INFLUENCE OF ANGIOTENSIN BLOCKADE DURING EXERCISE IN THE HEAT IN NORMAL MALES AND FEMALES

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INTRODUCTION

The use of angiotensin converting enzyme inhibitors (ACE-I) as a therapeutic modality in treating hypertension has become widely accepted. The decrease in blood pressure accompanying ACE-I has been attributed, in part, to a decrease in both angiotensin 11-mediated vasoconsmction and aldosterone release (Bauer, 1990). Whereas a reduction in both peripheral resistance and sodium retention are beneficial for lowering blood pressure in hypertensives at rest, circumstances leading to a reduced central blood pressure or volume (e.g. exercise in heat, orthostatic challenge) may require increased splanchnic and renal vasoconstriction as well as decreased sodium excretion for the maintenance of adequate hemodynamic and thermoregulatory function. Although recent evidence has shown reduced hemodynamic function with ACE-I during orthostatic challenge (Stadeager *et al.*, 1989), no studies to date have addressed the potential problem of ACE-I during exercise in the heat. The purpose of the present study was to evaluate the influence of blockade of the renin angiotensin system (RAS) on hemodynamic, thermoregulatory, and body fluid homeostasis, in normotensive males and females during moderate exercise in a hot environment. The clinical drug enalapril was used to reduce the level of circulating angiotensin II (angII) by inhibiting converting enzyme, which forms ang 11 from angiotensin I.

METHODS

Subjects. Six males and three females (age=24.6 ± 5.4yr, mass=72.0 ± 14.2kg, body fat= 13.6 ± 8.5%, A_D=1.83 ± .22m^2, VO_{2peak}=56.4 ± 9.1$ml \cdot kg^{-1} \cdot min^{-1}$) participated in the study following medical evaluation and giving informed consent. Body composition (6 skinfold thicknesses) and peak oxygen consumption (VO_{2peak}) was determined during a graded cycle ergometer test prior to heat exposures.

Protocol. The order of drug treatment was counterbalanced and tests were conducted at the same time of day but spaced one week apart. Females were studied during the follicular phase of their menstrual cycles. A double-blind procedure for drug administration was utilized with a gelatin capsule substituted during the placebo trial (PLAC) for enalapril (5mg, ENAL). Following 30 min rest in a thennoneutral environment (T_a=24.3°C, RH=31%), subjects performed cycle exercise at 60% VO_{2peak} in a heat chamber (T_a=35°C, RH=60%) for 45 min. Following exercise subjects returned to a thennoneutral environment (T_a=24.7°C, RH=33%) for 30 min. Esophageal (T_{es}) and mean *skin* (T_{sk}) temperatures, and heart rate (HR) were recorded every 5 min. Blood pressure was measured every 10 min. Venous blood samples were obtained at the midpoint of rest and recovery, and at the end of exercise. Samples were evaluated for plasma creatinine, sodium, potassium, protein, renin activity, aldosterone, osmolality, hematocrit and hemoglobin. Urine samples were obtained at the end of each phase by voluntary micturation and were analyzed for urine volume, osmolality, creatinine, sodium, and potassium concentrations. Changes in plasma volume (ΔPV) were calculated from hematocrit and hemoglobin values.

Data Analyses. Data were evaluated for differences between gender, drug treatments and measurement phases using a repeated measures ANOVA with $p < 0.05$ level of significance. Post-hoc comparisons were made using standard contrast procedures.

RESULTS

The increase in T_{es} (1.5 ± .1°C) and T_{sk} (5.5 ± .1°C) during exercise in the heat were similar between genders and were not influenced by ACE-I treatment. Two male subjects were unable to complete the 45 min exercise during PLAC as T_{es} increased above 39°C. Only one of these subjects was unable to complete the ENAL mal. The HR response during rest (PLAC=76

± 5 b·min^{-1}; ENAL=78 ± 3 b·min^{-1}), exercise in the heat (PLAC=156 ± 3 b·min^{-1}; ENAL= 154± 3 b·min^{-1}), and recovery (95 ± 3 b·min^{-1} both trials) was unaffected by gender or drug treatment Mean arterial pressure *(MAP)* was significantly reduced for each measurement phase during the ENAL trial. A gender by drug interaction was observed as the reduction in *MAP* was greater in females (Table). Additional evidence that the ACE-I was effective can be seen in

		PLACEBO			ENALAPRL		
Variable	Gender	Rest	Exer	Rec	Rest	Exer	Rec
MAP*,¶,§ (mmHg)	M	101.0 (1.6)	109.1 (3.0)	93.3 (2.1)	96.4 (1.6)	106.4 (2.5)	89.6 (2.1)
	F	88.0 (4.3)	89.0 (3.7)	81.8 (2.8)	74.5 (0.2)	79.9 (2.2)	69.2 (2.0)
PRA*,¶ (ngAI·ml^{-1}·h^{-1})	M	1.1 (0.2)	6.8 (1.7)	4.6 (1.1)	3.7 (0.9)	17.0 (4.0)	12.3 (3.7)
	F	2.1 (0.1)	9.0 (0.3)	4.2 (0.1)	2.4 (1.4)	16.0 (6.9)	6.1 (2.8)
ALDO¶ (pg·ml^{-1})	M	56(5)	387 (20)	291 (88)	50 (19)	344 (86)	272 (121)
	F	176 (47)	750 (149)	526 (98)	108 (39)	246 (13)	186 (28)
Pprot¶ (g·dl^{-1})	M	7.3 (0.1)	7.6 (0.2)	7.2 (0.2)	6.8 (0.2)	7.8 (0.1)	7.4 (0.3)
	F	6.8 (0.1)	7.1 (0.8)	7.2 (0.3)	6.6 (0.1)	7.3 (0.2)	6.4 (0.4)

* $p < 0.05$ v. PLAC ;¶ $p < 0.05$ v. Rest; § $p < 0.05$ v. Males

the plasma renin activity (PRA) response (Table). Both trials resulted in an exercise-induced elevation in PRA which remained during the recovery phase. However, PRA during exercise and recovery was greater with ENAL. The change in PV following exercise in the heat was unaffected by the drug treatment and was similar between genders (PLAC= -8.3 ± 1.6%; ENAL= -10.0 ± 2.5%). Also shown in this table is the plasma aldosterone and total plasma protein response to exercise in the heat. Although aldosterone is commonly linked to the renin-angiotensin system, both trials resulted in similar increases in aldosterone during and following exercise in the heat. The plasma protein response showing an elevation during exercise was also unaltered by the drug treatment. The acute administration of ACE-I did not influence the urine variables measured and there were no gender differences. Exercise in the heat resulted in a significant reduction in urine flow and urinary sodium excretion during both trials. The reduction in urinary potassium excretion was not significant for either trial.

CONCLUSIONS

In the present study, blockade of RAS with ACE-I in healthy, normotensive males and females did not compromise normal thermoregulatory function during exercise in the heat. Females displayed a greater reduction in *MAP* with enalapril, however, the pressure response to exercise was maintained. Aldosterone is commonly linked to RAS, however, the disassociation of aldosterone from the RAS observed in the present study during submaximal exercise in the hear, supports previous findings observed during maximal treadmill exercise (Wade *et al.*, 1987). Although the present data suggests that ACE-I does not alter temperature or body fluid homeostasis during these conditions in healthy, normotensive subjects, research to determine the influence of chronic angiotensin II blockade in hypertensives during exercise in the heat is warranted.

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