Acute plasma volume expansion: effect on metabolism during submaximal exercise

MATTHEW J. WATT,1 MARK A. FEBBRAIO,2 ANDREW P. GARNHAM,1 AND MARK HARGREAVES1

1School of Health Sciences, Deakin University, Burwood, Victoria 3125; and 2Department of Physiology, The University of Melbourne, Parkville, Victoria 3052, Australia

Watt, Matthew J., Mark A. Febbraio, Andrew P. Garnham, and Mark Hargreaves. Acute plasma volume expansion: effect on metabolism during submaximal exercise. J. Appl. Physiol. 87(3): 1202–1206, 1999.—To examine the effect of acute plasma volume expansion (PVE) on substrate selection during exercise, seven untrained men cycled for 40 min at 72 ± 2% peak oxygen uptake (V\textsubscript{O\textsubscript{2peak}}) on two occasions. On one occasion, subjects had their plasma volume expanded by 12 ± 2% via an intravenous infusion of the plasma substitute Haemaccel, whereas on the other occasion no such infusion took place. Muscle samples were obtained before and immediately after exercise. In addition, heart rate and pulmonary gas and venous blood samples were obtained throughout exercise. No differences in oxygen uptake or heart rate during exercise were observed between trials, whereas respiratory exchange ratio, blood glucose, and lactate were unaffected by PVE. Muscle glycogen and lactate concentrations were not different either before or after exercise. In addition, there was no difference in total carbohydrate oxidation between trials (control: 108 ± 2 g; PVE group: 105 ± 2 g). Plasma catecholamine levels were not affected by PVE. These data indicate that substrate metabolism during submaximal exercise in untrained men is unaltered by acute hypervolemia.

METHODS

Subjects. Seven healthy untrained men [age, 21 ± 1.6 yr; weight, 82.1 ± 5.6 kg (SD)] volunteered as subjects for the experiment. Each subject was informed of the risks associated with the procedures and signed a letter of informed consent before participation. The experiment was approved by the Deakin University Ethics Committee.

Preexperimental protocol. All subjects performed an incremental cycling test to volitional exhaustion on an electromagnetically braked cycle ergometer (LODE Instrument, Groningen, The Netherlands) to determine individual peak pulmonary oxygen uptake (V\textsubscript{O\textsubscript{2peak}}). The criteria used to determine V\textsubscript{O\textsubscript{2peak}} were a plateau in oxygen uptake (V\textsubscript{O\textsubscript{2}}) (<100 ml/min increase) with an increase in work rate and a respiratory exchange ratio (RER) > 1.10. Mean V\textsubscript{O\textsubscript{2peak}} was 3.36 ± 0.5 l/min. For the day preceding each trial, subjects were provided with a food parcel (~14 MJ, 80% carbohydrate), which they consumed, and were instructed to abstain from exercise and the ingestion of alcohol, caffeine, and tobacco. Additionally, subjects were instructed to consume 5 ml/kg body wt of water on the morning of each trial to ensure adequate hydration and similar pretrial plasma volume levels.

Experimental protocol. Each subject completed two submaximal exercise trials (72 ± 2% V\textsubscript{O\textsubscript{2peak}}) for 40 min at an ambient temperature of 21 ± 1°C. On one occasion, exercise was performed without any pretreatment (Con group); on the other, exercise was preceded by plasma volume expansion (PVE group). Plasma volume expansion was achieved by using a plasma substitute, Haemaccel (Behringwerke, Marburg, Germany), which was infused over 15–30 min via a catheter in an antecubital vein. Four subjects performed the PVE trial first and completed the Con trial at least 1 wk later. The order was reversed for the remaining three subjects. On arrival at the laboratory, subjects voided and were weighed. Subjects then rested quietly on a couch, and indwelling catheters were inserted into an antecubital vein for blood sampling and, when required, in the contralateral arm for infusion. The catheter for blood sampling was kept patent by flushing with 0.5 ml of 0.9% saline containing five units of heparin after each sample collection. After the subject lay

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Table 1. Effect of PVE on Hb, Hct, and changes in BV and PV preceding exercise at 72 ± 2% VO2peak

