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Effects of carbohydrate ingestion before and during exercise on glucose kinetics and performance

MARK A. FEBBRAIO,1 ALISON CHIU,1 DAMIEN J. ANGUS,1 MELISSA J. ARKINSTALL,2 AND JOHN A. HAWLEY2
1Exercise Physiology and Metabolism Laboratory, Department of Physiology, The University of Melbourne, Parkville, Victoria 3052; and 2Exercise Metabolism Group, Department of Human Biology and Movement Science, Royal Melbourne Institute of Technology University, Bundoora, Victoria 3083, Australia

Received 3 April 2000; accepted in final form 7 July 2000

Febbraio, Mark A., Alison Chiu, Damien J. Angus, Melissa J. Arkinstall, and John A. Hawley. Effects of carbohydrate ingestion before and during exercise on glucose kinetics and performance. J Appl Physiol 89: 2220–2226, 2000.—We investigated the effect of carbohydrate (CHO) ingestion before and during exercise and in combination on glucose kinetics, metabolism and performance in seven trained men, who cycled for 120 min (SS) at ~63% of peak power output, followed by a 7 kJ/kg body wt time trial (TT). On four separate occasions, subjects received either a placebo beverage before and during SS (PP); placebo 30 min before and 2 g/kg body wt of CHO in a 6.4% CHO solution throughout SS (PC); 2 g/kg body wt of CHO in a 25.7% CHO beverage 30 min before and placebo throughout SS (CC); or 2 g/kg body wt of CHO in a 25.7% CHO beverage 30 min before and 2 g/kg of CHO in a 6.4% CHO solution throughout SS (CP). Ingestion of CC and CP markedly (>8 mM) increased plasma glucose concentration ([glucose]) compared with PP and PC (5 mM). However, plasma [glucose] fell rapidly at the onset of SS so that after 80 min it was similar (6 mM) between all treatments. After this time, plasma [glucose] declined in both PP and CP (P < 0.05) but was well maintained in both CC and PC. Ingestion of CC and CP increased rates of glucose appearance (Ra) and disappearance (Rd) compared with PP and PC at the onset of, and early during, SS (P < 0.05). However, late in SS, both glucose Ra and Rd were higher in CC and PC compared with other trials (P < 0.05). Although calculated rates of glucose oxidation were different when comparing the four trials (P < 0.05), total CHO oxidation and total fat oxidation were similar. Despite this, TT was improved in CC and PC compared with PP (P < 0.05). We conclude that 1) preexercise ingestion of CHO improves performance only when CHO ingestion is maintained throughout exercise, and 2) ingestion of CHO during 120 min of cycling improves subsequent TT performance.

glucose uptake; glycogen

IT IS WELL ESTABLISHED THAT carbohydrate (CHO) feeding during prolonged (>120 min) exercise can increase work capacity by maintaining power output or speed (1, 5, 23) or by prolonging the time to fatigue at a fixed, submaximal workload (7, 21, 28). In contrast, studies that have examined the effect of preexercise CHO feedings on performance have produced conflicting results. This practice has been demonstrated to increase (11, 30), decrease (6, 10), or have no effect (9, 27) on exercise performance. This may, in part, be due to the hyperinsulinemia resulting from preexercise CHO ingestion. Rises in circulating insulin increase muscle glucose uptake at the onset of exercise but subsequently result in rebound hypoglycemia after ~30 min (18), thereby decreasing peripheral glucose availability. Increases in plasma insulin concentration during exercise also act to reduce lipolysis (32) and fat availability (27), which are likely to lead to increased intramuscular glycogen use (2) and a consequent reduction in exercise performance. Nonetheless, preexercise CHO ingestion has been demonstrated to increase both liver (24) and muscle (8) glycogen stores, and, therefore, this practice has the capacity to increase exercise performance.

If CHO ingestion during exercise is undertaken in conjunction with a preexercise CHO feeding, it is possible that the resulting hyperinsulinemia and increased muscle glucose uptake will be sustained as a result of a better maintenance of blood glucose concentration. Indeed, CHO feeding during exercise has been shown to increase muscle glucose uptake compared with the ingestion of a sweet placebo (19). Such an increase in blood glucose availability could, theoretically, more than compensate for any hyperinsulinemia-induced reduction in lipolysis while also reducing the reliance on intramuscular glycogen stores. Such a metabolic scenario is likely to lead to an enhanced exercise performance.

