Euglycemic hyperinsulinemic clamp to assess posthepatic glucose appearance after carbohydrate loading. 2. Evaluation of corn and mung bean starches in healthy men[1–3]

Vincent Lang, Francis RJ Bornet, Pierre Vaugelade, Marina van Ypersele de Strihou, Jing Luo, Nathalie Pacher, Florence Rossi, Philippe La Droitte, Pierre-Henri Duée, and Gérard Slama

ABSTRACT

Background: The rate of absorption of glucose from carbohydrates is important in several aspects of health. We recently validated a noninvasive technique in pigs, euglycemic hyperinsulinemic clamp plus oral carbohydrate loading (OC-Clamp), to quantify the rate of net posthepatic appearance of glucose after ingestion of carbohydrates.

Objective: The OC-Clamp procedure was performed in 8 healthy men to compare the net posthepatic appearance of glucose after ingestion of 1 of 3 carbohydrates.

Design: Human volunteers underwent the OC-Clamp procedure at an insulin infusion rate of 1.5 $mU \cdot kg^{-1} \cdot min^{-1}$ (n = 5). The oral carbohydrate load (1 g/kg) consisted of glucose, cornstarch, or mung bean starch. During the OC-Clamp procedure, the glucose infusion rate decreased during absorption to maintain plasma glucose steady state and the decrease reflected the net posthepatic appearance of glucose. In addition, carbohydrates were loaded without insulin infusion (n = 6) and glycemic indexes were calculated (with glucose as the reference).

Results: The mean (±SEM) glycemic index of cornstarch was higher (95 ± 18) than that of mung bean starch (51 ± 13). In the OC-Clamp experiments, the posthepatic appearance of glucose and cornstarch did not differ significantly and represented 79.4 ± 5.0% and 72.6 ± 4.0%, respectively, of the load after complete absorption (within 3 h). In contrast, the net posthepatic appearance of glucose from mung bean starch was significantly lower (35.6 ± 4.6% of the load, $P < 0.001$) than that from glucose and cornstarch, even 4.5 h postprandially.

Conclusions: The OC-Clamp technique allows a continuous assessment of net posthepatic appearance of glucose after ingestion of carbohydrates and significant discrimination between corn and mung bean starches. *Am J Clin Nutr* 1999;69:1183–8.

KEY WORDS Glucose, cornstarch, mung bean, corn, absorption, net splanchnic uptake, euglycemic clamp, men

INTRODUCTION

The rate of digestion of dietary carbohydrates and the rates of portal and posthepatic appearance of glucose partly control postprandial blood glucose concentrations. Moreover, the glycemic responses to foods may have implications in various aspects of health, including the control of food intake (1–4) and glucose and lipid metabolism in healthy and diabetic subjects and animals (5–12). Foods or diets with a low glycemic index are associated with higher satiety scores (2–4). In diabetes, diets with a low glycemic index reduce glycated hemoglobin by 9%, fructosamine by 8%, urinary C-peptide by 20%, and day-long integrated blood glucose concentrations by 16% (5). Diets with a low glycemic index may also be beneficial in lipid management (5–7).

The glycemic index of carbohydrate sources (ingested alone or in a mixed meal) has been evaluated extensively and tables of such have been compiled as a nutritional aid (13). Moreover, the development of low-glycemic-index foodstuffs (through progress in technologic processing, incorporation of new carbohydrate sources, or both) is still a challenge for the industry. Bearing this in mind, we previously characterized mung bean starch as a source of slowly digested carbohydrate in healthy and diabetic rats (6, 7) and in healthy humans (8). Mung bean starch was shown to produce small increases in the glycemic response in healthy subjects (8) and to modify glucose and lipid metabolism in rats (6, 7). However, the rate of absorption of mung bean starch has not been quantitatively measured in healthy humans.

Because the quantitative determination of the rate of glucose absorption from carbohydrate in the portal circulation is not ethically possible in humans, several qualitative methods have been developed. Indeed, the direct measurement of systemic glucose and insulin concentrations (2, 3, 8–12) as well as several indirect methods [intubation techniques (14), breath tests (15), and isotopic methods (16, 17)] provide only qualitative data on the kinetics of glucose absorption, as stated in the accompanying paper (18).

[1] From the INSERM U 341, Service de Diabétologie, Hôpital Hôtel-Dieu, Paris; Éridania Béghin-Say, Nutrition and Health Service, Vilvoorde, Belgium; Institut National de la Recherche Agronomique, Jouy-en-Josas, France; and Nutrition et Santé SA, Revel, France.