<table>
<thead>
<tr>
<th></th>
<th>Con</th>
<th>PVE (Pre)</th>
<th>PVE (Post)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb, g/dl</td>
<td>15.1 ± 0.3</td>
<td>15.0 ± 0.4</td>
<td>14.1 ± 0.5*</td>
</tr>
<tr>
<td>Hct, %</td>
<td>45.2 ± 1.2</td>
<td>44.4 ± 1.4</td>
<td>41.6 ± 1.6*</td>
</tr>
<tr>
<td>∆BV, %</td>
<td>6.8 ± 1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>∆PV, %</td>
<td>12.0 ± 2.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values are means ± SE (n = 7 men). PVE, plasma volume expansion; Hct, hematocrit; BV, blood volume; PV, plasma volume; ∆, change; Pre, before exercise; Post, after exercise; VO2peak, peak O2 uptake; Con, control. *Significantly different from PVE (Pre), P < 0.01.

supine for 20 min, a resting muscle sample was obtained from the vastus lateralis by the percutaneous needle-biopsy technique modified to include suction. Muscle samples were immediately (15 s) frozen in liquid nitrogen. After biopsy, a resting blood sample was obtained, after which 7 ml/kg body wt of Haemaccel were infused into the PVE group. A second resting blood sample was obtained at the conclusion of the infusion to determine the magnitude of plasma volume expansion from changes in Hb and hematocrit (Hct) (4).

At the completion of the rest period, subjects exercised for 40 min. Venous blood samples were obtained at 10-min intervals and were analyzed for plasma lactate, glucose, and catecholamines. Blood for glucose and lactate analysis was placed in fluoride-heparin tubes, whereas that for catecholamines was placed in tubes containing EGTA and reduced glutathione. The samples were spun, and the plasma was removed and stored at −20°C. For lactate, 125 µl of plasma were deproteinized in 250 µl of 8% perchloric acid, spun again, and the extract was stored at −80°C for later analysis. Expired gases were collected in Douglas bags at 10-min intervals during exercise for measurement of VO2 and RER. Heart rate was measured continuously via telemetry (Polar sports tester, Polar Electro, Finland) and recorded every 10 min. Immediately on cessation of exercise, a second muscle sample was obtained from a separate incision on the same leg and immediately (15 s) frozen. Subjects were not permitted to ingest fluid during the trials.

Analytical techniques. Oxygen and carbon dioxide contents of dried expirate were analyzed by using Applied Electrochemistry S-3A/I and CD-3A analyzers (Ametek, Pittsburgh, PA), whereas volumes were measured by using a Parkinson Cowan gas meter calibrated against a Tissot spirometer. Hb and Hct were measured by using an automated analyzer (Sysmet SE9000, Tao Electronics, Kobe, Japan). Plasma glucose was measured by using an automated glucose oxidase method (YSI 2300, Yellow Springs, OH), and lactate was determined by using an enzymatic spectrophotometric method (12). Plasma epinephrine and norepinephrine were analyzed by using a single-isotope (3H) radioenzymatic assay (TRK-995, Amersham). Muscle samples were weighed and freeze-dried, after which they were reweighed, dissected free of blood and connective tissue, powdered, and placed into two separate aliquots. One was extracted according to the procedures of Harris et al. (9) and analyzed for lactate by using standard enzymatic fluorometric techniques (12). Muscle glycogen concentrations were determined on the second aliquot (14). The data from the two trials were compared by a two-way analysis of variance for repeated measures, with significance at the P < 0.05 level. Specific differences were located by Newman-Keuls post hoc test. Where appropriate, paired comparisons were made by t-test. All values are reported as means ± SE.

RESULTS

After administration of Haemaccel, Hb and Hct were both reduced (P < 0.05) by 6%, resulting in a 12 ± 2%...
plasma volume expansion (Table 1). Although we did not measure Hb and Hct (and, therefore, plasma volume changes) during exercise, it has been demonstrated previously (5) that the magnitude of relative plasma volume expansion is maintained during exercise. VO\(_2\) and heart rate increased (\(P < 0.05\)) during both trials before stabilizing after 20 min. After an increase (\(P < 0.05\)) early in exercise, RER was reduced after 20 min (\(P < 0.05\)) and remained unaltered for the duration of exercise. However, plasma volume expansion did not affect either heart rate or RER during exercise (Table 2). Total carbohydrate oxidation was similar in the two trials (Con: 108 ± 6 2 g; PVE: 105 ± 6 2 g).