In this regard, Wright et al. (33) have previously demonstrated that a combination of CHO feeding before and during exercise has an additive effect on performance compared with when CHO is ingested only before, or only during, exercise. In that study (33), however, subjects ingested different amounts of CHO before and during exercise, and, therefore, the relative
importance of each practice could not be elucidated. In addition, neither muscle glycogen nor glucose kinetics were determined in the study of Wright et al. (33), so it was impossible to determine the underlying mechanism behind their observed performance enhancement.

The aim of the present study was to determine the effect of CHO ingestion before, during, or in combination on exercise metabolism and performance. We conducted a comprehensive study by obtaining glucose kinetic data throughout exercise, which allowed us to determine the rate of glucose disposal when different CHO feeding strategies are adopted. We hypothesized that a combination of CHO feeding before and throughout exercise would maintain euglycemia, and a modest hyperinsulinemia, thereby preserving high rates of glucose uptake by the contracting muscles. By reducing the reliance on muscle glycogen, we hypothesized that performance would be significantly improved when feeding was combined before and during exercise.

**METHODS**

**Subjects.** Seven endurance-trained men [age 26.9 ± 6.4 (SD) yr; weight 74.7 ± 9.0 kg; peak oxygen uptake (VO₂peak) 63.0 ± 4.4 ml·kg⁻¹·min⁻¹; height 181 ± 6 cm] were recruited as subjects for this study after being fully informed of the risks associated with the procedures and signing a letter of informed consent. The project was approved by the Research and Ethics Committees of the University of Melbourne and Royal Melbourne Institute of Technology University.

**Preliminary testing.** VO₂peak was determined during an incremental cycling test to volitional fatigue on an electrically braked cycle ergometer (Lode, Groningen, The Netherlands). Expired air was directed via a Hans Rudolph valve and plastic tubing into Douglas bags. The oxygen and carbon dioxide content of the Douglas bags was analyzed using Applied Electrochemistry (Ametek, Pittsburgh, PA) S-3A/II and CD-3A gas analyzers, respectively, calibrated before each test with a commercially prepared gas mixture of known composition. The volume of expired gases was determined using a gas meter (Parkinson-Cowan, Manchester, UK).

**Experimental trials.** Subjects reported to the laboratory on four occasions after an overnight fast, having abstained from alcohol, caffeine, tobacco, and strenuous exercise for the previous 24 h. To minimize differences in resting muscle and liver glycogen concentration, subjects were provided with preprepared food packages (~15.6 J, 71% CHO, 15% protein, 14% fat) for 24 h before each trial. Such a dietary-exercise regimen has previously been shown to minimize differences in preexperimental metabolism and substrate availability (1). Each experiment was separated by a minimum of 7 days.

During each trial, subjects cycled for 120 min (SS) at a workload (~64 ± 2% of peak power output) equivalent to ~70% of VO₂peak, followed by a performance cycle (TT) in which subjects completed 7 kJ/kg body wt as fast as possible. Trials were performed in random order using a double-blind protocol, and the identity of each trial was not revealed until after analyses. Subjects received either no CHO-electrolyte before or during SS (PP); a placebo-electrolyte beverage 30 min before and 2 g/kg body wt of CHO in a 6.4% CHO-electrolyte beverage (Lucozade Sport) throughout SS (PC); 2 g/kg body wt of CHO in a 25.7% CHO-electrolyte beverage (Lucozade) 30 min before and a placebo-electrolyte beverage throughout SS (CP); or 2 g/kg body wt of CHO in a 25.7% CHO-electrolyte beverage 30 min before and 2 g/kg body wt of CHO in a 6.4% CHO-electrolyte beverage throughout SS (CC). The CHO and placebo beverages were matched for electrolyte content. They were provided at the onset and at 15-min intervals during SS. During the TT, subjects had access to water ad libitum.

On arrival in the laboratory, the subjects voided, were weighed, and catheters (Terumo 20 gauge) were inserted into a vein in the antecubital space of each arm for blood sampling and infusion of the tracer (described subsequently). After a basal blood sample was collected, the catheter was flushed with 0.5 ml of saline containing heparin (10 IU/ml). A primed (3.3 mmol) continuous (~44 μmol/min) infusion of sterile [6,6-³H]glucose (Cambridge Isotope Laboratories, Cambridge, MA) commenced and was maintained for the 120 min of rest and throughout SS. The infusion was delivered via a peristaltic pump (Gilson, Minipuls 3, Villiers Le Bel, France) that was calibrated before and after each experiment. At the completion of SS, subjects rested for 1 min before they commenced the TT.