[2] Supported in part by the Ministère Chargé de la Recherche, Paris (grant no. 94 G 0267), and Nutrition et Santé SA, Revel, France. M van Ypersele de Strihou received an education grant from the Belgian Diabetic Association (grant S&J Pirart).

[3] Reprints not available. Address correspondence to G Slama, INSERM U 341, Service de Diabétologie, Hôpital Hôtel-Dieu, 1 Place du Parvis Notre Dame, 75181 Paris Cedex 04, France.

Received August 20, 1998.

Accepted for Publication December 17, 1998

We recently validated a noninvasive technique in pigs (combining the euglycemic hyperinsulinemic clamp and oral carbohydrate loading; OC-Clamp) to quantify the net posthepatic appearance of glucose after carbohydrate loading (18). In the present study, we applied this technique to 8 healthy male subjects to compare the glucose availability from 3 different sources of carbohydrates: glucose, cornstarch, and mung bean starch.

SUBJECTS AND METHODS

Subjects

Eight healthy nondiabetic men were included in the present study. Their mean (±SEM) weight, height, body mass index (in kg/m^2), waist-to-hip ratio, age, and fasting plasma glucose concentration were 71.6 ± 2.0 kg, 178 ± 2 cm, 22.7 ± 0.7, 0.81 ± 0.02, 27.2 ± 2.0 y, and 5.05 ± 0.01 mmol/L, respectively. All participants were instructed to eat carbohydrate-rich foods for 3 d before each experimental day at the laboratory. As established by food diary assessment, mean daily intakes were 3.15 ± 0.16 MJ, 356 ± 20 g carbohydrate, 137 ± 10 g fat, and 120 ± 7 g protein. No subject had a family history of diabetes or gastrointestinal or hepatic diseases, and none were taking any medication known to affect carbohydrate or glucose digestion, absorption, or metabolism. The purpose, nature, and potential risks of the study were explained in detail to all subjects, who gave their written, informed consent to the protocol, which was approved by the Medical Ethics Committee (Hôtel-Dieu Hospital, Paris).

Design

The subjects underwent an oral carbohydrate tolerance test (OC), OC-Clamp procedure, or both. Each type of experiment (OC and OC-Clamp) had a within-subjects design. The study compared the net posthepatic appearance of glucose after complex carbohydrate (cornstarch or mung bean starch) loading, as measured by the recently validated OC-Clamp technique (18), or by carbohydrate loading without a glucose clamp (OC). As a control, an isoenergetic amount of glucose was also used in both the OC and OC-Clamp experiments. The order of the 3 carbohydrate loads was randomized in both the OC and OC-Clamp experiments. For each volunteer, an interval of ≥6 d between 2 consecutive experiments was enforced. All studies were performed at 0900 after a 12-h overnight fast.

Carbohydrate load

Three types of carbohydrates (1 g/kg) were loaded: glucose as a 33% water solution, cornstarch [C*Top12410, ratio of amylose to amylopectin of 5:95, 0% resistant starch; Cerestar, Vilvoorde, Belgium (7)] powder prepared as a warmed (45°C) 11% solution, and mung bean starch [*Phasoleus aureus* starch in the form of Chinese noodles, ratio of amylose to amylopectin of 35:65, 10.7 ± 0.7% resistant starch, Pagoda Brand; Republic of China (7)] purchased in local Asian supermarkets in Paris and prepared as a cooked (7 min at 90°C) 11% solution cooled to 45°C. The 3 loads were pure carbohydrates. The taste of both starchy meals was improved with salt and pepper.

Procedure

OC-Clamp experiment

The glucose clamp technique was performed under euglycemic conditions to maintain plasma glucose and insulin concentrations at required concentrations (19). Infusates were administered through a cannulated vein. Arterialized (by warming at 55°C) venous blood was sampled through a cannulated antecubital vein from the other arm. A loading dose of insulin (30 mU/kg) was administered continuously over 2 min and was immediately followed by a constant infusion (1.5 $mU \cdot kg^{-1} \cdot min^{-1}$) for the next 450 min. The plasma glucose concentration was maintained at the basal concentration throughout the study by monitoring the glucose concentration at 5-min intervals and adjusting the infusion rate of a 20% glucose solution. Thus, plasma glucose and insulin were kept constant while the glucose infusion rate varied. Blood was collected before the clamp started and then at 20–30-min intervals to check the stability of plasma glucose, insulin, and C-peptide concentrations. Plasma K^+ concentrations were also checked regularly.

