Effects of human pregnancy on fluid regulation responses to short-term exercise

Aaron P. Heenan,1 Larry A. Wolfe,1,2 Gregory A. L. Davies,1,3 and Michael J. McGrath3

1School of Physical and Health Education, and Departments of 2Physiology, and 3Obstetrics and Gynaecology, Queen’s University, Kingston, Ontario, Canada K7L 3N6

Submitted 24 October 2002; accepted in final form 8 August 2003

Effects of human pregnancy on fluid regulation responses to short-term exercise. J Appl Physiol 95: 2321–2327, 2003. First published September 5, 2003; 10.1152/japplphysiol.00984.2002.—This study tested the hypothesis that human pregnancy alters fluid and electrolyte regulation responses to acute short-term exercise. Responses of 22 healthy pregnant women (PG; gestational age, 37.0 ± 0.2 wk) and 17 nonpregnant controls (CG) were compared at rest and during cycling at 70 and 110% of the ventilatory threshold (VT). At rest, ANG II concentration was significantly (P < 0.05) higher in PG vs. CG, whereas plasma osmolality and concentrations of AVP, sodium, and potassium were significantly lower. Atrial natriuretic peptide concentration at rest was similar between groups. ANG II and AVP concentrations increased significantly from rest to 110% VT in CG only, whereas increases in atrial natriuretic peptide concentration were similar between groups. Increases in osmolality, and total protein and albumin concentrations from rest to both work rates were similar between the two groups. PG and CG exhibited similar shifts in fluid during acute short-term exercise, but the increases in ANG II and AVP were absent and attenuated, respectively, during pregnancy. This was attributed to the significantly augmented fluid volume state already present at rest in late gestation.

angiotensin II; arginine vasopressin; atrial natriuretic peptide; progesterone; osmolality

Both pregnancy and strenuous exercise have striking effects on body fluid homeostasis, but, to our knowledge, their interactive effects have not been reported in any published study. Therefore, this study was conducted to examine the effects of human pregnancy on plasma electrolytes, osmolality, and circulating fluid balance hormone responses to short-term exercise above and below the ventilatory anaerobic threshold.

In early pregnancy, a reduction in systemic vascular tone attributed to gestational hormones activates “volume-restoring mechanisms,” an increase in blood volume, and a reduction in plasma osmolality (9, 23). The reduction in mean arterial pressure caused by the decrease in vascular tone activates the renin-ANGII system (RAAS) (9, 21, 32), causing sodium retention. Plasma renin concentration and plasma renin activity (PRA) remain elevated throughout pregnancy (9, 32). The elevated circulating ANG II concentration ([ANG II]) also stimulates AVP release, leading to water retention (5). The osmotic threshold for AVP release is also lowered in pregnancy along with the threshold for thirst (17).

The most important purpose of atrial natriuretic peptide (ANP) is to protect against excessive increases in central blood volume, and ANP is secreted in response to increased venous return and the resulting atrial distention. In human pregnancy, circulating plasma ANP concentrations ([ANP]) have been variously reported to decrease (29), increase (25), or remain unchanged (9) during pregnancy. Although blood volume and venous return are increased substantially by late gestation (20, 22, 23), this is also accommodated by the cardiac dilation mediated by gestational hormones that occurs in early pregnancy (20, 33). This may prevent an increase in resting left ventricular end-diastolic pressure (20) and presumably atrial stretch so that the stimulus to increase ANP release is not significantly affected.

In response to exercise, plasma osmolality, PRA, AVP concentration ([AVP]), [ANP], and Aldo concentration ([Aldo]) increase in healthy men (6, 7, 10, 11) and nonpregnant women (8, 12, 15, 28). Stimulation of the RAAS and AVP release is intensity-dependent, requiring an exercise intensity of ≥50–60% of maximal oxygen uptake (V O2 max) (7, 11), although others have reported a significant rise in PRA (6) and plasma [Aldo] (11) at 40% V O2 max. Plasma [ANP] increases significantly at exercise intensities as low as 25% V O2 max (11).