Neither plasma glucose nor lactate was different when comparing PVE trial with Con during exercise. In both trials, plasma glucose decreased (\(P < 0.05\)) and lactate increased (\(P < 0.01\)) during the first 10 min of exercise. Thereafter, concentrations of these metabolites were unaltered (Fig. 1). Plasma catecholamines increased (\(P < 0.05\)) progressively throughout exercise in both trials but were not different when PVE and Con trials were compared. At 10 min of exercise, plasma epinephrine concentrations were 1.12 ± 0.17 and 0.97 ± 0.15 nmol/l and increased (\(P < 0.01\)) to 2.50 ± 0.77 and 1.89 ± 0.52 nmol/l at the conclusion of exercise for the Con and PVE trials, respectively (Fig. 2). Plasma norepinephrine levels were 11 and 28% lower, respectively, in the PVE group compared with Con at 10 and 40 min (Fig. 2, \(P = 0.06\)). However, when plasma catecholamine (Cat) values were corrected \(\text{[Cat]}_{\text{corrected}} = \text{[Cat]}_{\text{measured}} \times [1 + (\Delta PV/100)]\) for the increased plasma volume (PV), assuming it was maintained during exercise (5), this tendency for a difference was abolished.

Muscle glycogen content was not different when PVE and Con groups were compared either before or after exercise (Fig. 3). Although muscle glycogen use was slightly higher in Con trial (Con: 324 ± 39 vs. PVE 261 ± 54 mmol glucosyl units/kg dry mass), post hoc analysis revealed no significant difference. Muscle lac-
tate content was not different when PVE group was compared with Con either before or after exercise.

**DISCUSSION**

The results of the present study suggest that acute plasma volume expansion, similar in magnitude to that seen after short-term endurance training, has no effect on either muscle carbohydrate metabolism or plasma catecholamine levels during 40 min of submaximal exercise in untrained men. This observation suggests that the reduced glycogen use and lactate accumulation, previously observed in response to short-term endurance training (17), are mediated by factors other than vascular hypervolemia.

The 12% increase in plasma volume that we induced in the PVE trial was similar to that seen after short-term training (3). In contrast with the well-accepted changes in carbohydrate metabolism that result from short-term training (6, 7, 19), we observed no change in muscle metabolism. This was reflected in the muscle glycogen, RER, blood glucose, and blood and muscle lactate data. Although we observed a 19% reduction in glycogen use in PVE trial, this was largely due to the results of one subject who, for reasons we cannot explain, had a marked decrease in glycogen use in the PVE trial. In fact, three of seven subjects had an increased net glycogen use when PVE group was compared with Con and, therefore, we are confident that plasma volume expansion had no effect on substrate metabolism. Our data are in agreement with previous investigations that have demonstrated no change in whole body carbohydrate and fat utilization (10, 15) or glucose kinetics and estimated glycogen oxidation (10) in untrained men after plasma volume expansion by dextran infusion. Hence, the changes in substrate metabolism that result from short-term endurance training appear to be mediated by factors other than vascular hypervolemia.

In contrast with previous studies that have employed similar protocols as the present study (5, 10), plasma catecholamines were unaltered by acute hypervolemia. An early adaptation to prolonged exercise training is a reduction in the sympathoadrenal response during exercise (8, 13, 20). Although the exact mechanism remains unclear, the hypervolemia observed at the onset of endurance training appears to significantly reduce the sympathoadrenal response during exercise (5, 7, 10). The reduction in sympathoadrenal activity is reflected by lowered plasma epinephrine and norepinephrine concentrations during the early stages of endurance training (8). Importantly, the reductions observed after 10 days of endurance training are not further manifested after 12 wk (13). The absence of a blunted plasma catecholamine response to exercise in the present study suggests that sympathoadrenal activity during exercise is unaffected by acute vascular hypervolemia of the magnitude we employed, a conclusion different from that in two previous studies (5, 10). Possible explanations for this result include differences in exercise intensity (72 vs. 46 and 60% VO_{2peak}) and duration (40 vs. 120 and 90 min) as well as the agent used to obtain plasma volume expansion (Haemaccel vs. dextran).

In summary, the present study has demonstrated that acute plasma volume expansion, to a level comparable to that obtained with short-term endurance training, failed to alter carbohydrate oxidation, muscle glycogen utilization, or plasma catecholamines during submaximal exercise in untrained subjects. This suggests that plasma volume expansion is unlikely to account for the changes in substrate metabolism observed during the early stages of endurance training.

The authors acknowledge the assistance of Dr. Kirsten Howlett. Address for correspondence: M. Hargreaves, School of Health Sciences, Deakin University, Burwood, Victoria 3125, Australia (E-mail: mharg@deakin.edu.au).

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