After 2–3 h of the insulin infusion in healthy subjects, the glucose infusion rate was at steady state (*see* Results). Under these conditions, hepatic glucose production is totally suppressed as proven in a previous experiment carried out in our laboratory (20). This suppression of hepatic glucose production was also obtained in glucose clamp experiments performed in healthy men with comparable body mass indexes by using an insulin infusion rate of 1.5 $mU \cdot kg^{-1} \cdot min^{-1}$ (21, 22). The moment that the steady state glucose infusion rate was achieved (time 0), 1 of the 3 carbohydrate loads was ingested by the subjects and the glucose infusion rate was adjusted to maintain plasma glucose at steady state. Glucose concentrations were then monitored for 270 min postprandially. The variation in the glucose infusion rate compensated for the net posthepatic appearance of glucose after the oral carbohydrate load. This assumption was derived from previous validation of the OC-Clamp technique in an animal model (18). Indeed, the posthepatic appearance of glucose after a carbohydrate load can be assessed with a euglycemic hyperinsulinemic clamp, taking into account that hepatic glucose production is totally suppressed and overall glucose utilization is kept constant (18). Because hepatic glucose uptake remains proportional to the rate of glucose absorbed and the rate of intestinal glucose uptake only represents a small part of splanchnic glucose uptake, the OC-Clamp technique validated previously in pigs could be extended to human studies. Moreover, a close relation between the posthepatic appearance of glucose and the rate of portal appearance of glucose from various starches was shown in pigs (18). Complete absorption of the load was indicated when the glucose infusion rate reached the steady state infusion level again. As reported below in the Results section, the glucose infusion rate after mung bean starch ingestion only reached the steady state infusion level for transient periods of time; therefore, complete absorption could not be determined.

OC experiment

Six subjects were given 3 oral carbohydrate loads with the meals provided in the OC-Clamp experiments. Peripheral venous blood was drawn before the subjects ingested the meal and sampling was then repeated at 20–30-min intervals for 250 min. Plasma glucose and insulin concentrations were determined in the samples.

Biochemical analyses

Plasma glucose was analyzed by using the glucose-oxidase method (Beckman, Galway, Ireland) with an Autoanalyzer II (Beckman, Fullerton, CA). Plasma insulin and C-peptide concen-