Activation of the RAAS during exercise is attributed to sympathetic stimulation of juxtaglomerular cells and reduced renal blood flow (6). An increase in plasma osmolality, due to the shifting of water out of the vasculature, stimulates AVP release from the neurohypophysis and promotes water retention. Increased circulating [ANG II] also stimulates AVP secretion via type 1 (AT1) angiotensin receptors located outside the blood-brain barrier (5). Stimulation of these fluid retention mechanisms during exercise helps to...
preserve plasma volume to maintain cardiovascular function and thermoregulation. Also during dynamic exercise, enhanced venous return and atrial stretch result in augmented ANP secretion. However, because strenuous exercise is associated with antidiuresis and antinatriuresis, there is a dissociation between changes in plasma ANP levels and the normal effect of ANP to excrete sodium and promote fluid loss (11).

Acute expansion of plasma volume in men results in a blunted PRA (24), Aldo (13, 24), and AVP response to exercise (24). The greater the plasma volume expansion, the less pronounced the Aldo response (13). Plasma volume expansion also has been observed to result in lower plasma [AVP] (13) and higher [ANP] (13, 24) during exercise as a result of changes in resting levels of these hormones (13, 24).

This study compared the fluid regulation responses of pregnant and nonpregnant women to short-term (7 min) exercise at intensities corresponding to 70 and 110% of the ventilatory threshold (VT). Based on the findings of Grant et al. (13) and Roy et al. (24) on the effects of acute plasma volume expansion in men, we hypothesized that the plasma volume expansion of pregnancy would attenuate the normal response for ANG II and AVP to exercise.

METHODS

Subjects. Subjects were 22 healthy, nonsmoking, physically active pregnant women [pregnant group (PG); aged 30.0 ± 0.8 yr, mean gestational age 37.0 ± 0.2 wk] and 17 healthy nonpregnant women [control group (CG); aged 27.1 ± 1.4 yr] with similar physical and demographic characteristics. Prospective subjects were recruited from local prenatal fitness classes and from the general population via media advertisements, posters, flyers, and contact with local obstetricians. Medical clearance for pregnant subjects was obtained from the physician or midwife monitoring their pregnancy with the Physical Activity Readiness Medical Examination for Pregnancy. Nonpregnant subjects completed the Revised Physical Activity Readiness Questionnaire. Both forms are available online from the Canadian Society for Exercise Physiology (www.csep.ca/forms.asp).

Written, informed consent was obtained from all subjects before entry into the study. The study protocol and consent form were approved by the Research Ethics Board, Faculty of Medicine, Queen’s University and the US Army Medical Research and Materiel Command, Human Subjects Protection Branch.

Basic physical measurements included body height, body mass, and resting blood pressure. Body mass index was calculated as body mass/body height² (kg/m²). PG and CG values were equated for mean age, body height, prepregnancy body mass (as reported by subject), parity, and aerobic fitness. Members of PG performed the two exercise tests for the study between 34 and 38 wk of gestation. Subjects in CG were not using oral contraceptives.

Exercise testing protocols. Subjects performed two exercise tests on a Sensor Medics cycle ergometer (model 800S; Sensor Medics, Yorba Linda, CA) constant work rate protocol on separate days, at least 1 day apart. To help standardize nutritional status and to ensure normal hydration, subjects consumed a standard meal (350 kcal, 40% carbohydrate, 40% fat, 20% protein) 1–2 h before both tests and avoided strenuous physical activity and caffeine on the day of testing. The first test was used to determine VT and to assess aerobic working capacity (14). The protocol involved 5 min of resting data collection and a 4-min warm-up at 20 W, followed by an increase in work rate of 20 W/min until a heart rate (HR) of 170 beats/min was reached (14). Respiratory responses and oxygen uptake (VO₂) were measured on a breath-by-breath basis by using a computerized system (First Breath, St. Agatha, Ontario, Canada) that incorporates a respiratory mass spectrometer (MGA 1100; Marquette Electronics, Milwaukee, WI) with a volume turbine (VMM-2; Interface Associates, Also, Viejo, CA) as described previously (14). The V-slope method (2) was used to identify VT. Heart rate (HR) was monitored with both a Polar Vantage monitor (Polar Electro, Woodbury, NY) and Marquette Max-1 electrocardiograph (Marquette Electronics). Oxygen pulse (VO₂/HR) at a HR of 170 beats/min was calculated as an index of aerobic working capacity (14).

