Atrial natriuretic factor responses to submaximal and maximal exercise

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The aim of this study was to evaluate and compare the plasma concentration of atrial natriuretic factor (ANF), K⁺, Na⁺, blood lactate, heart rate, and blood pressure in moderately trained women. Ten healthy women were studied on a cycle ergometer during 20 min of constant submaximal and maximal exercise, as well as during recovery. The ANF concentration was determined by radioimmunoassay. The results show that, except for Na⁺, all the other variables increased significantly with an increase in the duration and intensity of the exercise (P < 0.05, P < 0.001). In recovery, the values fell (P < 0.01, P < 0.001). Submaximal and maximal exercise both cause increases in ANF and this increase is due to the duration and intensity of exercise. However, maximal exercise, rather than submaximal exercise, is the major stimulus for the concentration of plasma ANF. ANF concentration may be a useful test for evaluating the releasing function of ANF in the heart.

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Atrial natriuretic factor (ANF), or atriopeptin, is a cyclic polypeptide secreted from human atrial tissues in response to increased intra-atrial pressure.1-2 It induces vasodilatation and blood pressure reduction, decreases renal and hepatic blood flow, and produces a natriuretic and diuretic effect.3-7

It has been suggested that the determination of plasma ANF can help to estimate the seriousness of heart disease, act as a sensitive diagnostic indicator, and be a significant index of the physical evolution of the disease.8-11 Resting plasma ANF concentrations have been reported to be raised in a spectrum of heart and renal diseases12-16 in trained compared with normal individuals, and as well in untrained controls.17-19 On the other hand Fellmann10 reported that there was no significant difference in resting or maximum exercise ANF values between trained and untrained subjects.

Numerous studies have suggested that higher plasma ANF values are found in disease conditions associated with a pressure or fluid overload of the heart.19 Of clinical importance are the findings that both the increase in resting ANF and the much higher plasma ANF found in response to exercise are directly related to the severity of the disease.21 It has been shown that strenuous and prolonged physical activity causes a significant increase in plasma ANF.22

Knowledge about the effect of short to moderate duration exercise at constant submaximal workload on ANF concentrations is limited. Furthermore, little information exists about maximum exercise intensity on ANF concentrations and their relationship to blood pressure, sodium (Na⁺), potassium (K⁺), and blood lactate concentrations in moderately trained subjects. Thus the aim of this study was to evaluate and compare the ANF secretory patterns during short term constant submaximal and maximal exercise, as well as during recovery, in moderately trained women.

Methods

Ten healthy female physical education students and volleyball players (mean age (SD) = 20,5(1.04) years, height 180.6(5.4) cm, weight 68(5.5) kg) participated in this study. All volunteers were informed about the purpose and possible risks of the study before giving their voluntary written consent to participate. All subjects attended the laboratory early in the morning after an overnight fast from 2100 the previous evening. The subjects were instructed to avoid smoking and strenuous exercise the previous day and to rest in the laboratory for 10 minutes before the blood sampling. The exercise test was performed on an electronic cycle ergometer (Monark) at a pedal rate of 50 rpm indicated by a metronome. All tests were performed in the morning. No warm up was allowed before exercise.

The exercise test started with a submaximal work rate of 100 W for 20 min followed by increments of 25 W every minute until exhaustion. Heart rate was monitored continuously on an electrocardiograph. Blood pressure, with a cuff, and blood samples were obtained at rest, at 10 min, 20 min, and immediately after maximum exercise, as well as 10 min after the end of the maximum exercise (recovery). Blood samples were drawn by a catheter from the brachial vein. The catheter was kept patent with heparinized saline

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throughout the testing period. Blood samples for plasma ANF concentration were collected in prechilled tubes containing EDTA-2Na (1.5 mg/ml blood) and aprotinin (500 KIU/ml blood), placed on ice, and immediately centrifuged at 1500 g for 10 min at 4 °C. Plasma was frozen and stored at −70 °C until the assay was performed. The plasma ANF concentration was determined by radioimmunoassay (RIA), using a commercial kit (Amersham). The intra- and interassay coefficients of variation were 6.8% and 9.8% respectively and the sensitivity was 7 pg/ml. Serum K+ and Na+ levels were measured by flame photometry (Eppendorf EDOX 5053). Blood lactate concentration was measured by an enzymatic method (Boehringer, Mannheim). The special characteristics of the method were: (1) specificity: the antibodies bound 100% of ANF; (2) sensitivity: 7 pg/ml; (3) the coefficient of variance (CV %) within assay was 6.5% and 9.8% between different assays (n = 10).

The significance of intraindividual differences was tested using the Wilcoxon test. Pearson product-moment correlation coefficients were also determined. The significance of differences between means was determined by a one way analysis of variance (ANOVA). A value of P < 0.05 was considered significant.

