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Substrate source utilization during moderate intensity exercise with glucose ingestion in Type 1 diabetic patients

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Robitaille M, Dubé M-C, Weisnagel SJ, Prud'homme D, Massicotte D, Péronnet F, Lavoie C. Substrate source utilization during moderate intensity exercise with glucose ingestion in Type 1 diabetic patients. *J Appl Physiol* 103: 119–124, 2007. First published April 12, 2007; doi:10.1152/japplphysiol.01462.2006.—Substrate oxidation and the respective contributions of exogenous glucose, glucose released from the liver, and muscle glycogen oxidation were measured by indirect respiratory calorimetry combined with tracer technique in eight control subjects and eight diabetic patients (5 men and 3 women in both groups) of similar age, height, body mass, and maximal oxygen uptake, over a 60-min exercise period on cycle ergometer at 50.8% (SD 4.0) maximal oxygen uptake [131.0 W (SD 38.2)]. The subjects and patients ingested a breakfast (containing ~80 g of carbohydrates) 3 h before and 30 g of glucose (labeled with ^{13}C) 15 min before the beginning of exercise. The diabetic patients also received their usual insulin dose [Humalog = 9.1 U (SD 0.9); Humulin N = 13.9 U (SD 4.4)] immediately before the breakfast. Over the last 30 min of exercise, the oxidation of carbohydrate [1.32 g/min (SD 0.48) and 1.42 g/min (SD 0.63)] and fat [0.33 g/min (SD 0.10) and 0.30 g/min (SD 0.10)] and their contribution to the energy yield were not significantly different in the control subjects and diabetic patients. Exogenous glucose oxidation was also not significantly different in the control subjects and diabetic patients [6.3 g/30 min (SD 1.3) and 5.2 g/30 min (SD 1.6), respectively]. In contrast, the oxidation of plasma glucose and oxidation of glucose released from the liver were significantly lower in the diabetic patients than in control subjects [14.5 g/30 min (SD 4.3) and 9.3 g/30 min (SD 2.8) vs. 27.9 g/30 min (SD 13.3) and 21.6 g/30 min (SD 12.8), respectively], whereas that of muscle glycogen was significantly higher [28.1 g/30 min (SD 15.5) vs. 11.6 g/30 min (SD 8.1)]. These data indicate that, compared with control subjects, in diabetic patients fed glucose before exercise, substrate oxidation and exogenous glucose oxidation overall are similar but plasma glucose oxidation is lower; this is associated with a compensatory higher utilization of muscle glycogen.

indirect respiratory calorimetry; carbon isotopes; insulin; muscle glycogen; plasma glucose oxidation

INGESTION OF CARBOHYDRATES (CHO) immediately before exercise is advocated in patients with Type 1 diabetes to avoid hypoglycemia during and/or after exercise (8, 15). There is however a paucity of data on the effect of CHO ingestion on substrate oxidation during moderate exercise in diabetic patients (7, 11, 22–24), and only two studies have compared the oxidation rate of exogenous glucose during exercise in diabetic patients and control subjects (11, 24). In both studies, compared with the observation in the control subjects, exogenous glucose oxidation was not significantly different in diabetic patients over 4 h of exercise at ~45% maximal oxygen uptake ($\dot{V}O_{max}$) (11) or 60 min of exercise at ~60% $\dot{V}O_{max}$ (24). However, the oxidation of exogenous glucose was delayed in the diabetic patients; in the study by Riddell et al. (24), the contribution of exogenous glucose oxidation to the energy yield was significantly lower in the diabetic patients than in control subjects (9 vs. 12%).

