Gastrointestinal function during exercise: comparison of water, sports drink, and sports drink with caffeine

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Received 8 March 1999; accepted in final form 26 April 2000

Van Nieuwenhoven, M. A., R.-J. M. Brummer, and F. Brouns. Gastrointestinal function during exercise: comparison of water, sports drink, and sports drink with caffeine. J Appl Physiol 89: 1079–1085, 2000.—Caffeine is suspected to affect gastrointestinal function. We therefore investigated whether supplementation of a carbohydrate-electrolyte solution (CES) sports drink with 150 mg/l caffeine leads to alterations in gastrointestinal variables compared with a normal CES and water using a standardized rest-exercise-rest protocol. Ten well-trained subjects underwent a rest-cycling-rest protocol three times. Esophageal motility, gastroesophageal reflux, and intragastric pH were measured by use of a transnasal catheter. Orocecal transit time was measured using breath-H2 measurements. A sugar absorption test was applied to determine intestinal permeability and glucose absorption. Gastric emptying was measured via the13C-acetate breath test. In the postexercise episode, midesophageal pressure was significantly lower in the CES + caffeine trial compared with the water trial (P = 0.017). There were no significant differences between the three drinks for gastric pH and reflux during the preexercise, the cycling, and the postexercise episode, respectively. Gastric emptying, orocecal transit time, and intestinal permeability showed no significant differences between the three trials. However, glucose absorption was significantly increased in the CES + caffeine trial compared with the CES trial (P = 0.017). No significant differences in gastroesophageal reflux, gastric pH, or gastrointestinal transit could be observed between the CES, the CES + caffeine, and the water trials. However, intestinal glucose uptake was increased in the CES + caffeine trial.

carbohydrate; gastric emptying; glucose absorption; orocecal transit time; permeability

Participants in endurance events frequently suffer from gastrointestinal (GI) symptoms such as abdominal pain, urge to defecate, diarrhea, heartburn, nausea, and vomiting. This suggests that exercise can influence GI function.

The underlying etiology of GI symptoms associated with exercise has been rarely studied and remains speculative. One of the most common theories includes an exercise-induced reduction in GI blood flow. Although it is very difficult to measure GI blood flow during exercise, it has been reported that at maximal exercise intensity the flow may be reduced to 20% of the resting value in both trained and untrained people (7). Sympathetic output plays an important role in redistributing blood flow during exercise. Blood flow may be decreased to critical levels during maximal sympathetic stimulation. As a result, GI motility, intestinal absorption, and mucosal integrity may be disturbed. This may be a cause for exercise-induced GI symptoms. Training status, exercise intensity, hydration state, and nutrition seem to play an important role. GI symptoms during strenuous physical activity occur more frequently in untrained people compared with trained people and more in women than in men. In “gliding” sports such as cycling, skating, and swimming, the prevalence of GI symptoms is lower compared with running (4).

Several studies have reported an increase of gastrointestinal reflux during exercise (5, 10, 20, 21). Gastric emptying may also be altered as a result of physical exercise (3). There is no consensus about the effect of exercise on the orocecal transit time (OCTT), i.e., the time that elapses between oral ingestion and the arrival of the nonabsorbed fraction of the meal in the proximal colon (4). Data concerning the effect of exercise on intestinal permeability are also scarce. Økstedal et al. (15) and Moses et al. (14) observed an increase in intestinal permeability. Ryan et al. (19) observed no change in permeability in relation to exercise.

It has been suggested that a reduction of mesenteric blood flow by >50% causes a linear fall in the rate of glucose absorption (26).