Results
The results of the present study showed that heart rate and systolic blood pressure (Figure 1A), blood lactate and ANF concentrations (Figure 1B), Na+ and K+ (Figure 1C) increased significantly in response to the duration and intensity of the exercise. After 10 min and 20 min of exercise all variables except Na+ showed a significant increase in comparison to the rest values (P < 0.01 to P < 0.001). All variables reached their highest values during maximum exercise. The measurements showed that the maximum values (SEM) over basal level increased as follows: ANF from 49.8(3.3) to 95.7(18.1) pg/ml (P < 0.01); systolic blood pressure from 110(2.1) to 200(8.2) mm Hg (P < 0.001); K+ from 4.1(0.1) to 5.1(0.2) mmol l⁻¹ (P < 0.01); and plasma lactate concentration from 0.67(0.06) to 11.9(0.23) mmol l⁻¹ (P < 0.001). The correlations between the different variables after 10 min and 20 min of exercise were low. The maximum values of plasma ANF concentrations were not correlated with the maximum values of the other variables. However, significant correlations were found between systolic blood pressure and blood lactate (r = 0.65). Ten minutes after maximum exercise (recovery period) the values of all variables except Na+ decreased significantly in comparison to the maximum values (P < 0.005 for ANF, and P < 0.001, for heart rate, systolic blood pressure, blood lactate and K+).

Discussion
The heart rate when measured at an exercise intensity of 100 W indicated that the subjects were exercising at about 40–50% of their maximum heart rate. Most of the variables increased significantly in response to exercise. This increase is not only due to the effect of the exercise intensity, but also to exercise duration. This is shown by there being no increase in exercise intensity until 20 minutes, but a significant increase in heart rate, plasma ANF concentration, blood pressure, and blood lactate. All peak values appear at maximum exercise, which confirms that exercise intensity is a prime factor when exercise is used stimulating plasma ANF production. Mannix et al.17 and Goodman et al.17 have shown that maximum plasma ANF and K+ concentrations do not appear at the end of maximal exercise, but occur in the first 4 minutes of recovery. The different maximum values of plasma ANF and serum K+ between the present study and these previous investigations may be due to methodological differences.

When looking at plasma ANF concentrations in relation to exercise intensity, Tanaka et al.23 and Mannix et al.3 found increases in plasma ANF concentration at only 30% of maximum aerobic power in untrained subjects. In contrast, Saito et al.24 found no increase in ANF concentration during mild exercise.

The present study shows that exercise duration appears to be an important factor in the increase in ANF concentration. The question is whether the long exercise duration of the same continuous submaximal workload could be a prime factor in the further rise in ANF concentration, as has occurred in maximal exercise.24–27

Ten minutes after the end of the exercise (recovery), plasma ANF was significantly reduced, suggesting an immediate reduction in ANF secretion by the heart. This finding is in agreement with previous observations by Brooks et al.26 and Follenius and Branderberger.29

Heart rate and blood pressure are known to increase significantly with increasing work rates. Some investigators postulate that the exercise tachycardia itself might play a role in ANF stimulation.21,30 Saito et al.24 and Somers et al.31 reported that the increase in heart rate during exercise was positively correlated to the changes in ANF. The increase in heart rate itself does not appear to play a major role in the exercise stimulated rise in plasma ANF concentration. Plasma concentrations of ANF during exercise and its potential haemodynamic or cardiovascular effects are known.32

The experimental design of the present study was, for the main part, to investigate the changes of plasma ANF concentrations during constant submaximal workload. The results have shown that under these conditions plasma ANF concentration increases with the increase in the duration of the exercise. However, maximal exercise rather than submaximal exercise is the major stimulus for an increase in plasma ANF. This is probably due to different haemodynamic adjustments which occur in the two intensities of exercise. The purpose of most previous studies was to estimate the seriousness of heart and renal disease. In the present study it is shown that plasma ANF concentration increases with exercise intensity and that this response depends on the duration and intensity of the exercise. Exercise in healthy subjects is shown to be a useful test to evaluate the releasing function of ANF in the heart. The determination of plasma ANF provides information on the strain on the cardiovascular system.
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**Figure 1.** Metabolic and physiological variables at rest, at submaximal and maximal exercise, and at recovery. (A) Heart rate and systolic blood pressure; (B) blood lactate and ANF (a-ANP); (C) Na⁺ and K⁺. Values are means, error bars = SEM. *P < 0.05; **P < 0.01; ***P < 0.001

The increase in blood lactate concentration and serum potassium during the 10 and 20 minutes of continuous submaximal constant workload could be due to local fatigue of the quadriceps muscle. On the other hand, the unchanged value of sodium during the submaximal and maximal exercise is difficult to explain.

In conclusion, our study clearly shows that plasma ANF concentration increases in response to the intensity of exercise, indicating that an exercise test can evaluate not only cardiorespiratory function but also the endocrine function of the heart. Further study is needed to determine whether long duration exercise until exhaustion can lead to maximal ANF concentrations. Also, the ANF response during a long period of constant submaximal workload in these individuals remains to be investigated.

**References**

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