In the present study, substrate oxidation during a 60-min exercise period at 50% $\dot{V}O_{max}$ after ingestion of 30 g of glucose was compared in diabetic patients receiving their usual insulin dose and in control subjects. The glucose ingested was artificially labeled with ^{13}C to compute the oxidation of exogenous glucose, plasma glucose, glucose released from the liver, and muscle glycogen from calorimetry data and $^{13}CO_2$ production at the mouth, and from the ^{13}C enrichment of plasma glucose (3, 5, 6, 9, 20). On the basis of data from Krzentowski et al. (11) and Riddell et al. (24), we hypothesized that, during exercise, exogenous and endogenous CHO oxidation, respectively, will not be different in the diabetic patients and control subjects. However, Raguso et al. (21) have shown that, compared with control subjects, in response to a 30-min exercise period at 45% $\dot{V}O_{max}$ without glucose ingestion, the rate of plasma glucose disappearance was lower in diabetic patients, presumably because of a defective recruitment of glucose transporters. In addition, recent data from Chokkalingam et al. (4) suggest that the oxidation rate of plasma glucose in diabetic patients during exercise could be lower than its rate of disappearance. From these results and from the observation that endogenous CHO oxidation during exercise with glucose ingestion was not significantly different in diabetic patients and control subjects (11, 24), we hypothesized that the oxidation of plasma glucose and of glucose released from the liver could be lower, whereas that of muscle glycogen could be higher in diabetic patients than in control subjects.

METHODS

Eight control subjects and eight diabetic patients (5 men and 3 women in each group), with similar average age, height, body mass, and $\dot{V}O_{max}$ on cycle ergometer (Table 1), gave their written informed consent to participate in this study. The study was approved by the

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Table 1. *Characteristics of the control subjects and diabetic patients*

	Control Subjects (n = 8)	Diabetic Patients (n = 8)
Age, yr	24.0 (1.8)	26.5 (6.8)
Body mass, kg	79.0 (19.0)	78.1 (12.3)
Height, cm	175.4 (13.0)	175.5 (8.7)
Body-mass index, kg/m^2	25.5 (4.8)	25.2 (2.2)
Duration of diabetes, yr	N/A	12.8 (6.8)
Daily insulin dose, U/day,	N/A	69.0 (19.5)
Glycated hemoglobin (hemoglobin A_{1c}), %	5.0 (0.4)	7.4 (0.4)*
Max power ouput, W	259.4 (77.9)	256.3 (77.6)
$\dot{V}O_{2max}$, ml·kg^{-1}·min^{-1}	42.3 (6.6)	42.9 (10.3)

Values are means (SD). $\dot{V}O_{2max}$, maximal oxygen uptake. *Significantly different from control subjects, $P < 0.05$.

Ethic Committees on the use of human subjects in research of the Université Laval and the Université du Québec à Trois-Rivières. Both control subjects and diabetic patients were lean, nonsmokers and were moderately active (2–5 h/wk). The women in both groups were taking oral contraceptives and were studied in the follicular phase of the menstrual cycle (5–7 days after the beginning of menstruation). Insulinotherapy for the diabetic patients included the insulin analog Humalog (Lispro, Eli Lilly Canada, Scarborough, Ontario, Canada) before every meal and Humulin N (Eli Lilly Canada) before breakfast and at bedtime. The concentration of glycated hemoglobin (Table 1) indicated that, at the time of experiment, the patients were in good metabolic control and all of them were free of diabetic complications as assessed by their physicians. No episode of hypoglycemia was reported by the diabetic patients for at least 24 h before the experiment. During the 2 days preceding the experiment, all subjects refrained from exercising and from ingesting alcohol and caffeine. They also avoided ingesting foods containing CHO with a high ^{13}C content (e.g., corn, sugar cane), which may modify the background ^{13}C enrichment of plasma glucose and expired CO_2 (12). On the day before the experiment, the evening meal was standardized and taken between 0700 and 0800 (~13 kcal/kg; ~20% proteins, ~35% lipids, and ~45% CHO).

Maximal aerobic power on cycle ergometer (Lode Instruments) and $\dot{V}O_{max}$ (open-circuit spirometry: Vacumetrics, Ventura, CA) were measured 1 wk before the experiment. On the day of experiment, the subjects reported to the laboratory at 7:15 AM after a 12-h overnight fast and ingested a standardized breakfast at 7:30 AM (~8 kcal/kg; ~20% proteins, ~30% lipids, and ~50% CHO). Immediately before the breakfast, the diabetic patients were given their usual morning insulin dose [Humalog = 9.1 U (SD 0.9); Humulin N = 13.9 U (SD 4.4)]. Three hours later, the subjects exercised for 60 min (from 10:30 to 11:30 AM) on the ergocycle at 50% $\dot{V}O_{max}$ and were observed during an additional 60-min recovery period (11:30 AM to 12:30 PM). At the end of the recovery period and before leaving the laboratory (~1:00 PM), the subjects ingested a lunch containing 75 g of CHO. To prevent possible postexercise-induced hypoglycemia in the diabetic patients, the usual dose of insulin administered before this lunch was reduced by 50% (~4–5 U Humalog).