Heart rate (HR), ratings of perceived exertion (RPE), VO₂, carbon dioxide production (VCO₂), and respiratory exchange ratio (RER) were measured at 15-min intervals during SS. In addition to the basal blood sample, further samples were obtained 10, 20, and 30 min postprandial and at 20-min intervals during SS.

**Analytic techniques.** HR was measured by telemetry (Polar, Kempele, Finland), and RPE was estimated using a 19-point scale (3). VO₂, VCO₂, and RER values were analyzed using Douglas bags as previously described, and the values were used to estimate rates of whole body CHO and fat oxidation according to the equations of Peronnet and Massicotte (25). Because estimated rates of substrate oxidation were contingent on precise pulmonary gas measures, the analyzers were calibrated before each measure, and the Douglas bags were analyzed on collection.

Ten milliliters of blood were collected at each sampling time; ~5 ml were placed in a tube containing fluoride heparin and spun in a centrifuge. The plasma was stored at ~80°C and later analyzed for plasma glucose concentration using an automated method (EML-105, Electrolyte Metabolite Laboratory, Radiometer, Copenhagen, Denmark) and plasma insulin concentration by radioimmunoassay (Incstar, Stillwater, MN). A further aliquot of blood was mixed in a tube containing lithium heparin and spun in a centrifuge. Two hundred and fifty microliters of plasma were placed into a tube containing 250 μl of ice-cold 3 M perchloric acid, mixed vigorously on a vortex mixer, and spun. Four hundred microliters of this supernatant were added to a tube containing 100 μl of 6 M KOH, mixed, and spun. The resultant supernatant was analyzed for plasma glyceral concentration using an enzymatic spectrophotometric analysis as previously described (1). The further aliquot of this plasma was stored for measurement of [6,6-³H]glucose enrichment as previously described (12). Briefly, 500 μl of plasma were mixed with 500 μl of 0.3 M Ba(OH)₂ and 500 μl of ZnSO₄, and spun. The supernatant was passed down an ion-exchange column (Dowex 2 × 8, 200–400 mesh, Bio-Rad, Richmond, CA) washed with distilled water (3 × 1-ml aliquots), and dried. The samples were then resuspended with distilled water, placed in glass vials, dehydrated overnight, and derivatized with the addition of pyridine and acetic anhydride. The derivatized samples were measured using a gas chromatograph-mass spectrometer (5890 series 2 gas chromatograph, 5971 mass spectrometer detector, Hewlett-Packard, Avondale, PA). The rates of glucose appearance (Rₐ) and glucose disappearance (Rₜ) were determined from changes in the
percent enrichment in the plasma of [6,6-2H]glucose, calculated using the one-pool non-steady-state model (29), assuming a pool fraction of 0.65 and estimating the apparent glucose space as 25% of body mass. Glucose oxidation was estimated by assuming that glucose $R_d$ during exercise was approximately equal to the amount of glucose oxidized (16). An estimate of glycogen oxidation was then calculated by subtracting glucose oxidation from total CHO oxidation obtained from pulmonary measures.

Two milliliters of whole blood were added to an aliquot of preservative consisting of EGTA and reduced glutathione in normal saline, mixed gently, and spun in a centrifuge. Plasma was decanted, placed in vials and stored at $-80^\circ C$. These samples were later analyzed for plasma free fatty acids (FFAs) using an enzymatic colorimetric method (22). The remaining blood (2 ml) was added to a lithium heparin tube containing 200 $\mu$l of a protease inhibitor (10% Trasylol), mixed gently, and spun in a centrifuge. Plasma was decanted, placed in vials, and stored at $-80^\circ C$ until analysis of plasma glucagon concentration by immunoradiometric assay (Biodione, Marrickville, Australia) as previously described (12).