During strenuous physical exercise, liquids are the major energy source consumed. Liquids are also necessary for rehydration. An ideal sports drink is a good thirst quencher, provides sufficient energy and electrolytes, is rapidly absorbed, and has a good palatability. Recently, it has been established that caffeine enhances endurance performance, even below the International Olympic Committee limit (6, 22). Hence supplementation of sports drinks with caffeine is a logical step, with the prerequisite that the resulting levels in urine remain below the reference limit of 12 mg/l, as the costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.
A second prerequisite for beneficial use of caffeine ingestion during exercise is that caffeine does not induce GI upset. There are no recent studies on the effect of caffeine on GI tract. Studies carried out in the 1970s and earlier indicate that caffeine may increase gastric acid secretion (18, 27). Other researchers did not find an effect of caffeine on acid secretion (1, 8).

Caffeine has also been suspected to induce gastroesophageal reflux by lowering the lower esophageal sphincter (LES) pressure (9). However, this characteristic is not very well established. Caffeine in high doses has been suggested to induce jejunal secretion. Wald and co-workers (25) carried out a triple lumen intestinal perfusion study in which they observed a net jejunal secretion in all subjects after administration of test solutions containing caffeine doses of 1,000 and 2,000 mg/l. It was suggested that this secretion might accelerate small bowel transit and hence give rise to lower GI symptoms. The effect of caffeine on esophageal motor function, GI motility, intestinal permeability, and jejunal glucose absorption is unknown.

The aim of the present study was to investigate whether a sports drink or supplementation of a sports drink with caffeine leads to alterations in GI variables compared with water. We compared a carbohydrate-electrolyte solution (CES), CES with the addition of 150 mg caffeine/l, and water in a standardized rest-cycling-rest protocol that was as noninvasive as possible.

METHODS

Subjects

Ten well-trained male subjects (age 18–25 yr), who did not suffer from exercise-induced GI symptoms, were studied on 4 different days. Their diet was standardized during 24 h preceding the test days. This period is sufficient for removal of most of the caffeine that might be present in the plasma of the subjects. The subjects were not allowed to consume fiber-rich or spicy food products, alcohol, caffeine-containing products, or drugs or to perform physical exercise the day preceding the test days.

Design of the Study

First, the subjects underwent a slow pull-through manometry to locate the LES and to exclude gross manometric abnormalities. Subsequently, they underwent a maximal power output (Wmax) cycling test (11) to determine their Wmax. On the 3 actual testing days, the subjects underwent a rest-cycling-rest protocol. The test drinks were studied in randomized order.

Test Protocol

After an overnight fast, the subject arrived at the laboratory at 8:00 AM. A thin catheter allowing the registration of esophageal motility, gastroesophageal reflux, and intragastric pH (Koningsberg) was inserted transnasally. The pH was simultaneously measured 5 cm above the LES and in the fundus of the stomach, 10 cm below the LES. Esophageal pressure was measured at 13 (P1) and 3 (P3) cm above the LES. The catheter was connected with an ambulatory data recorder (MMS, Enschede, The Netherlands), thus allowing continuous registration of pH and pressure. Subsequently, the subjects received a standard liquid breakfast (4 ml/kg body wt, pH 5.8) and remained seated in a chair for 60 min. During this period, resting values for esophageal motility, gastric pH, and gastroesophageal reflux were obtained. Subsequently, the subjects emptied their bladder and mounted a stationary bicycle ergometer (Lode, Groningen, The Netherlands). A warm-up was performed for 10 min at 100 W. During the final minute of this warm-up, 2 ml/kg body wt of the test drink were ingested. The composition of the test drinks and of the semiliquid meal is displayed in Table 1. These drinks, which were commercially available sports drinks, contained some other compounds as well as carbohydrates and electrolytes. These compounds, however, are not very likely to affect GI function. At time (t) = 0 of the subsequent exercise episode, the cycling intensity was increased to a load of 70% of the subject’s previously determined Wmax, which was maintained for 90 min. However, if the subject was not able to maintain this load, the exercise intensity was decreased in 5% steps until the subject was able to complete the 90-min cycling. During this period, the subject received 2 ml/kg body wt of the test drink at t = 20 min and 5 ml/kg body wt of the test drink at t = 40 min to compensate for sweat losses and to minimize dehydration. All drinks were at room temperature (19°C). At t = 90 min, the subject dismounted the cycle ergometer and remained normally seated in a comfortable chair for 210 min to obtain postexercise resting values. At t = 150 min, the subjects received a standard liquid lunch (4 ml/kg body wt). For each breath sample, the subjects breathed for 2 min through a mouthpiece, which was connected to a mixing chamber. Breath samples for H2 and 14CO2 analysis were collected from the mixing chamber at 15 min and at 5-min intervals, respectively. From t = 0 min to t = 300 min, the total urinary production was collected.