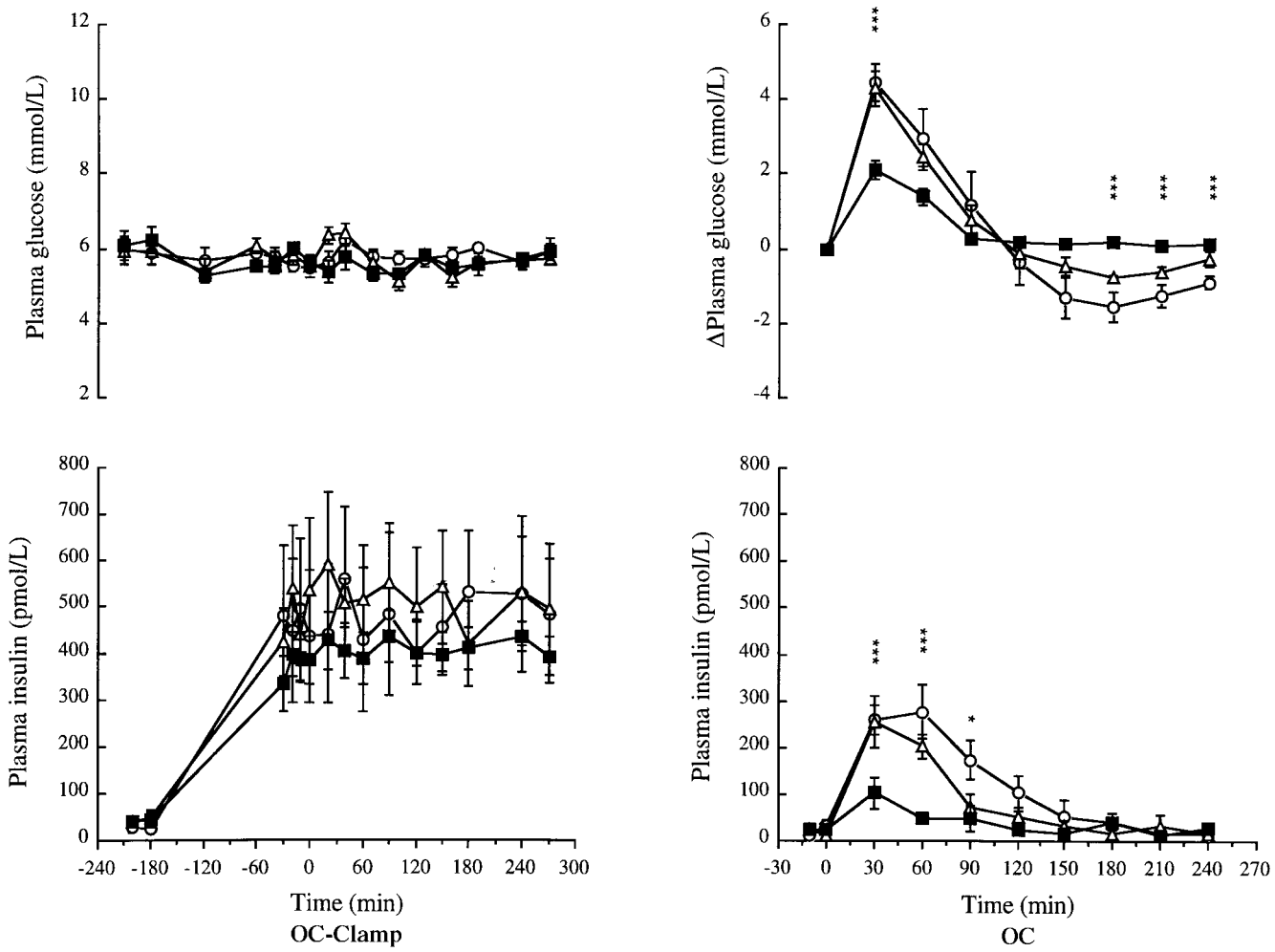

FIGURE 1. Mean (±SEM) plasma glucose and insulin concentrations after an oral carbohydrate load (OC; $n = 6$) (right panels) and after both an OC load and a euglycemic hyperinsulinemic clamp (OC-Clamp; $n = 5$) (left panels). The OC loads were glucose (○), cornstarch (△), and mung bean starch (■). In the OC-Clamp experiments, glucose and insulin responses to the 3 carbohydrates were not significantly different. In the OC experiments, main effects of time and time × carbohydrate interactions were observed for glucose and insulin responses ($P = 0.0001$–0.008); main effects of type of carbohydrate were observed for insulin ($P = 0.001$). *,***Significant differences between responses to mung bean starch and glucose and cornstarch (post hoc Scheffe's test): $^{*}P < 0.05$, $^{***}P < 0.005$.

trations were measured by radioimmunoassay (ERIA Diagnostics Pasteur, Marnes-la-Coquette, France).

Calculations and statistical analyses

In the OC experiments, areas under the curve were calculated for each plasma index according to the trapezoidal method and reported for 250 min postprandially. The glycemic index was calculated as the mean of the individual ratio of the area under the plasma glucose curve to a given carbohydrate and the area under the plasma glucose curve to the control glucose load. The insulinemic index was calculated in the same way but with plasma insulin data.

In the OC-Clamp experiments, the posthepatic appearance of glucose was calculated by integrating the difference between steady state glucose infusion rate and glucose infusion rate (*see* reference 18 for more details). Repeated-measures analysis of variance with time and type of load as the within-subjects factors was used to analyze plasma glucose, insulin, and C-peptide concentrations. Post hoc analyses were based on the Scheffe's test. Analyses were performed by using SUPERANOVA (version 1.11; Abacus Concepts, Berkeley, CA) and STATVIEW (version 1.03; Abacus Concepts) software. All data were expressed as means ± SEMs. Significance was assumed at $P < 0.05$.

RESULTS

Plasma glucose, insulin, and C-peptide concentrations

In the OC experiments, as expected, both plasma glucose and insulin concentrations increased after the carbohydrate load (**Figure 1**), peaked 30–60 min after the carbohydrate load, and returned to basal concentrations 60–90 min after the mung bean starch meal and 90–120 min after the glucose and cornstarch meals. Peak glucose and insulin values were significantly higher after the glucose and cornstarch meals than after the mung bean starch meal. Moreover, significant postprandial reactive hypoglycemia was only observed after the glucose and cornstarch loads ($P < 0.001$; Figure 1).