The second exercise test involved a 10-min resting data collection period, followed by a 3-min warm-up at 0 W and a ramp increase in work rate, over a 30-s time period, to a work rate corresponding to 70 or 110% VT (14). Both work rates were continued for 7 min after achievement of the prescribed work rate. Subjects rested for 20 min between levels. Before this test, an indwelling catheter was inserted into a dorsal hand vein situated as far from the thumb as possible. The hand and lower arm were soaked in a warm water bath before insertion of the catheter and then placed in a Plexiglas heating box (45°C) to promote vasodilation. Arterialized blood samples were then collected at rest and during the minute 6 of exercise at 70 or 110% VT.

Blood samples for the determination of oxygen tension, arterial Pco₂ and H⁺ concentration were collected in a syringe containing lyophilized heparin and analyzed immediately by using a Radiometer ABL 30 acid-base analyzer at a standard temperature of 37°C. Tympanic temperature measurements confirmed no significant deviation from 37°C with pregnancy or exercise with the use of the present protocol (14). Quality control checks using four control liquids were done on all testing days. The remaining blood was used for plasma electrolyte, total protein (TP), and albumin analysis. Blood for plasma osmolality determination was collected in a 4.5-ml syringe containing lithium heparin (Monovette, Sarstedt). Blood samples for plasma analysis of [ANG II], [AVP], and [ANP] were collected in 10-ml chilled vacuum tubes containing EDTA (Becton-Dickinson) to which aprotonin (100 µl of 100,000 KIU/ml solution) was immediately added to the whole blood and peptatin A (20 µl of 1 mg/ml solution) and O-phenanthroline (20 µl of 50 mM solution) added to 2 ml of fresh plasma for ALI determination. Blood for serum determination of progesterone concentration was collected in a vacutainer containing no additive and placed in ice for 0.5–1 h to allow time to clot. All blood collected for plasma and serum analysis was centrifuged for 10 min at 2,500 rpm (532 g), and the plasma or serum was frozen at −80°C for later analysis, as described below.

Plasma concentrations of sodium ([Na⁺]), potassium ([K⁺]) and chloride ([Cl⁻]) were analyzed by using ion-selective electrodes. Total calcium concentration was measured using a dye-binding assay. Ionized calcium concentration ([Ca²⁺]) was calculated from total calcium concentration. Plasma osmolality was determined by using the freezing-point depression technique (Osmette A, model 5002, Precision Systems, Natick, MA). TP concentration ([TP]) was measured by using the direct Biuret method. Albumin concentration ([Alb]) was determined by using a conventional dye-binding method.
ANG II was measured with a radioimmunoassay kit using 125I-labeled ANG II (Nichols Institute Diagnostics, San Juan Capistrano, CA) (30). The extraction recovery was 70%. AVP and ANP were measured by radioimmunoassay developed by Sarda et al. (26, 30). Intra- and interassay coefficients of variation were 11 and 8% for AVP and 3.8 and 9.1% for ANP. The assays for AVP and ANP have a sensitivity of within 0.2 and 15 pg/ml (1.5 pg/tube), respectively. Progesterone was measured by radioimmunoassay by the Core Lab at Kingston General Hospital.

Statistical analyses. Physical characteristics, VO2 at VT, and oxygen pulse at 170 beats/min were compared between groups by using Student’s t-statistics for independent samples. Data at rest and during exercise at 70 and 110% VT were compared within and between subjects by using a two-way ANOVA (groups vs. rest/exercise level) with repeated measures on the second factor. When a significant between-group main effect was observed, a Tukey’s post hoc test was used to identify significant differences between group means at rest, at 70% VT, and at 110% VT. When a significant within-subjects main effect or group × time interaction was observed, Tukey’s post hoc tests were also used to detect significant differences between rest, 70% VT, and 110% VT within each group. The critical alpha for significance was P < 0.05.

RESULTS

By design, there were no significant differences between groups in age, body height, or parity (Table 1). As expected, body mass and body mass index of the PG was significantly greater than that of the CG at the time of testing. However, the prepregnancy body mass and body mass index of the PG were similar to those of the CG. There were also no significant differences between the groups in VO2 at VT or O2 pulse at 170 beats/min, confirming that the two groups had a similar level of aerobic fitness. Of the 22 subjects in the PG and the 17 subjects in the CG, not all subjects produced complete data sets for [ANG II], [AVP], [ANP], [progesterone], and [TP] due to hemolysis of individual blood samples or individual blood sample acquisition problems. Only subjects with complete data sets (i.e., data at rest, 70% VT, and 110% VT) were included in a variables analysis. The sample sizes used in the analysis of each variable are shown in Tables 2–5 and Figs. 1–3.