Testing Procedures

Esophageal manometric variables. Two solid-state pressure sensors measured esophageal pressure at P1 and P3. The catheter was connected with an ambulatory data recorder (MMS), thus allowing continuous registration of pH and pressure. The stored data were transferred from the ambulatory data logger to a personal computer system and edited using specialized manometry software (MMS). In each episode of the experiments, the following variables were evaluated: number of peristaltic contractions, mean

Table 1. Composition of the CES, the CES + caffeine, and the liquid meal

<table>
<thead>
<tr>
<th>Content of CES/100 ml</th>
<th>Content of CES + caffeine/100 ml</th>
<th>Content of Liquid Meal/100 ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>30.0 kcal</td>
<td>Caffeine 15 mg</td>
<td>122.4 kcal</td>
</tr>
<tr>
<td>CHO 6.88 g</td>
<td>CHO 6.88 g</td>
<td>CHO 37.5 g</td>
</tr>
<tr>
<td>Vitamins 10.6 mg</td>
<td>Vitamins 10.6 mg</td>
<td>Protein 5.4 g</td>
</tr>
<tr>
<td>Electrolytes 119 mg</td>
<td>Electrolytes 119 mg</td>
<td>Lactose 0.27 g</td>
</tr>
<tr>
<td>Amino acids 21 mg</td>
<td>Amino acids 21 mg</td>
<td>Fiber 1.08 g</td>
</tr>
<tr>
<td>Myoinositol 5.1 mg</td>
<td>Myoinositol 5.1 mg</td>
<td>Electrolytes 130 mg</td>
</tr>
<tr>
<td>Choline 10 mg</td>
<td>Choline 10 mg</td>
<td>Vitamins 3.9 mg</td>
</tr>
<tr>
<td>pH 4.95</td>
<td>pH 4.75</td>
<td>pH 5.8</td>
</tr>
</tbody>
</table>

CES, carbohydrate-electrolyte solution; CHO, carbohydrates.
peristaltic pressure at P1 and P3, mean duration of peristaltic pressure events at P1 and P3, and the peristaltic velocity.

Gastroesophageal reflux. Esophageal pH was measured by using a solid-state pH electrode at 5 cm above the LES. A reflux episode was defined as a period in which the pH in the esophagus, at 5 cm above the LES, was <4. The following variables were determined during each episode of the experiments: number of reflux episodes and duration of the reflux episodes as a percentage of time.

Gastric pH. The intragastric pH was measured in the fundus of the stomach at 10 cm below the LES via a solid-state pH electrode. The following variables were determined during each episode of the experiments: median pH in the fundus and percentage of time in which the pH in the fundus was <4.

These variables were determined during the preexercise episode, the cycling episode, and the postexercise episode. No corrections were made for pH changes due to the ingested drinks and liquid meals, because they were similar for the three trials.