In the OC-Clamp experiment, the plasma glucose concentration was 5.95 ± 0.13 mmol/L before insulin infusion. Steady state

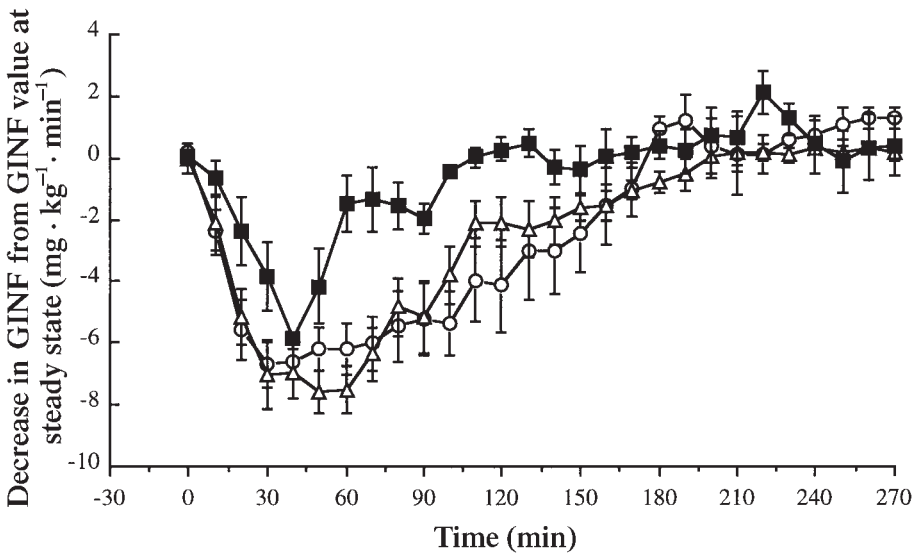

FIGURE 2. Mean (±SEM) decreases in glucose infusion rates (GINFs) from GINFs at steady state over 270 min after glucose (○), cornstarch (△), and mung bean starch (■) loads. $n = 5$.

plasma glucose was achieved at 5.64 ± 0.07 mmol/L (Figure 1). The plasma glucose concentration did not change significantly during carbohydrate absorption (5.71 ± 0.04 mmol/L). Basal plasma insulin and C-peptide concentrations were 34.7 ± 4.9 and 643 ± 48 pmol/L, respectively. Insulin infusion significantly increased plasma insulin concentrations to reach steady state 1 h before carbohydrate administration (449 ± 31 pmol/L; $P < 0.01$; Figure 1) and significantly decreased plasma C-peptide concentrations (486 ± 46 pmol/L; $P < 0.01$). The plasma insulin concentration remained significantly constant during absorption (472 ± 20 pmol/L), regardless of the carbohydrate ingested (Figure 1). Plasma C-peptide concentrations rose transiently over the postprandial period (556 ± 23 pmol/L), but this small increase did not significantly affect plasma insulin concentrations (Figure 1).

Glycemic and insulinemic indexes

As calculated from the responses of plasma indexes in the OC experiments, glycemic and insulinemic indexes were 95 ± 18 and 83 ± 6 for cornstarch and 51 ± 13 and 20 ± 5 for mung bean starch, respectively. For both indexes, responses to the mung bean starch load were significantly different from responses to the cornstarch load ($P < 0.05$).

Glucose infusion rates

During the OC-Clamp, the glucose infusion rate increased to reach steady state (48.6 ± 0.4 μmol · kg^{-1} · min^{-1}) within 120–180 min. After the oral carbohydrate load, the glucose infusion rate decreased significantly ($P < 0.01$, **Figure 2**), but returned to the prior steady state value ≈180 min after the glucose or cornstarch load. In 3 of the 5 men, the glucose infusion rate after the mung bean starch load did not reach the steady state glucose infusion rate even after 270 min of absorption.