A 30-g glucose load dissolved in 300 ml of water was ingested 15 min before the beginning of exercise. The glucose derived from corn (Biopharm, Laval, Canada; $^{13}C/^{12}C = -11.0‰$ [δ-^{13}C]PDB) was artificially enriched with [U-^{13}C]glucose ($^{13}C/C > 99\%$; Isotec, Miamisburg, OH) to achieve a final isotopic composition of 400‰ [δ-^{13}C]PDB. This high ^{13}C enrichment of exogenous glucose provides a strong signal in plasma glucose as well as in expired CO_2 and allows the neglect of the comparatively small changes in background enrichment of expired CO_2 observed from rest to exercise (19).

Observations were made at rest before glucose ingestion, before the beginning of exercise, and every 15 min during the exercise period. Fat and CHO oxidation were computed from indirect respiratory calorimetry corrected for protein oxidation. For this purpose, oxygen consumption ($\dot{V}O_2$) and carbon dioxide production ($\dot{V}CO_2$) were measured by open-circuit spirometry (5-min collection period), and urea excretion in urine was measured over 5 h (from 7:30 AM to 12:30 PM). For the measurement of the isotopic composition ($^{13}C/^{12}C$) of expired CO_2, 10-ml samples of expired gas were collected in vacutainers. Finally, at rest before ingestion of [^{13}C]glucose and at regular intervals during the exercise period, 10-ml blood samples were withdrawn through a catheter (Cathlon Clear, Johnson & Johnson), which was placed in an antecubital vein at the beginning of the experiment, for the measurement of plasma glucose and insulin concentrations and of $^{13}C/^{12}C$ in plasma glucose. Between the samplings that were made, the catheter was kept patent by a slow infusion of sterile isotonic saline.

Plasma samples were stored at −80°C until analyses. In addition, in diabetic patients, plasma glucose concentration was measured at 5-min intervals throughout the period of exercise and the 60-min recovery period to verify that hypoglycemia did not develop (One Touch Ultra glucose meter; LifeScan, Milpitas, CA).

Substrate oxidation was computed from $\dot{V}O_2$ and $\dot{V}CO_2$ (in l/min) (18):

$$\text{CHO (g of glucose/min)} = 4.59\,\dot{V}CO_2 - 3.23\,\dot{V}O_2 \quad (1)$$

$$\text{Fat (g/min)} = 1.70(\dot{V}O_2 - \dot{V}CO_2) \quad (2)$$

In these computations, $\dot{V}O_2$ and $\dot{V}CO_2$ were corrected for the average rate of protein oxidized over the 5-h period of observation [38 mg/min (SD 12) and 35 mg/min (SD 10) in control subjects and diabetic patients; not significantly different].

Plasma glucose $^{13}C/^{12}C$ was measured as previously described (3). Briefly, plasma glucose was separated by double-bed ion-exchange chromatography (AG 50W-X8 H^+ and AG 1-X8 chloride, 200–400 mesh; Bio-Rad, Mississauga, ON, Canada) after deproteinization with barium hydroxide and zinc sulfate (0.3 N). The eluate was evaporated to dryness (Virtis Research Equipment, New York, NY) and combusted (60 min at 400°C with copper oxide), and the CO_2 was recovered for the isotopic analyses.

Measurement of $^{13}C/^{12}C$ in expired CO_2 and in CO_2 from combustion of plasma glucose was performed by mass spectrometry (Prism, Manchester, UK). The isotopic composition of ingested glucose, expired CO_2, and plasma glucose was expressed in ‰ difference by comparison with the PDB Chicago Standard: ‰ [δ-^{13}C]PDB-1 = [(Rspl/Rstd) − 1] × 1,000, where Rspl and Rstd are the ^{13}C-to-^{12}C ratios in the sample and standard (1.1237%), respectively (3).