Gastric emptying: Assessment and mathematical evaluation of \(^{13}\)C enrichment. The drink administered at \(t = 40\) min during the cycling episode contained 150 mg sodium \([1-{\textsuperscript{13}}}\)C acetate (99%; Cambridge Isotope Laboratories, Andover, MA) to determine the gastric emptying rate using the \(^{13}\)C-acetate breath test. Breath samples for \(^{13}\)CO\(_2\) enrichment analysis were drawn from the mixing chamber at 5-min intervals from \(t = 40\) min to \(t = 90\) min using Vacutainer tubes. One breath sample was taken before administration of the drink at \(t < 40\) min to determine background enrichment. The collected breath samples were analyzed for \(^{13}\)C isotopic enrichment of the expired CO\(_2\) using Isotope Ratio Mass Spectrometry (Finnigan MAT 252). The \(^{13}\)C enrichment of CO\(_2\) was expressed as the delta (δ) per mil difference between the \(^{13}\)C-to-\(^{12}\)C ratio of the breath sample and a known laboratory reference standard according to the formula

\[
\delta^{13}C \ (\text{per mil}) = \left\{\frac{[\text{^{13}C/^{12}C}]_{\text{sample}}}{[\text{^{13}C/^{12}C}]_{\text{standard}}} - 1\right\} \times 10^3
\]

The δ value was then related to an international standard, Pee Dee Belemnite. The data from the breath enrichment were fitted by nonlinear regression analysis according to a dual-exponential function with the following features

\[
y(t) = a + \left[b e^{-a(t-i)} + c \left(1 - e^{-b(t-i)}\right) + j\right] \times 10^{-3}
\]

where \(a, b, c, d, f, g, h, i\) and \(j\) are constants, \(t\) is the time, and \(j\) is the background enrichment. A dual-compartment description of \(^{13}\)CO\(_2\) production \(a e^{-\beta t} + f e^{-\beta t}\) is applied because acetate is oxidized both in the splanchic area and in the working muscles. The decrease in \(^{13}\)CO\(_2\) enrichment is also described in two factors: the first factor \(c e^{-a t}\) describes washout of \(^{13}\)CO\(_2\) through the body bicarbonate pool via the breath, and the second factor \(d e^{-b t}\) describes other processes of \(^{13}\)CO\(_2\) removal, namely, sequestration of \(^{13}\)CO\(_2\) in bone, excretion via urine, and incorporation into glucose.

In the present study, the results are based on the time to peak \(^{13}\)C enrichment in the breath samples \((^{13}\text{C-TTP})\) derived from the dual-exponential function. The \(^{13}\text{C-TTP}\) was interpreted from the curve using the GraphPad software and was considered as the parameter of gastric emptying (24).

OCTT. The drink administered at \(t = 0\) of the cycling episode contained a nondigestible soluble carbohydrate (5 g lactulose, Centrafarm syrup, 670 mg/ml, Etten-Leur, The Netherlands), allowing the measurement of OCTT via H\(_2\) measurement in breath. As soon as the lactulose enters the colon, bacterial fermentation will take place, and H\(_2\) gas will be produced (13). Breath samples for H\(_2\) analysis were collected from the mixing chamber via a 140-ml syringe at 15-min intervals, starting at \(t = 0\), and were analyzed for H\(_2\) enrichment by use of a sensitive electrochemical exhaled hydrogen monitor (GMI Medical, Renfrew, Scotland). The OCTT was determined using the time of onset of a sustained increase in breath H\(_2\), which is the first breath sample that shows a higher breath H\(_2\) than the preceding one, followed by two or more breath samples that show a further increase.

Intestinal permeability and glucose absorption. The drink administered at \(t = 0\) of the cycling episode contained 5 g lactulose (Centrafarm syrup, 670 mg/ml), 0.5 g rhamnose, and 0.35 g 3-O-d-methyl-m-glucose (3-OMG) (Sigma Chemical, St. Louis, MO), allowing the measurement of intestinal permeability and intestinal glucose absorption (17). At the end of the experiment, at \(t = 300\) min, total urine production was collected, its volume was determined, and a small portion was stored at −80°C for lactulose, rhamnose, and 3-OMG determination. The urinary lactulose, rhamnose, and 3-OMG excretion was determined by a validated, sensitive, newly developed fluorescent detection HPLC method, which is extensively described by Rooyackers et al. (17). Subsequently, the lactulose and rhamnose recoveries and the lactulose-to-rhamnose and 3-OMG-to-rhamnose ratios were calculated.

