall metabolic control. This treatment appears effective but it is onerous and ongoing concerns with mechanical pump failure and tube dislodgement remain (Leonard and Dunger 1978; Rake et al 2002a.) Daytime meals can be frequent (<2 h interval) and consequently several studies looked at slow glucose-releasing dietary starches to extend this period of euglycaemia (Chen et al 1984; Sidbury et al 1986; Smit et al 1988; Wolfsdorf and Crigler 1997).

The introduction of UCCS into the dietary regimen in the 1980s improved daytime management and allowed some patients to replace nocturnal pump feeds of glucose polymer with a dose of cornstarch. An important consequence of the introduction of these dietary therapies was an improved quality of life and prognosis (Moses 2002). While many patients clearly benefit from UCCS, some patients do not have sustained normoglycaemia and many have symptoms of bloating, flatulence and gastrointestinal disturbance. In some patients these symptoms may be related to incomplete digestion of starch (Bodamer et al 2002). However, it has become increasingly clear that there is substantial morbidity in older patients, including the development of hepatic adenoma and potentially hepatocellular carcinoma, renal tubular and glomerular disease and fractures related to osteopenia (Lee and Leonard 1995; Lee et al 1995a,b,c; Weinstein and Wolfsdorf 2002). While the pathophysiology of all these processes is not clear, improved primary and secondary metabolic control is associated with less morbidity. Therefore, current management protocols recommend strategies to improve metabolic control (Rake et al 2002b). For some patients, including adults, improved metabolic control continues to require frequent meals or UCCS and nocturnal nasogastric pump feeds. Such intensive strategies may have a major impact on quality of life and psychosocial well-being.

It has thus been a goal of many research groups to find a dietary starch that improves metabolic control for a sustained period. Starch is a glucose polymer. Variation in physical properties and granular organization gives a starch its unique digestibility profile. In particular, the amylose (linear chain) to amylopectin (branched chain) ratio, particle size and proportion and nature of the crystalline structure determine the digestibility of any given starch (Smit et al 1988). However, the physical properties of starch can be modified by chemical, heat, pressure or enzymatic treatment, which subsequently alters its digestibility.

The physiology of an individual also greatly determines to what extent glucose is liberated from available dietary starch. Factors such as gastrointestinal transit time, abundance of pancreatic α-amylase and gastrointestinal mucosal integrity determine the extent to which this occurs. Undigested starch undergoes fermentation by colonic bacterial flora, releasing hydrogen, which is absorbed into the bloodstream and excreted in the breath. Measurement of breath hydrogen excretion is a well-recognized technique for assessing starch malabsorption (Casellas et al 2004; Metz et al 1975).

The authors' clinical research group has approached the development of a dietary starch in a number of ways. We have tried various synthetic starches with different ratios of amylose/amylopectin but have not found the desired metabolic profile. High amylose content, for example in high-amylose maize, is difficult to digest (Tester et al 2004). The use of products with delayed gastrointestinal time and the use of pancreatic enzyme supplements have not appeared effective in our hands. However, by controlled heat–moisture processing of cornstarch, we have found that the new 'reorganized' cornstarch (WMHM20) can offer better metabolic control than traditional UCCS.

Having performed this study as a pilot study on one and then five patients from our clinic (unpublished data), we invited all patients in our clinic with GSD Ia, Ib and III who take cornstarch as part of their treatment to participate in the full study protocol to see whether there is any evidence of benefit in the broader GSD population To this end, the overall test duration of the novel starch appears beneficial for the majority of patients. The glucose and lactate profiles also appear favourable, but some of these data were not statistically significant. There was also no statistical difference in the area under the curve for each of these glucose profiles owing to the relatively higher peak glucose of the UCCS (Fig. 2a) and the shorter test durations of these patients. We believe the lower peak glucose and gradual sustained decline of the glucose curve conferred by WMHM20 is the more desirable metabolic profile, despite the equivalent area that each curve yields.

Ideally, starch load tests and hydrogen/$^{13}CO_2$ breath tests should be performed after a substantial fast to discriminate interference from other ingested substances, but this is rarely possible in patients with GSD. In addition, there should also ideally be a pre-test 'washout' of ^{13}C-containing food. This again is not possible in this study population, who are dependent on regular cornstarch with high ^{13}C content, leading to a statistically different baseline breath $^{13}CO_2$ when compared to the normal population (Bodamer et al 2002.) The best compromise was to recommend that patients' pre-test management be identical for each load, with patients acting as their own controls. We assumed that day-to-day variation was minimal on the two test days, yet this was not always the case.

There was increased hydrogen excretion compatible with increased colonic delivery and fermentation of UCCS compared to WMHM20, suggesting greater malabsorption of UCCS. If the criterion for malabsorption of peak hydrogen excretion>20 ppm was used, eight UCCS subjects and four WMHM20 met the criterion (Metz et al 1975). Increased breath hydrogen excretion was not demonstrated in two previous studies of patients with GSD I, but those studies were in children and adults all under the age of 22 years (Smit et al 1984; Visser et al 2002.) Our results indicate a lower mean hydrogen excretion for starch load duration for those patients aged 14 years and under compared with those aged 15 years and over. Hydrogen excretion seems to increase with age, implying that there is acquired malabsorption in this patient group. We cannot, however, exclude that the differences between this study and those published previously are due to differences in dose or regional variations in management. Further work is required to elucidate more precisely the physiology of starch digestion in GSDs, including fermentation and malabsorption of different starches in these patients. Our data demonstrate peak colonic fermentation of starch at 300 min. Therefore, studies to assess fermentation and utilization of starch should extend beyond this time in order to assess this variable effectively, However, our primary test endpoint was duration of normoglycaemia and consequently several subjects did not have studies that lasted beyond 300 min. These findings in our study are consequently preliminary and further analysis of each of these specific variables within separate trial protocols would be desirable.

We studied a small number of heterogeneous patients with large differences in age, burden of disease and management. In addition, different types of GSD were studied. In such a varied group of patients, who often require meticulous individualized management, it is difficult to implement a standardized trial protocol. This resulted in variation of baseline biochemistry and duration of tests, leading to difficulty with statistical analysis. The converse of stratifying data by disease, disease severity or age resulted in loss of statistical power in this cohort and inconclusive findings. For safety reasons, patients were also managed conservatively during the starch loads, resulting in premature termination of some studies. This contributed to the variations

observed, as fewer patients contribute data from their load towards the end.

The data presented indicate that WMHM20 has an improved lactate and glucose metabolic profile without concomitant increase in insulin, compared with UCCS. The data indicate greater fermentation and potentially malabsorption of UCCS. These preliminary data appear favourable for WMHM20. As such, this would be the first advance in dietary therapy for over 20 years for these disorders. It is necessary to examine the role of this novel starch as part of the standard dietary regimen of larger numbers of patients for a greater period of time. Even a modest improvement in fasting tolerance may have a clinically significant impact on quality of life for this group of patients as their feeding patterns integrate better with their peers.

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