The oxidation rate of exogenous glucose (in g/min) was computed as follows (19):

$$\text{Exogenous glucose (g/min)} = \dot{V}CO_2\,[(\text{Rexp} - \text{Rref})/(\text{Rexo} - \text{Rref})]/k \quad (3)$$

In this equation, $\dot{V}CO_2$ (not corrected for protein oxidation) is in liters per minute, Rexp is the observed isotopic composition of expired CO_2, Rref is the isotopic composition of expired CO_2 at rest before ingestion of [^{13}C]glucose, Rexo is the isotopic of the exogenous glucose ingested, and k (0.747 l/g) is the volume of CO_2 provided by the complete oxidation of glucose. In addition, based on the isotopic composition of plasma glucose (Rglu), the oxidation rate of plasma glucose (in g/min) was computed as follows (5, 20):

$$\text{Plasma glucose (g/min)} = \dot{V}CO_2\,[(\text{Rexp} - \text{Rref})/(\text{Rglu} - \text{Rref})]/k \quad (4)$$

The oxidation rate of muscle glycogen (in g/min), either directly or through the lactate shuttle (2), was computed by the difference between the rate of total glucose oxidation (*Eq. 1*) and the oxidation rate of plasma glucose (*Eq. 4*). Finally, the oxidation rate of glucose released by the liver was estimated by the difference between the oxidation rate of plasma and exogenous glucose. These computations

are based on the observation that, during exercise, ^{13}C provided from [^{13}C]glucose is not irreversibly lost in pools of tricarboxylic acid cycle intermediates and/or bicarbonate and that $^{13}CO_2$ recovery in expired gases is thus complete or almost complete (25, 29). However, the $^{13}C/^{12}C$ in expired CO_2 only slowly equilibrates with $^{13}C/^{12}C$ in the CO_2 produced in tissues (17). To take into account the delay between $^{13}CO_2$ production in tissues and at the mouth, exogenous and plasma glucose oxidation and oxidation of glucose released from the liver and muscle glycogen were only computed during the last 30 min of exercise, thus allowing for a 30-min equilibration period.

Plasma glucose concentration was measured by a spectrophotometric assay (Sigma Diagnostics, Mississauga, ON, Canada), whereas plasma insulin concentration was measured with a radioimmunoassay (KTSP-11001, Immunocorp Sciences, Montreal, QC, Canada).

Results are presented as means (SD). Comparisons were made by one-way or two-way ANOVA (diabetic patients vs. control subjects × time) with repeated measures on one factor (time). When appropriate, Newman-Keuls post hoc tests were performed. The comparisons were made at the 0.05 level of significance.

RESULTS

No significant difference was observed for gas exchanges between control subjects and diabetic patients at rest and during the exercise period (Table 2). In both groups, the contribution of CHO oxidation to the energy yield significantly decreased, whereas that of fat oxidation significantly increased from *minutes 0–30* to *minutes 30–60* during the exercise period (Table 3). However, the oxidation of CHO and fat and their respective contributions to the energy yield were not significantly different in control subjects and in diabetic patients.

The isotopic composition of expired CO_2 at rest before ingestion of [^{13}C]glucose was not significantly different in diabetic patients and control subjects {−23.9‰ [δ-^{13}C]PDB-1 (SD 0.89) vs. −23.8‰ [δ-^{13}C]PDB-1 (SD 1.2), respectively} (Fig. 1). In response to [^{13}C]glucose ingestion, the progressive increase in $^{13}C/^{12}C$ in expired CO_2 was slower in diabetic patients than in control subjects (main effect with interaction). The amount of exogenous glucose oxidized, computed between *minutes 30* and *60* during the exercise period, was ~20% higher in the control subjects than in the diabetic patients. However, this difference *1*) did not reach statistical significance (Table 4) and *2*) could be partly because exogenous glucose oxidation was underestimated in the diabetic patients because $^{13}C/^{12}C$ in expired CO_2 only started to level off at *minute 45* vs. *minute 30* in the control subjects (Fig. 1). The percentage of exogenous glucose, which was actually oxidized between *minute 30* and *60* [21% (SD 4) and 17% (SD 5) in the control subjects and the diabetic patients], and the contribution of exogenous glucose oxidation to the energy