Statistics

Differences among the episodes between the three trials were analyzed by use of Friedman’s nonparametric tests. The level of confidence was set at \(P = 0.05\). If Friedman’s analysis demonstrated a significant difference, Wilcoxon’s signed-rank test was performed, corrected for multiple comparisons with a Bonferroni correction, which is the level of confidence \((P = 0.05)\) divided by the number of comparisons, in this case three. This correction results in a level of confidence of \(P = 0.017\). Differences between two related samples were analyzed using Wilcoxon’s signed-rank test. The level of confidence was set at \(P = 0.05\). Data are presented as median (range). All statistical analyses were performed using the SPSS 7.5 for Windows statistical package.

RESULTS

All the subjects were able to complete the 90-min cycling episode. However, it was frequently necessary to decrease the cycling load in 5% steps. The progress of the relative median cycling loads was 70% Wmax (70–70%) at \(t = 0\), 65% Wmax (65–70%) at \(t = 30\), 60% Wmax (60–65%) at \(t = 60\), and 60% Wmax (55–65%) at \(t = 90\). The median initial load (70% Wmax) was 243.5 (217–350) W, and the median load at the end of the 90-min cycling episode was 215.5 (185–325) W. During the experiments, body weight decreased 0.8 kg from 72.3 (55.7–88.7) at the start to 71.5 (54.5–87.8) kg at the end of the experiment. This indicates that not much dehydration occurred.

Esophageal Motility

The data from the esophageal measurements and the \(P\) values from the Friedman tests are displayed in Table 2. In the postexercise episode, the peristaltic pressure at P1 was significantly lower in the CES + caffeine trial. After Bonferroni correction, Wilcoxon’s
Table 2. Results of the manometric measurements of the esophagus in the three trials during the cycling and postexercise episodes

<table>
<thead>
<tr>
<th>CES</th>
<th>CES + Caffeine</th>
<th>Water</th>
<th>Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cycling</td>
<td>Postexercise</td>
<td>Exercise</td>
<td>Postexercise</td>
</tr>
<tr>
<td>Number of contractions</td>
<td>24.0 (17.0–73.0)</td>
<td>35.0 (21.0–146.0)</td>
<td>31.0 (8.0–64.0)</td>
</tr>
<tr>
<td>Pressure at P1, cmH2O</td>
<td>73.4 (45.3–89.0)</td>
<td>71.3 (55.6–103.8)</td>
<td>68.2 (50.2–78.8)</td>
</tr>
<tr>
<td>Pressure at P3, cmH2O</td>
<td>74.8 (62.9–162.5)</td>
<td>87.4 (53.9–148.0)</td>
<td>73.8 (49.5–160.9)</td>
</tr>
<tr>
<td>Duration at P1, s</td>
<td>1.7 (1.3–2.0)</td>
<td>1.7 (1.4–2.2)</td>
<td>1.5 (1.3–2.0)</td>
</tr>
<tr>
<td>Duration at P3, s</td>
<td>1.7 (1.3–2.7)</td>
<td>1.8 (1.4–2.5)</td>
<td>1.5 (1.1–2.4)</td>
</tr>
<tr>
<td>Velocity, cm/s</td>
<td>4.9 (4.2–7.1)</td>
<td>4.8 (3.2–5.9)</td>
<td>5.3 (4.6–8.5)</td>
</tr>
</tbody>
</table>

Values are medians with ranges given in parentheses (n = 10). P1 and P3, 13 and 3 cm, respectively, above the lower esophageal sphincter. *Significant difference (P ≤ 0.05).

The signed-rank test demonstrated no significant difference between CES + caffeine and CES (P = 0.028) and a significant difference between CES + caffeine and water (P = 0.017).