Table 1. Physical characteristics of subjects

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pregnant Group (n = 22)</th>
<th>Control Group (n = 17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>30.0 ± 0.8</td>
<td>27.1 ± 1.4</td>
</tr>
<tr>
<td>Gestational age, wk</td>
<td>37.0 ± 0.2</td>
<td>n/a</td>
</tr>
<tr>
<td>Height, cm</td>
<td>163 ± 2</td>
<td>165 ± 1</td>
</tr>
<tr>
<td>Body mass, kg</td>
<td>75.8 ± 2.0*</td>
<td>61.4 ± 1.7</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>28.4 ± 0.6*</td>
<td>22.5 ± 0.5</td>
</tr>
<tr>
<td>Pre-pregnant body mass, kg</td>
<td>62.4 ± 2.0</td>
<td>n/a</td>
</tr>
<tr>
<td>Pre-pregnant body mass index, kg/m²</td>
<td>23.3 ± 0.6</td>
<td>n/a</td>
</tr>
<tr>
<td>Parity</td>
<td>0.5 ± 0.2</td>
<td>0.4 ± 0.2</td>
</tr>
<tr>
<td>VO2 at VT, l/min</td>
<td>1.67 ± 0.06</td>
<td>1.80 ± 0.04</td>
</tr>
<tr>
<td>O2 pulse at 170 beats/min, ml/beat</td>
<td>12.1 ± 0.5</td>
<td>13.0 ± 0.4</td>
</tr>
</tbody>
</table>

Values are means ± SE. VO2, O2 uptake; VT, ventilatory threshold. *Significant difference between groups (P < 0.05).

HR was significantly higher in the PG vs. the CG at rest, whereas VO2 was not (Table 2). There was no difference between groups in VO2 at 70 or 110% VT. HR was significantly higher in the PG vs. the CG at 70% VT but not at 110% VT. Both VO2 and HR increased in both groups from rest to 70% VT and 70 to 110% VT.

Osmolality was significantly lower in the PG vs. CG at rest and at both work rates. Osmolality increased significantly from rest to 70% VT and from 70 to 110% VT in both groups (Table 3). There was a significant interaction between group and exercise level for osmolality. [Na+] and [K+] were significantly lower in the PG vs. the CG at rest and both work rates. [Na+] and [K+] increased significantly from rest to 70% VT and from 70 to 110% VT in both groups, except for [Na+] in the CG from 70 to 110% VT. There was no significant interaction between group and exercise level for [Na+] and [K+]. [Ca2+] was not significantly different between groups at rest but was significantly higher in the PG vs. the CG at 70 and 110% VT. [Ca2+] increased from rest to 70% VT in the PG and from 70 to 110% VT in both groups. There was a significant interaction be-

![Fig. 1. Plasma ANG II concentration ([ANG II]) at rest and at 2 work rates. VT, ventilatory threshold. *Significant difference (P < 0.05) between groups. #Significant difference (P < 0.05) within group from rest. †Significant change (P < 0.05) within group from cycling at 70% VT to cycling at 110% VT.](image-url)
between group and exercise level for \([\text{Ca}^{2+}]\). \([\text{Cl}^-]\) increased from rest to 70% VT in the PG and rest to 110% VT in both groups. There was no significant interaction between group and exercise level for \([\text{Cl}^-]\).

Both TP and albumin levels were significantly lower in the PG compared with the CG at all measurement times (Table 4). Both TP and albumin levels increased significantly from rest to 70% VT and from 70% to 110% VT in both groups. There was no significant interaction between group and exercise level for TP or albumin levels.