Table 2. *Gas exchanges at the mouth at rest and over the 60-min exercise period*

		Control Subjects (n = 8)	Diabetic Patients (n = 8)
	Rest		
$\dot{V}O_2$, l/min		0.40 (0.11)	0.38 (0.07)
$\dot{V}CO_2$, l/min		0.34 (0.10)	0.31 (0.08)
RER		0.856 (0.036)	0.804 (0.064)
	Exercise		
$\dot{V}O_2$, l/min	*Minute* 0–30	1.68 (0.48)	1.72 (0.42)
	Minute 30–60	1.68 (0.46)	1.69 (0.50)
$\dot{V}CO_2$, l/min	*Minute* 0–30	1.51 (0.45)	1.60 (0.42)
	Minute 30–60	1.47 (0.42)	1.50 (0.48)
RER	*Minute* 0–30	0.894 (0.031)	0.928 (0.028)
	Minute 30–60	0.875 (0.028)*	0.884 (0.037)*

Values are means (SD). $\dot{V}O_2$, oxygen consumption; $\dot{V}CO_2$, carbon dioxide production; RER, respiratory exchange ratio. *Significantly different from the interval *minute 0–30,* $P < 0.05$.

Table 3. *Total CHO and fat oxidation and percent contribution to the energy yield during rest and exercise*

		Control Subjects (n = 8)	Diabetic Patients (n = 8)
	Rest		
CHO, g/min		0.26 (0.12)	0.17 (0.14)
%Energy		49.2 (11.8)	30.7 (23.8)
Fat, g/min		0.08 (0.03)	0.11 (0.03)
%Energy		41.6 (12.0)	60.0 (22.0)
	Exercise		
CHO, g/min	*Minute* 0–30	1.47 (0.57)	1.77 (0.58)
	Minute 30–60	1.32 (0.48)	1.42 (0.63)*
%Energy	*Minute* 0–30	65.2 (10.2)	76.3 (9.2)
	Minute 30–60	59.0 (9.2)*	61.8 (12.4)*
Fat, g/min	*Minute* 0–30	0.28 (0.09)	0.19 (0.08)
	Minute 30–60	0.33 (0.10)*	0.30 (0.10)*
%Energy	*Minute* 0–30	32.7 (10.3)	21.8 (9.1)
	Minute 30–60	38.9 (9.4)*	36.2 (12.0)*

Values are means (SD). The contribution of protein oxidation to the energy yield averaged 2–3%. CHO, carbohydrate; %energy, percent contribution to the energy yield. *Significantly different from *minutes 0–30,* $P < 0.05$.

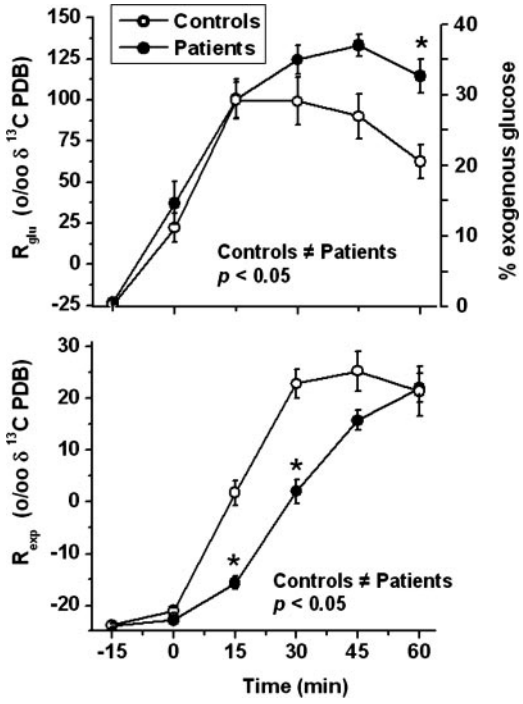

Fig. 1. Isotopic composition ($^{13}C/^{12}C$) of expired CO_2 (Rexp; *bottom*) and plasma glucose (Rglu; *top*) and percentage of plasma glucose arising from exogenous glucose (*top*) after [^{13}C]glucose ingestion in control subjects and diabetic patients. Values are means and SD; n = 8 subjects. *Significantly different in the control subjects and diabetic patients (main effect with interaction for Rglu and Rexp) and significantly different from the control subjects by two-way ANOVA (group × time) with repeated measures on one factor (time): $P < 0.05$.