Gastric pH

The results of the gastric pH measurements are displayed in Table 3.

Between the trials. Friedman’s analysis showed no significant differences between the three drinks for median gastric pH during the preexercise (P = 0.924), cycling (P = 0.060), and postexercise episodes (P = 0.531). Friedman’s analysis showed also no significant differences between the three drinks for the percentage of time in which the gastric pH was <4 during the preexercise (P = 0.497), cycling (P = 0.062), and postexercise episodes (P = 0.325).

Within the trials. Friedman’s analysis demonstrated a significant difference in median gastric pH within the CES trial (P = 0.002), the CES + caffeine trial (P = 0.001), and the water trial (P = 0.02). After Bonferroni correction, Wilcoxon’s signed-rank test demonstrated significant difference in the CES trial between the preexercise and the cycling episode (P = 0.008) and between the preexercise and the postexercise episode (P = 0.012), in the CES + caffeine trial between the preexercise and the cycling episode (P = 0.005) and between the preexercise and the postexercise episode (P = 0.007), and in the water trial between the preexercise and cycling episode (P = 0.012) and between the preexercise and postexercise episode (P = 0.017).

Friedman’s analysis demonstrated a significant difference in the percentage of time in which the gastric pH was <4 in the CES trial (P = 0.002) and in the water trial (P = 0.004) but not in the CES + caffeine trial (P = 0.273). After Bonferroni correction, Wilcoxon’s signed-rank test demonstrated a significant difference in the CES trial between the preexercise and the cycling episode (P = 0.008) and between the preexercise and postexercise episode (P = 0.012) and in the water trial between the preexercise and cycling episode (P = 0.005) and between the preexercise and postexercise episode (P = 0.011). However, these results could be expected as a result of the ingestion of drinks and liquid meals.

Gastroesophageal Reflux

The results of the gastroesophageal reflux measurements are displayed in Fig. 1. Friedman’s analysis showed no significant differences between the preexercise, cycling, and postexercise episodes in either the number of reflux episodes (P = 0.129, 0.610, and 0.786, respectively) or the duration of reflux as a percentage of time (P = 0.237, 0.612, and 0.463, respectively).

The results of the analyses of differences in gastroesophageal reflux as a percentage of time within the trials are displayed in Table 4. The P values from Wilcoxon’s signed-rank test showed no significant diff-

Table 3. Results of the gastric pH measurements in the three trials during the preexercise, cycling, and postexercise episodes

<table>
<thead>
<tr>
<th>CES</th>
<th>CES + Caffeine</th>
<th>Water</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median pH</td>
<td>5.5 (4.8–6.9)</td>
<td>5.8 (4.4–6.3)</td>
</tr>
<tr>
<td>% pH &lt;4</td>
<td>2.6 (0.0–27.4)</td>
<td>2.6 (0.1–53.2)</td>
</tr>
</tbody>
</table>

Values are medians with ranges given in parentheses (n = 10).
ference in reflux duration as a percentage of time within the three trials.

**Gastric Emptying and OCTT**

Neither gastric emptying nor the OCTT show differences between the three trials. $^{13}$C-TTP in the CES trial was 22.8 (15.7–50.0) min, in the CES + caffeine trial it was 24.2 (19.8–26.4) min, and in the water trial it was 19.2 (14.2–24.1) min ($P = 0.066$). OCTT in the CES trial was 140.0 (105.0–195.0) min, in the CES + caffeine trial it was 120.0 (95.0–180.0) min, and in the water trial it was 110.0 (95.0–200.0) min ($P = 0.772$).