Rates of net posthepatic appearance of glucose

The net posthepatic appearance of glucose in the OC-Clamp study was not significantly different between the glucose and cornstarch loads (**Figure 3**). Similarly, the cumulative posthepatic appearance of glucose 270 min postprandially, expressed as a percentage of the glucose load, was not significantly different between the loads: 79.4 ± 5.0 with the glucose load and 72.6 ± 4.0 with the cornstarch load. Completion of the posthepatic appearance of glucose was achieved at similar times with both loads: 185.2 ± 12.6 and 184.6 ± 13.8 min with the glucose and cornstarch loads, respectively. The posthepatic appearance of glucose was lowest after the mung bean starch load, despite a time-course pattern that was similar to that after the glucose and cornstarch loads; it was significantly lower (35.6 ± 4.6% of load) than that after the other 2 loads 270 min postprandially. The completion time for the posthepatic appearance of glucose could not be calculated because glucose was still appearing at the posthepatic level at 270 min.

DISCUSSION

A previous study validated the OC-Clamp technique in pigs as a method of performing a quantitative assessment of the net posthepatic appearance of glucose after glucose loading (18). Furthermore, the rate of net posthepatic appearance of glucose (deduced from the decrease in glucose infusion rate) reflected the rate of net portal glucose appearance directly and proportionally, as shown in pigs fed various carbohydrate sources (18). Thus, the OC-Clamp technique is a noninvasive method that directly provides information on the kinetics of absorption of carbohydrates in humans.

In the present study, peripheral plasma insulin and glucose concentrations were maintained at a steady state concentration over the absorption period so that the OC-Clamp calculations could be performed. We showed that the OC-Clamp technique allows significant discrimination between various carbohydrate sources with different glycemic indexes. Mung bean starch was absorbed significantly more slowly than was cornstarch or glucose (Figure 3). This result is consistent with that of several studies that showed low digestibility in vitro (7) and a low glycemic index in vivo (6–8) for mung bean starch. In vitro hydrolysis, measured 30 min postinfusion in a

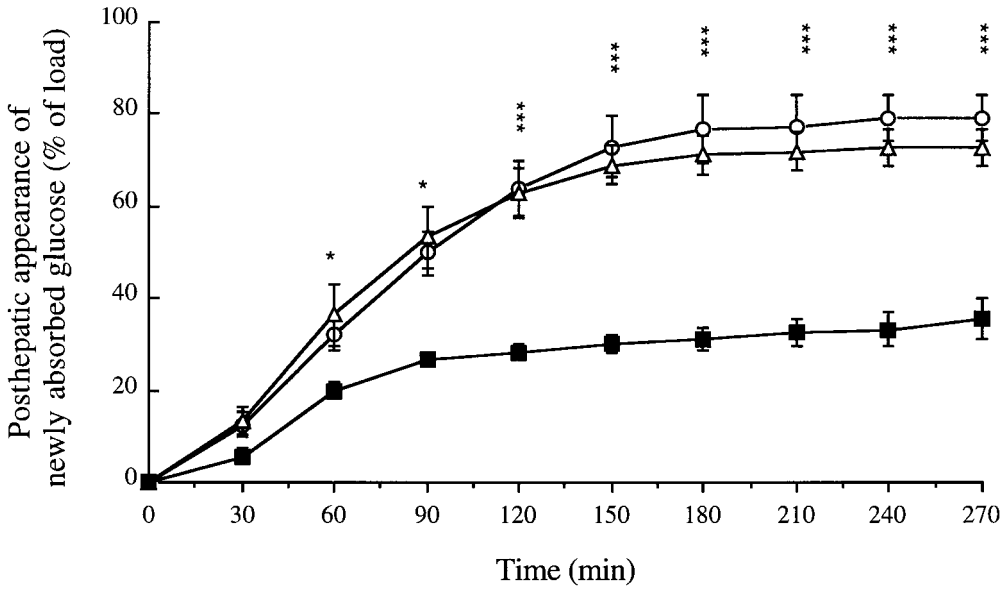

FIGURE 3. Mean (±SEM) cumulative, net posthepatic appearance of glucose over 270 min after glucose (○), cornstarch (△), and mung bean starch (■) loads. Main effects of time (P = 0.0001), type of carbohydrate (P = 0.013), and time × type of carbohydrate interaction (P = 0.0001) were observed. *,***Significant differences between responses to mung bean starch and responses to glucose and cornstarch (post hoc Scheffe analysis): $^{*}P < 0.05$, $^{***}P < 0.005$.There were no significant differences between responses to glucose and cornstarch loads at any time. n = 5.

buffer solution with α-amylase (37°C), was significantly lower for mung bean starch than for cornstarch: 46 ± 3% and 60 ± 4% of the load, respectively (7). In normal rats, glycemic and insulinemic responses to mung bean starch were 63% and 62%, respectively, of the corresponding responses to cornstarch. In the present study, the glycemic and insulinemic responses to mung bean starch were 54% and 24%, respectively, of the responses to cornstarch. Bornet et al (8) assessed glucose and insulin responses to various raw, gelled, and industrially processed starches (eg, mung bean, extruded wheat, and tapioca) in healthy subjects. There was a smaller hyperglycemic response to mung bean starch than to wheat starch: 28 ± 10 and 109 ± 31 mmol/kg, respectively, 180 min postprandially.