Table 4. *Oxidation of glucose from various sources over the last 30 min of exercise in control subjects and diabetic patients*

	Control Subjects (n = 8)	Diabetic Patients (n = 8)
Total glucose, g	39.5 (14.5)	42.5 (19.0)
Exogenous glucose, g	6.3 (1.3)	5.2 (1.6)
Plasma glucose, g	27.9 (13.3)	14.5 (4.3)*
Glucose from liver, g	21.6 (12.8)	9.3 (2.8)*
Muscle glycogen, g	11.6 (8.1)	28.1 (15.5)*

Values are means (SD). *Significantly different from control subjects, $P < 0.05$.

yield (Fig. 2) were not significantly different in the control subjects and diabetic patients.

Figure 1 also shows the $^{13}C/^{12}C$ in plasma glucose and the percentage of plasma glucose deriving from the [^{13}C]glucose ingested. In response to exercise and [^{13}C]glucose ingestion, the percentage of plasma glucose deriving from exogenous glucose significantly increased (main effect). This increase was significantly higher in the diabetic patients than in control subjects (main effect with interaction). The values were similar over the first 30 min of exercise. However, over the second 30-min period of exercise, the percentage of plasma glucose deriving from exogenous glucose was higher in diabetic patients than in control subjects.

Table 4 and Fig. 2 show that, over the last 30 min of exercise, compared with the observations in control subjects, the oxidation of plasma glucose and of glucose released from the liver and their respective contribution to the energy yield were ~50–55% lower in diabetic patients. In contrast, the oxidation of muscle glycogen and its contribution to the energy yield were significantly 250% higher.

In control subjects, plasma glucose concentrations significantly increased in response to glucose ingestion [from 4.8 mmol/l (SD 0.7) to 6.1 mmol/l (SD 1.3) at *minute 15* during the exercise period] and then returned to preingestion levels (Fig. 3). In diabetic patients, plasma glucose concentration, which was significantly higher than in control subjects over the entire period of observation (main effect), also significantly increased in response to glucose ingestion [from 9.6 mmol/l (SD 2.9) to 11.7 mmol/l (SD 3.1) at *minute 15* during the exercise period] but then significantly decreased below the value observed at rest before exercise [7.5 mmol/l (SD 3.4) at the end of exercise period]. In control subjects, glucose ingestion transiently increased plasma insulin concentration over basal values at *minute 0*. In diabetic patients, plasma insulin concentration was significantly higher than that shown in control subjects at rest and exercise (main effect) and slowly decreased over the observation period (Fig. 3).

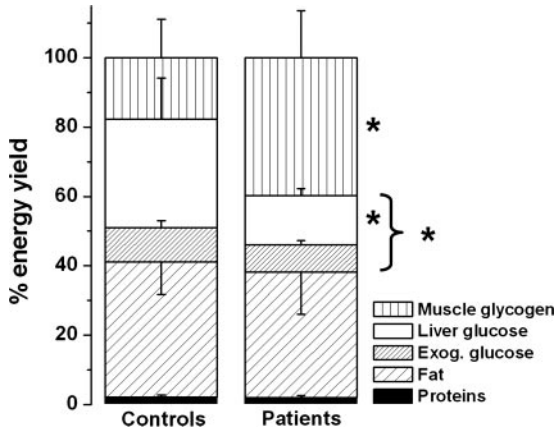

Fig. 2. Oxidation of glucose from various sources between *minute 30* and *60* during exercise in control subjects and diabetic patients. Values are means and SD; n = 8 subjects. Exog, exogenous. *Significantly different from the control subjects by one-way ANOVA for independent measures: $P < 0.05$.