**Intestinal Permeability and Glucose Absorption**

The results of the intestinal permeability and the 3-OMG absorption measurements are displayed in Fig. 2. There was no significant difference in the lactulose-to-rhamnose ratio between the three trials [CES: 0.0067 (0.0017–0.0141), CES + caffeine: 0.0039 (0.0042–0.0181), respectively; $P = 0.301$]. No significant difference could be observed in the urinary lactulose, rhamnose, and 3-OMG recoveries [lactulose: CES 0.089 (0.038–0.173), CES + caffeine 0.093 (0.006–0.149), water, 0.106 (0.055–0.249), $P = 0.497$; rhamnose: CES 15.00 (8.54–23.99), CES + caffeine 13.24 (0.70–15.68), and water, 12.01 (6.09–16.66), $P = 0.061$; 3-OMG: CES 36.15 (21.06–62.12), CES + caffeine 40.18 (2.10–50.45), and water 39.23 (15.93–55.76), $P = 0.905$]. Friedman’s analysis, however, demonstrated a significant difference in the 3-OMG-to-rhamnose ratio between the three trials [CES: 2.64 (2.03–3.91), CES + caffeine: 3.24 (2.36–4.34), and water: 2.91 (2.45–4.69); $P = 0.007$]. After Bonferroni correction, Wilcoxon’s signed-rank test demonstrated a significant increase in the 3-OMG-to-rhamnose ratio in the CES + caffeine trial compared with CES ($P = 0.017$), which almost reached significance in the CES compared with water trial ($P = 0.037$). The individual changes in 3-OMG-to-rhamnose ratio are displayed in Fig. 3.

**DISCUSSION**

The esophagus is composed of skeletal (striated) and smooth muscle. The proximal 5% of the esophagus is striated, and the proportion of smooth muscle increases distally. The distal 50–60% consists entirely of smooth muscle. The results of the present study indicate that caffeine decreases the peristaltic pressure in the mixed striated and smooth muscle part of the esophagus (P1) in the postexercise episode. The control mechanisms of esophageal motor function are complex and not completely elucidated yet. The extrinsic innervation of the esophagus occurs via the vagal fibers. The striated muscle part of the esophagus is innervated by axons of cholinergic lower motoneurons with their cell bodies in the nucleus ambiguus. The smooth muscle of the esophagus is innervated by the dorsal motor nucleus of the vagus.

This observation might be explained by caffeine-induced inhibition of the cholinergic innervation of the

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**Table 4. P values of Wilcoxon’s signed-rank test and comparison of relative reflux time within the trials**

<table>
<thead>
<tr>
<th>Trial Analysis</th>
<th>Reflux Time, Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>CES</td>
<td></td>
</tr>
<tr>
<td>Pre vs. ex</td>
<td>$P = 0.6$</td>
</tr>
<tr>
<td>Pre vs. post</td>
<td>$P = 0.25$</td>
</tr>
<tr>
<td>Ex vs. post</td>
<td>$P = 0.89$</td>
</tr>
<tr>
<td>CES + caffeine</td>
<td></td>
</tr>
<tr>
<td>Pre vs. ex</td>
<td>$P = 1.0$</td>
</tr>
<tr>
<td>Pre vs. post</td>
<td>$P = 0.50$</td>
</tr>
<tr>
<td>Ex vs. post</td>
<td>$P = 0.37$</td>
</tr>
<tr>
<td>Water</td>
<td></td>
</tr>
<tr>
<td>Pre vs. ex</td>
<td>$P = 0.09$</td>
</tr>
<tr>
<td>Pre vs. post</td>
<td>$P = 0.31$</td>
</tr>
<tr>
<td>Ex vs. post</td>
<td>$P = 0.09$</td>
</tr>
</tbody>
</table>

Pre, preexercise episode; ex, cycling episode; post, postexercise episode ($n = 10$).
striated muscle component, because no changes in the distal esophagus (P3), which is composed entirely of smooth muscle, could be observed. The alteration found in the simultaneous and nontransmitted pressure events during the cycling episode are unlikely to be of physiological significance because of the small number of simultaneous contractions.