\([\text{ANG II}]\) was significantly higher in the PG vs. CG at rest but not at either work rate. In the transition from rest to 110% VT, \([\text{ANG II}]\) increased significantly in the CG but not in the PG (Fig. 1). There was a significant group \(\times\) time interaction for \([\text{ANG II}]\). Plasma \([\text{AVP}]\) was significantly lower in the PG vs. CG at rest and both work rates. Arginine vasopressin concentration increased significantly from rest and 70% VT to 110% VT in the CG (Fig. 2). There was no significant interaction between group and exercise level for \([\text{AVP}]\). ANP was not significantly different at rest or either work rate between groups. \([\text{ANP}]\) increased significantly from rest to 70% VT and from 70% to 110% VT in the PG and was significantly higher at 110% VT than at rest in both groups (Fig. 3). There was no significant interaction between group and exercise level for \([\text{ANP}]\).

As expected, values for circulating plasma progesterone were substantially higher in the PG vs. CG under all experimental conditions (Table 5). Values within the CG reflected the fact that subjects were tested in varying phases of the menstrual cycle. Progesterone levels increased significantly in the PG from rest to 110% VT and from 70 to 110% VT. There was a significant interaction between group and exercise level for progesterone.

**DISCUSSION**

This study tested the hypothesis that pregnancy attenuates \([\text{ANG II}]\) and \([\text{AVP}]\) responses to short-term dynamic exercise. As postulated, the main finding was that the normal response for the activation of the renin-angiotensin system and the secretion of \([\text{AVP}]\) in response to exercise was blunted in late gestation. In contrast, ANP responses were not attenuated.

Although changes in blood volume were not measured directly in this study, the use of plasma protein measurements to reflect fluid volume shift in response to exercise has been used successfully in previous studies of pregnant (3) and nonpregnant women (4). This practice is based on the assumption that macromolecules such as albumin and other plasma proteins do...
not cross vascular barriers in important amounts in response to hydrostatic and osmotic forces during exercise. In this regard, Pivarnik et al. (23) reported moderate increases in exercise-induced loss of total plasma protein and albumin at 29–33 wk of gestation; values in late gestation (33–36 wk) were similar to postpartum control. These losses were small under all experimental conditions.

Resting measurements from this study reflected the substantial expansion of plasma volume and hemodilution that occurs in normal human pregnancy. In this regard, values for TP and albumin were significantly lower in the PG vs. nonpregnant subjects in the resting state. In response to exercise, hemoconcentration was observed in both groups at both work rates as TP and albumin concentrations and osmolality increased significantly from rest. The two groups were similar in the extent of the hemoconcentration as indicated by similar changes in TP and albumin concentration. Both TP and albumin concentrations increased in the PG from rest to 70% VT by ~5% and from rest to 110% VT by ~10–11%, with the CG increasing by 3–4 and ~8%, respectively. This is consistent with the findings of Pivarnik et al. (23), who observed similar decreases in plasma volume in women 33–36 wk pregnant compared with 4 wk postpartum in response to 5 min of cycling at 75 W.

The significantly higher [ANG II] of the PG vs. CG at rest is consistent with the findings of other studies, which have found elevated plasma renin concentration (9), PRA (32), and [ANG II] (21) in pregnancy. The lower circulating [AVP] in the PG vs. the CG at rest may be the result of a large increase in the metabolic clearance rate of AVP during pregnancy (16). Progesterone may also contribute to the lowering of [AVP] as progesterone administration has been demonstrated to decrease AVP levels in women (31). However, elevated circulating estrogen concentration (not measured in this study) is the probable stimulus for the decrease in the osmotic threshold for AVP release during pregnancy (17) because this hormone decreases the osmotic threshold for AVP release in nonpregnant women (27). The level of ANP at rest was not different between the PG and CG. Atrial enlargement during pregnancy (33) may reduce atrial stretch from the expanded blood volume and contribute to the maintenance of normal ANP levels.

As hypothesized, the ANG II response to exercise was attenuated in the PG but not in the CG as reflected by a significant group × time interaction. Although the rise in [ANG II] in the CG group in response to exercise is consistent with the literature on the response of the RAAS to dynamic exercise in the CG (6, 7, 11) values in the PG did not rise at either intensity. This may indicate that blood flow to the kidney was not reduced in pregnancy during the exercise, and thus renin production was not stimulated. If renin concentration did not change, then ANG I levels and subsequently [ANG II] would not rise. The large increase in blood volume during pregnancy (18, 23) may have resulted in improved renal perfusion during exercise. Grant et al. (13) and Roy et al. (24) also hypothesized that the blunted plasma [Aldo] response to exercise observed in men after acute plasma volume expansion was related to improved renal blood flow during exercise.