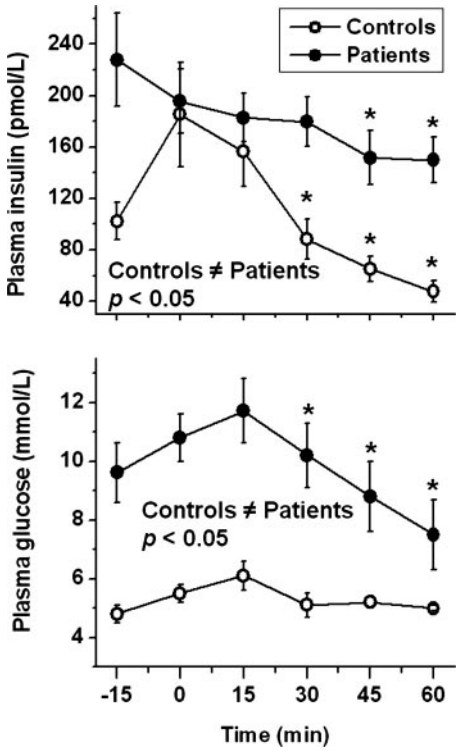

Fig. 3. Plasma glucose (*bottom*) and insulin (*top*) concentrations in control subjects and diabetic patients. Values are means and SD; n = 8 subjects. *Significantly different from the corresponding peak value and significantly different in control subjects and diabetic patients (main effect with interaction for both variables) by two-way ANOVA (group × time) with repeated measures on one factor (time): $P < 0.05$.

DISCUSSION

Data from Wahren et al. (30), Lyngsoe et al. (13), and Ramires et al. (22) show that, in diabetic patients deprived of insulin for 12–24 h during prolonged moderate exercise without glucose ingestion, the respiratory exchange ratio is lower, and thus fat oxidation is higher, than that shown in control subjects. In contrast, when insulin is administered to diabetic patients before or during moderate exercise without ingestion of glucose, fuel selection is not significantly different than that shown in control subjects (14, 21, 24). Ingestion of glucose immediately before exercise is advocated in diabetic patients receiving a normal or reduced dose of insulin (1) to avoid exercise-induced hypoglycemia (8, 15). However, there is a paucity of data on substrate utilization in this situation (7, 11, 24). In the study by Francescato et al. (7), which were conducted at various time intervals after insulin injection and with different amounts of glucose ingested, fat oxidation and CHO oxidation were not significantly different, respectively, from those observed in control subjects. However, the control sub-

jects did not receive any exogenous glucose. In the studies by Riddell et al. (24) and Krzentowski et al. (11), both the control subjects and the insulin-treated diabetic patients ingested glucose before and/or during exercise. In these two studies, the oxidations of fat and CHO were not significantly different in the two groups. Results from the present experiment are well in line with these observations: in diabetic patients receiving their usual insulin dose along with the breakfast 3 h before exercise and a 30-g glucose load 15 min before exercise, total CHO and total fat oxidations were not significantly different from those observed in control subjects during a 60-min period at 50% $\dot{V}O_{max}$.

In the studies by Krzentowski et al. (11) and by Riddell et al. (24), the glucose ingested was labeled with ^{13}C to measure exogenous glucose oxidation. In both studies, the progressive increase in production of $^{13}CO_2$ at the mouth was slower and reached its maximum later in diabetic patients (11, 24); in the study by Riddell et al. (24), the percent contribution of exogenous glucose oxidation to the energy yield was significantly lower in diabetic patients than in control subjects. However, the amount of exogenous glucose oxidized over the exercise period was only slightly and not significantly lower in diabetic patients than in control subjects (11, 24). Because total CHO oxidation was not significantly different in diabetic patients and control subjects, endogenous glucose oxidation was not significantly different in the two groups described in Krzentowski et al. (11) and Riddell et al. (24). Results from the present experiment confirm these findings. The appearance of ^{13}C in expired CO_2 was delayed over the first 30 min of exercise; however, over the second part of exercise (*minutes 30–60*), the amount of exogenous glucose oxidized, and its contribution to the energy yield was not significantly different in the diabetic patients and control subjects. Endogenous glucose oxidation was also similar over the last 30-min period of exercise in diabetic patients and in control subjects [37 g/30 min (SD 18) vs. 33 g/30 min (SD 14), contributing 54% (SD 13) vs. 49% (SD 11) to the energy yield, respectively]. These results from Krzentowski et al. (11) and Riddell et al. (24) and from the present experiment together show that, in diabetic patients receiving insulin, overall fuel selection, including the oxidation of exogenous glucose, is not different from that observed in control counterparts.