In the present study, complete absorption of glucose and cornstarch was achieved ≈180 min postprandially. The net splanchnic glucose uptake was 20.6 ± 3.3% and 27.4 ± 2.7% of the load, respectively, after glucose and cornstarch. These values correspond to those generally reported in healthy subjects (23, 24). In contrast, net splanchnic glucose uptake could not be calculated for mung bean starch because the complete posthepatic appearance of glucose was not achieved. An important question raised by our data deals with the fate of glucose originating from digestion and absorption of mung bean starch because only a small fraction of the carbohydrate load is quantified at the posthepatic level. First, a larger splanchnic glucose uptake could occur. However, in pigs, the net hepatic glucose extraction ratio (net hepatic glucose uptake:net hepatic glucose load) is the same for mung bean and cornstarch (18). As mentioned previously (18), intestinal uptake (and utilization) of ingested glucose is negligible. Both observations strongly suggest that an increased splanchnic glucose uptake cannot explain a lower posthepatic appearance of glucose. Second, ≈11% of mung bean starch is resistant starch, which escapes small-intestinal digestion and absorption. However, this undigestible fraction cannot fully account for the large difference obtained at 270 min. Third, kinetics of digestion and absorption (intestinal availability) are significantly lower for mung bean starch. This is supported by in vitro data (*see* above) and by in vivo observations underlying the fact that absorption of some carbohydrates may, at least in animal models such as pigs, continue over an 8-h postprandial period (25). In the present experiment, as suggested by the determination of net posthepatic appearance, glucose originating from mung bean starch was still entering the body after 270 min (Figure 3).

In the accompanying paper, the net posthepatic appearance of glucose was shown to be closely related to the net portal entry of absorbed glucose (18). In addition, the present study showed that the OC-Clamp technique allowed detection of the net posthepatic appearance of glucose, whereas at the same time the excursion of glycemia was blunted in the OC experiment, as observed for mung bean starch 120 min postprandially (Figure 1). The existence of a clear relation between glucose concentration at a given time and its rate of absorption is debatable (16, 17). In the present study, even if such a link could be established for the early responses (30 min), no relation was found for the later responses. Indeed, the glucose concentration at 120 min was close to basal values, although glucose was still entering the body. Nevertheless, more exhaustive evaluation of various carbohydrate sources after various loads should provide valuable information on the existence of such a relation.

Furthermore, the glycemic index is now a well-established method of classifying carbohydrate sources according to their rate of digestion and absorption. However, for carbohydrates presenting delayed digestion or absorption and a high glycemic index, their discrimination against rapidly digested products with a high glycemic index may be missed if only the glycemic index method is used. Consequently, the use of methods allowing a continuous quantitative assessment of glucose entry are likely to be required.

In conclusion, the present study illustrates the effectiveness of the noninvasive OC-Clamp technique for routinely assessing the

net posthepatic appearance of glucose after carbohydrate loading. Moreover, this method can continuously discriminate between 2 carbohydrates during the absorption period. The OC-Clamp technique can also effectively quantify the amount of glucose available from new carbohydrate sources, alone or in a mixed meal. Thus, this method can be useful for indicating what carbohydrates may help prevent the metabolic complications of various diseases.