Attenuation of the RAAS response to exercise in pregnancy was similar qualitatively to that reported by Grant et al. (13) and Roy et al. (24) in response to acute plasma volume expansion in men. The size of this effect appears to be related to the extent of hypervolemia. Since plasma volume is usually increased by 45–55% in pregnancy (18, 23) our results may be viewed as an extension of the investigations of Grant et al. (13) and Roy et al. (24). Grant et al. used plasma volume expansion of 14 and 21% in a study of responses of untrained men to prolonged exercise (120 min at 46% of maximal aerobic power). The subsequent study by Roy et al. examined the effects of a 16% plasma volume expansion on responses of similar subjects to 90 min of exercise at 62% of maximal aerobic power. Thus the results from the study of the larger plasma volume expansion in the pregnant state continued the trend for a decreasing RAAS response with increasing plasma volume expansion, established by Grant et al. and Roy et al., by using smaller percentage increases in plasma volume.

A reduced sympathetic drive (i.e., lower epinephrine and norepinephrine levels) was also observed by Grant and Roy et al. (24). Exercise was attenuated in the PG but not in the CG as reflected by a significant group × time interaction. Although the rise in [ANG II] in the CG group in response to exercise is consistent with the literature on the response of the RAAS to dynamic exercise in the CG (6, 7, 11) values in the PG did not rise at either intensity. This may indicate that blood flow to the kidney was not reduced in pregnancy during the exercise, and thus renin production was not stimulated. If renin concentration did not change, then ANG I levels and subsequently [ANG II] would not rise. The large increase in blood volume during pregnancy (18, 23) may have resulted in improved renal perfusion during exercise. Grant et al. (13) and Roy et al. (24) also hypothesized that the blunted plasma [Aldo] response to exercise observed in men after acute plasma volume expansion was related to improved renal blood flow during exercise.

Attenuation of the RAAS response to exercise in pregnancy was similar qualitatively to that reported by Grant et al. (13) and Roy et al. (24) in response to acute plasma volume expansion in men. The size of this effect appears to be related to the extent of hypervolemia. Since plasma volume is usually increased by 45–55% in pregnancy (18, 23) our results may be viewed as an extension of the investigations of Grant et al. (13) and Roy et al. (24). Grant et al. used plasma volume expansion of 14 and 21% in a study of responses of untrained men to prolonged exercise (120 min at 46% of maximal aerobic power). The subsequent study by Roy et al. examined the effects of a 16% plasma volume expansion on responses of similar subjects to 90 min of exercise at 62% of maximal aerobic power. Thus the results from the study of the larger plasma volume expansion in the pregnant state continued the trend for a decreasing RAAS response with increasing plasma volume expansion, established by Grant et al. and Roy et al., by using smaller percentage increases in plasma volume.

A reduced sympathetic drive (i.e., lower epinephrine and norepinephrine levels) was also observed by Grant

Table 5. Serum progesterone at rest and at 2 work rates

<table>
<thead>
<tr>
<th>Group</th>
<th>Rest</th>
<th>70% VT</th>
<th>110% VT</th>
</tr>
</thead>
<tbody>
<tr>
<td>PG</td>
<td>716±55*</td>
<td>756±59*</td>
<td>828±53†‡</td>
</tr>
<tr>
<td>CG</td>
<td>15±4</td>
<td>15±4</td>
<td>19±5</td>
</tr>
</tbody>
</table>

Values are means ± SE in nmol/l; n = 20 for PG and n = 16 for CG. *Significant change (P < 0.05) within group from rest. †Significant change (P < 0.05) within group from cycling at 70% VT to cycling at 110% VT.
et al. (13) and Roy et al. (24) and was hypothesized to be a potential contributor to the observed lower [Aldo] (13). Sympathetic activity reduces renal blood flow and causes the juxtaglomerular cells of the kidney to increase their renin secretion. This in turn results in elevated circulating [ANG II] and [Aldo]. In our laboratory, a reduction in sympathetic activity has also been observed during exercise in similar pregnant subjects in late gestation at work rates corresponding to 60 and 110% VT as indicated by lower epinephrine levels at 60% VT and lower epinephrine and norepinephrine levels at 110% VT (1). Thus the reduced [ANG II] during exercise in the PG may also be the consequence of a reduction in sympathetic drive. Regardless of the cause, the lack of rise in [ANG II] means that Aldo secretion will not be stimulated to increase Na+ retention during exercise in pregnancy.