We are not aware of any study of plasma glucose oxidation during prolonged moderate exercise in Type 1 diabetic patients, and there are only a limited number of studies of the rate of plasma glucose disappearance (4, 21, 26, 27, 32). In addition, all of these studies have been conducted without administration of glucose, except for the recent study by Chokkalingam et al. (4), which was conducted under a slightly hyperglycemic (8 mmol/l)-hyperinsulinemic clamp. No significant differences were observed for rates of plasma glucose disappearance between control subjects and diabetic patients in work by Shilo et al. (26), Zinman et al. (32), and Simonson et al. (27). In contrast, in the study by Raguso et al. (21), the increase in rate of plasma glucose disappearance was similar in diabetic patients and in control subjects at 75% $\dot{V}O_{max}$ but was ~50% lower in diabetic patients than in control subjects at 45% $\dot{V}O_{max}$. In addition, data from Chokkaligam et al. (4) suggest that, in diabetic patients, plasma glucose oxidation could be much lower than its rate of disappearance. Unfortunately, no control subjects were included in that study. In line with these observations, in the present experiment, despite higher plasma glucose and insulin concentrations in diabetic patients than in control subjects, the oxidation of plasma glucose and that of glucose derived from the liver (Table 4), as well as their respective contributions to the energy yield (Fig. 2), were much lower in the diabetic patients than in control subjects. As discussed by Raguso et al. (21) and Chokkalingam et al. (4), this is probably due to a defect in insulin-mediated glucose transport in the muscle fiber in patients with Type 1 diabetes. This hypothesis is supported by data from Klip et al. (10) in rats with streptozotocin-induced diabetes. Compared with control rats, the number of GLUT4 transporters in the intracellular pool was lower and their redistribution on plasma membrane after insulin stimulation was also lower. As a consequence, insulin-stimulated glucose uptake was also ~50% lower. Nuutila et al. (16) and Yki-Jarvinen et al. (31) also showed that insulin-stimulated muscle plasma glucose uptake was ~25–45% lower in Type 1 diabetic patients than in control subjects.

In the present experiment, total CHO oxidation was not significantly different in the two groups, indicating a larger oxidation of glucose derived from muscle glycogen, which compensated for the lower oxidation rate of plasma glucose in the diabetic patients (Table 4 and Fig. 2). This observation differs from that of Raguso et al. (21), in which the reduction in plasma glucose oxidation (assumed to be equal to rate of plasma glucose disappearance) was compensated for by an increased intramuscular triglyceride oxidation, whereas muscle glycogen oxidation was not significantly different in diabetic patients and control subjects. Standl et al. (28) also reported that the reduction in muscle glycogen content over a 60-min exercise period at 50–60% $\dot{V}O_{max}$ without glucose ingestion was not significantly different in well-controlled diabetic patients and in control subjects. However, the diabetic patients but not the control subjects ingested 36 g of CHO during the exercise period, and this could have resulted in muscle glycogen sparing. As for the difference between results from the present experiment and from that by Raguso et al. (21), it could stem from the fact that, in Raguso et al., the two groups were studied after a 12-h fast, whereas in the present experiment the diabetic patients and the control subjects both ingested a breakfast 3 h before and 30 g of glucose 15 min before the beginning of exercise.

In conclusion, results from the two studies available in the literature (11, 24) and results from the present experiment suggest that, compared with control subjects, when exogenous glucose is ingested immediately before or during exercise in diabetic patients, although its availability could be slightly delayed, its oxidation rate is not significantly reduced. Moreover, these results suggest that, when glucose is ingested before exercise, diabetic patients rely more on muscle glycogen and less on plasma glucose oxidation than control subjects.

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