REFERENCES

1. Grossman SP. The role of glucose, insulin and glucagon in the regulation of food intake and body weight. Neurosci Behav Rev 1986;10:295–315.
2. Holt SHA, Miller JCB, Petocz P. Interrelationships among postprandial satiety, glucose and insulin responses and changes in subsequent food intake. Eur J Clin Nutr 1996;50:788–97.
3. Holt S, Miller J. Increased insulin responses to ingested foods are associated with lessened satiety. Appetite 1995;24:43–54.
4. Lavin JH, Read NW. The effect on hunger and satiety of slowing absorption of glucose: relationship with gastric emptying and postprandial blood glucose and insulin responses. Appetite 1995;25:89–96.
5. Brand Miller JC. Importance of glycemic index in diabetes. Am J Clin Nutr 1994;59(suppl):747S–52S.
6. Lerer-Metzger M, Rizkalla S, Luo J, et al. Effects of long-term low-glycaemic index starchy food on plasma glucose and lipid concentrations and adipose tissue cellularity in normal and diabetic rats. Br J Nutr 1996;75:723–32.
7. Kabir M, Rizkalla S, Champ M, et al G. Dietary amylose-amylopectin starch content affects glucose and lipid metabolism in adipocytes of normal and diabetic rats. J Nutr 1998;128:35–43.
8. Bornet F, Fontvieille A, Rizkalla S, et al. Insulin and glycemic responses in healthy humans to native starches processed in different ways: correlation with in vitro α-amylase hydrolysis. Am J Clin Nutr 1989;50:315–23.
9. Behall K, Howe JC. Effect of long-term consumption of amylose vs amylopectin starch on metabolic variables in human subjects. Am J Clin Nutr 1995;61:334–40.
10. Byrnes S, Miller J, Denyer G. Amylopectin starch promotes the development of insulin resistance in rats. J Nutr 1995;125:1430–7.
11. Frost G, Keogh B, Smith D, Akinsanya K, Leeds A. The effect of low-glycemic carbohydrate on insulin and glucose responses in vivo and in vitro in patients with coronary heart disease. Metabolism 1996;45:669–72.
12. Jenkins DJA, Wolever TMS, Collier GR, et al. Metabolic effects of a low-glycemic-index diet. Am J Clin Nutr 1987;46:968–75.
13. Englyst H, Veenstra J, Hudson G. Measurement of rapidly available glucose (RAG) in plant foods: a potential in vitro predictor of the glycaemic response. Br J Nutr 1996;75:327–37.
14. Stephen A, Haddad A, Phillips S. Passage of carbohydrate into the colon. Direct measurements in humans. Gastroenterology 1983;85:589–95.
15. Levitt M, Hirsh P, Fetzer C, Sheahan M, Levine A. H_2 excretion after ingestion of complex carbohydrates. Gastroenterology 1987;92:383–9.
16. Jackson R, Roshania R, Hawa M, Sim B, DiSilvio L. Impact of glucose ingestion on hepatic and peripheral glucose metabolism in man: an analysis based on simultaneous use of forearm and double isotope techniques. J Clin Endocrinol Metab 1986;63:541–9.
17. Normand S, Pachiaudi C, Khalfallah Y, Guilluy R, Mornex R, Riou J. ^{13}C appearance in plasma glucose and breath CO_2 during feeding with naturally ^{13}C-enriched starchy foods in normal humans. Am J Clin Nutr 1992;55:430–5.
18. Lang V, Vaugelade P, Bernard F, et al. Euglycemic hyperinsulinemic clamp to assess posthepatic glucose appearance after carbohydrate loading. 1. Validation in pigs. Am J Clin Nutr 1999;69:1174-82.
19. DeFronzo R, Tobin J, Andres R. Glucose clamp technique: a method for quantifying insulin secretion and resistance. Am J Physiol 1979;273:E214–23.
20. Luo J, Rizkalla S, Alamowitch C, et al. Chronic consumption of short-chain fructooligosaccharides by healthy subjects decreased basal hepatic glucose production but had no effect on insulin-stimulated glucose metabolism. Am J Clin Nutr 1996;63:939–45.
21. DeFronzo R, Ferrannini E, Hendler R, Felig P, Wahren J. Regulation of splanchnic and peripheral glucose uptake by insulin and hyperglycemia in man. Diabetes 1983;32:35–45.
22. Rizza RA, Mandarino LJ, Gerich JE. Dose-response characteristics for effects of insulin on production and utilization of glucose in man. Am J Physiol 1981;240:E630–9.
23. Consoli A. Pathways of glucose metabolism following ingestion of an oral glucose load. Diab Nutr Metab 1994;7:97–107.
24. Ludvik B, Nolan J, Roberts A, et al. A noninvasive method to measure splanchnic glucose uptake after oral glucose administration. J Clin Invest 1995;95:2232–8.
25. Rérat A, Vaissade P, Vaugelade P. Absorption kinetics of some carbohydrates in conscious pigs. 2. Quantitative aspects. Br J Nutr 1984;51:517–29.