The AVP response to exercise in the PG differed from that of the CG. Again, the CG responded as expected, increasing significantly in response to strenuous exercise, but not in response to the less intense exercise (7, 11). Values in the PG, however, did not increase in response to either work rate. Both groups had similar increases in osmolality at the 110% VT work rate, and thus it would be expected that the stimulus for AVP release would be similar in both groups. However, because the [ANG II] response of the PG was blunted, there may have been a lesser stimulus for AVP release. Roy et al. (24) observed a similar blunting of the AVP response to exercise after plasma volume expansion, especially during the first hour of their protocol.

Whether other cardiovascular pressure receptors and reflexes are involved in the blunted ANG II and AVP responses to exercise is an open question. Although blood pressure during exercise was not measured during the present study, an earlier study from this laboratory (1), which used a very similar cycling test protocol and many of the same subjects, observed no significant differences in systolic blood pressure immediately before exercise (sitting) or during short bouts of exercise (7 min) at 60 and 110% VT, respectively, in late pregnancy vs. the nonpregnant state. Thus there is no solid basis at this time to suggest that cardiovascular pressure or volume receptors are involved in these blunted hormone responses. However, further study is needed to clarify this issue.

Despite minor statistical differences, [ANP] rose in both groups at both work rates, and responses were similar from a physiological viewpoint. The increase in ANP in response to exercise in both groups in the present study was expected at both the 70 and 110% VT work rates because relative intensity exceeded the usual threshold to evoke an ANP response. This is consistent with the earlier findings of Grant et al. (13) and Roy et al. (24), who showed that the response in normal subjects to increase ANP in response to exercise was also present in subjects with acute plasma volume expansion. The fact that, in the present study, ANP levels at rest and in response to exercise were generally similar in the pregnant vs. nonpregnant state may be that the augmented venous return observed at rest and during standard submaximal exercise in pregnancy is offset by atrial enlargement (33) so that the degree of atrial distention and stimulus for ANP release is not affected. Thus the acute plasma volume expansion in the Grant et al. and Roy et al. studies, which resulted in higher ANP values compared with controls at rest, with the higher levels also persisting into exercise, may have resulted because the acute plasma volume expansion (resulting in enhanced venous return) would not be offset by atrial enlargement.

The fact that the RAAS and AVP were affected by pregnancy during exercise and ANP responses were not can be explained by the fact that the stimuli for activation of the two systems are different (19). In this regard, the RAAS-AVP axis responds primarily to changes in blood volume, renal perfusion pressure, and sympathetic stimulation (with osmotic changes also being a major stimulus for AVP), whereas the ANP secretion is stimulated by increased venous return and atrial distention (19).

In conclusion, our results support our original hypothesis that pregnant subjects exhibit blunted RAAS and AVP responses to short-term exercise. This effect may have been the result of reduced sympathetic drive to the kidney and/or reduced circulating norepinephrine resulting in an attenuation of the normal decrease in renal blood flow in response to exercise and reduced renin output of juxtaglomerular cells of the kidney. Lower ANG II levels may then account for the observed blunting of AVP responses to exercise. In contrast, the ANP response to exercise above VT were similar to the CG. Despite the differences in the ANG II and AVP responses to exercise, the two groups exhibited similar changes in osmolality and TP and albumin concentrations, suggesting similar overall water balance adjustments during the exercise bouts.

Because this study examined the effects of human pregnancy responses to short-term exercise, future studies should be conducted to determine the effects of pregnancy on responses to prolonged exercise (>40 min duration). The study of renal blood flow during exercise in pregnancy would also be useful to understand the mechanisms responsible for possible discrepancies in hormonal responses.

DISCLOSURES

This study was supported by US Army Medical Research and Materiel Command Contract no. DAMD17-96-C-6112, Ontario Thoracic Society, Ontario Respiratory Disease Foundation (Block-Term Grant Funding), and Natural Sciences and Engineering Research Council of Canada. A. P. Heenan was supported by an Ontario Graduate Scholarship for Science and Technology and an Ontario Thoracic Society training award.

REFERENCES