Statistical analyses. The metabolic data from the four trials was compared using two-factor (time and treatment) ANOVA with repeated measures. A one-way ANOVA was used to compare time to complete the performance cycle. Newman-Keuls post hoc tests were used to locate differences when ANOVA revealed a significant interaction. A Statistica computer software program was used to compute these statistics. The alpha level to reject the null hypothesis was set at $P < 0.05$. All values are expressed as means $\pm$ SE.

RESULTS

Mean $\dot{V}O_2$, $\dot{V}CO_2$, RER, HR, and RPE during SS were not different between trials (Table 1). However, RER was higher ($P < 0.05$) in CC compared with other trials at 105 and 120 min (data not shown). Preexercise CHO consumption resulted in a higher ($P < 0.01$) plasma glucose concentration 10, 20, and 30 min postingestion in CC and CP compared with PC and PP (Fig. 1). During the first 90 min of SS, no differences in plasma glucose concentration were observed between trials. However, during the last 30 min of SS, plasma glucose concentration was higher in CC and CP compared with PC and PP (Fig. 1). Neither plasma FFA nor glycerol concentrations were different between trials during the first 60 min of SS. However, during the final 60 min of SS, both plasma FFA and glycerol concentrations were elevated ($P < 0.05$) in PP compared with CC, CP, and PC (Fig. 2). Plasma FFA concentrations during this period were not different between CC, CP, or PC (Fig. 2), although plasma glycerol was higher ($P < 0.05$) when comparing PP with PC at 120 min. Preexercise CHO ingestion resulted in a higher ($P < 0.01$) plasma insulin concentration 10, 20, and 30 min postingestion in CC and CP compared with PC and PP. However, shortly after the start of exercise, plasma insulin concentrations were similar between trials (Fig. 3). Although plasma glucagon concentration increased ($P < 0.05$) as exercise progressed, this hormone was not different between trials (Fig. 3). Glucose $R_g$ and $R_d$ were higher ($P < 0.05$) in CC and CP compared with PC and PP after beverage ingestion and at the onset of SS. In addition, for reasons not readily apparent, glucose $R_g$ was higher ($P < 0.05$) in CC compared with CP 10 min after ingestion. No differences in glucose $R_g$ or $R_d$ were observed between trials during the first 105 min of SS. However, during the last 15 min of SS, glucose $R_g$ and $R_d$ were higher ($P < 0.05$) in CC compared with PC and PP (Fig. 4). The rates of total CHO oxidation were not different between trials for the first 105 min of SS but were higher ($P < 0.05$) in CC compared with other trials at 105 and 120 min. Because we assumed that glucose $R_d$ during exercise was approximately equal to the amount of glucose oxidized, we were able to obtain an indirect measure of glucose oxidation and CHO oxidation derived from other sources (i.e., glycogen). These calculations demonstrated that glucose oxidation was different ($P < 0.05$) when comparing the four trials, with CC > CP >
PC/H11022PP. However, the contribution of glucose to total substrate oxidation was minimal, ranging from 38 to 43 g (8–11% of total energy). Hence, estimated total glycogen oxidation and fat utilization were not different when comparing the four trials (Fig. 5). Despite this, the time taken to complete 7 kJ/kg was lower (P < 0.05) when comparing CC and PC with PP. No difference in exercise performance was observed when comparing PP with CP (Fig. 6).

**DISCUSSION**

The results from this study demonstrate that even when relatively high amounts of CHO are fed in combination before and during exercise, the contribution of CHO and fat to total substrate use were not affected when compared with ingestion of a placebo. Nonetheless, when CHO was ingested both before and during exercise, endurance performance was increased compared with the ingestion of a placebo. In addition, when equal amounts of CHO were consumed either 30 min before or throughout exercise, endurance performance was increased only when CHO was consumed throughout exercise, despite the fact that the contribution of glucose to energy turnover was higher when glucose was ingested before exercise.