The present study showed no significant differences in gastroesophageal reflux, GI transit time, or gastric pH during a rest-cycling-rest protocol between a CES, a caffeine-supplemented CES, and water. It has been hypothesized that both exercise and caffeine can induce gastroesophageal reflux. Earlier studies in our department, however, showed that exercise on a stationary bicycle itself does not increase either the number of gastroesophageal reflux episodes or the percentage of time of reflux if the experiments are conducted in a well-controlled laboratory setting (23). These observations are confirmed by the results of the present study for all three test drinks. The results obtained in the present study do not rule out the possibility that changes in reflux may occur at near-maximal exercise intensities or at higher dosages of caffeine. In this respect, Soffer et al. (20, 21) demonstrated that a significant increase in reflux occurred only at the highest intensity (90% maximal O2 uptake for 10 min) in a graded exercise protocol.

Gastroesophageal reflux has also been associated with increased gastric acid production. Some studies in the past reported an increase in acid secretion due to caffeine. Our pH measurements failed to confirm these observations. This may be due to the relatively low dosage of caffeine (~120 mg). It can not, however, be excluded that exercise and/or caffeine induce an alteration in basal gastric acid output.

Within the trials, significant differences for both the median gastric pH and the percentage of time in which the gastric pH was <4 were observed. This is possibly explained by the pH of the drinks used and by the effect of the ingested pre- and postexercise liquid meals on the gastric pH, and not by an effect of caffeine or exercise on the gastric pH.

Ingestion of caffeine in dosages from 75 to 300 mg/150 ml is known to induce jejunal secretion, which lasts at least 15 min. This does not, however, result in a change in the liquid OCTT (25). This is in contrast to the small intestinal secretion induced by an osmotic load (12) or cholera enterotoxins (2). The latter conditions do lead to a decrease of the OCTT. The explanation for the present observation that caffeine does not affect intestinal transit might be that caffeine induced a relaxation of the intestinal smooth muscle, which, in turn, induced an increased intestinal volume capacity, resulting in an unchanged intestinal flow rate.

Caffeine did not induce a significant change in urinary lactulose and rhamnose recovery or in lactulose-to-rhamnose ratio. Intestinal glucose absorption, however, was affected by caffeine. Intestinal glucose uptake is a carrier-mediated transport process. There was a significant difference in rhamnose-to-3-OMG ratio between the CES and the CES + caffeine. The 3-OMG uptake in the water trial was higher than in the CES trial. This observation may be explained by caffeine-induced enhancement of sodium-glucose-linked transporter protein activity, thus leading to an increased jejunal glucose uptake. Each glucose molecule is transported together with two sodium ions, which is an energy-requiring transport process involving later basolateral removal of sodium in exchange for potassium through the sodium-potassium-ATPase, creating a gradient for the sodium-glucose-linked transporter. A second transporter, GLUT-2, is responsible for glucose transport from the enterocyte to the blood. A possible effect of caffeine may also involve the latter two mechanisms. These possible mechanisms might explain the observations of Pizzio et al. (16), who recently observed that oral caffeine intake induces a rise in blood glucose levels that is insulin independent. This mechanism may contribute to the ergogenic effect of caffeine on endurance performance.

In summary, it was demonstrated that 90-min cycling at an intensity of 70% Wmax does not induce gastroesophageal reflux or alterations in gastric pH. It can be concluded that ingestion of water, a CES, or CES with added caffeine (150 mg/l) does not lead to significant differences in gastroesophageal reflux, gastric pH, or GI transit in a controlled experimental rest-cycling-rest protocol in healthy trained individuals. Therefore, it is safe to use at least moderate amounts of caffeinated sports drinks with respect to adverse effects on GI function. It appears that caffeine inhibits the cholinergic innervation of the striated muscle component of the esophagus, leading to a lower peristaltic pressure in the midesophagus, and that caffeine stimulates glucose uptake in the small bowel.

This study was supported with grants from Novartis Nutrition and the Dutch Olympic Committee.
REFERENCES