In the present study, ~150 g of glucose were fed before exercise and an equal amount was fed during exercise in CC. Despite this high oral glucose load and the fact that plasma insulin concentration increased markedly (Fig. 2), providing an added stimulus other than muscle contraction for glucose disposal, the estimated contribution from glucose to total substrate oxidation was only 11%, representing an average rate of oxidation of only 0.4 g/min. This result was somewhat unexpected but demonstrates that, in endurance-trained humans, the contribution of glucose to total energy turnover during exercise is relatively minor. These data support those of Juekendrup et al. (17), who observed that the ingestion of 354 g of CHO during 120 min of low-intensity (50% maximal oxygen uptake) cycling resulted in glucose contributing <1 g/min to the total substrate turnover. In fact, several studies have demonstrated that glucose oxidation is limited during exercise despite marked hyperglycemia and hyperinsulinemia (13, 14, 17, 26, 31). In the present study, we were unable to determine what percentage of glucose Ra came from exogenous glucose. Nonetheless, even if hepatic glucose production was completely suppressed, as is possible when large amounts of glucose are ingested during exercise (17), we cannot account for all of PC > PP. However, the contribution of glucose to total substrate oxidation was minimal, ranging from 38 to 43 g (8–11% of total energy). Hence, estimated total glycogen oxidation and fat utilization were not different when comparing the four trials (Fig. 5). Despite this, the time taken to complete 7 kJ/kg was lower (P < 0.05) when comparing CC and PC with PP. No difference in exercise performance was observed when comparing PP with CP (Fig. 6).
the ingested glucose appearing in the plasma and/or being taken up by tissue. Therefore, our data are in agreement with the previous suggestion that the rate of exogenous glucose oxidation may be limited by digestion, absorption, and glucose Ra into the bloodstream (16). It must be noted that, in the present study, we assumed that glucose Rd matches glucose oxidation because we were unable to directly measure glucose oxidation using 6,6-2H. However, we are confident that this assumption is valid because it has been previously demonstrated that ~98% of glucose Rd is oxidized during exercise (16).

It is important to note that the calculated rate of glucose oxidation was higher in CP compared with PC, even though the amount of glucose ingested during both of these trials was equal. It is likely that the small, but nonetheless significant, increase in glucose uptake and oxidation during exercise was due to marked hyperinsulinemia after ingestion in CP, which was not apparent in PC (Fig. 3). Insulin and contraction have a synergistic effect on muscle glucose uptake (4). Despite this observation, exercise performance was increased in PC, but not CP, when compared with PP (Fig. 6). These data support the previous investigations that have demonstrated that the ergogenic benefit of CHO consumption during prolonged exercise is a consistent and reproducible finding (1, 5, 7, 21, 23, 28) but
that the efficacy of preexercise CHO ingestion on performance is equivocal (6, 9–11, 27, 30). It has been suggested that the differences seen when comparing the effect of preexercise CHO ingestion with feeding throughout exercise are related to the negative effects of hyperinsulinemia associated with preexercise CHO ingestion. Increased insulin reduces the lipolytic rate and limits the availability of plasma FFAs in the circulation (32). Such a reduction in FFA availability augments muscle glycogen utilization (2). However, in the present study, despite the relative hyperinsulinemia when comparing CP with PC (Fig. 2), we found no evidence of impaired fat availability (Fig. 2) or fat utilization (Fig. 4). Furthermore, CHO utilization was not different between these two trials (Fig. 4). Hence, we found no evidence that the superior exercise performance in PC compared with CP and PP was related to substrate metabolism. It is important to note, however, that, in the two trials that produced increased exercise performance, plasma glucose concentration was better maintained in the final hour of SS (Fig. 1). It is possible that this better maintenance of plasma glucose concentration had a positive effect on mechanisms other than those associated with substrate turnover. It has been previously demonstrated that CHO ingestion can increase exercise performance during a 60-min TT (15) or when CHO is ingested throughout, as opposed to only during the final 30 min of a 120-min cycle (20). Similar to the present observations, the authors of these respective studies found little evidence of a metabolic basis for their observed performance improvement. Hence, it appears that the maintenance of high (i.e., 6 mM) plasma glucose concentrations typically associated with the ingestion of CHO throughout exercise may improve exercise performance by mechanisms other than alterations in substrate utilization, such as negative central nervous system changes, as previously suggested (20).

In summary, our data demonstrate that, even when CHO is ingested in large quantities before and during exercise, the amount of glucose disappearance is relatively minor. However, the maintenance of high plasma glucose concentrations throughout exercise appears to increase exercise performance.

We acknowledge the excellent technical assistance of Rebecca Starkie and Dr. Dominic Cardi from the School of Life Sciences of Victoria University of Technology (Footscray, Victoria, Australia) for the use of the gas chromatography-mass spectrometer.

This study was supported by a grant from SmithKline Beecham Consumer Healthcare (UK).

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