Natriuretic peptide and exercise

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Abstract Natriuretic peptide (NP) release is mainly stimulated by stretching of the myocardium. NP causes diuresis, natriuresis and vasodilation. NP release increases during exercise. Increased NP plays a counter-regulatory role in increased blood pressure during exercise and makes it lower. The source of ANP released during exercise seems to depend on the experimental conditions. Exercise affected guanylate cyclase activity in the kidney and adrenals. Plasma NP concentration is increased in the hypertensive state. Also, exercise increases plasma NP concentration. But when hypertensive model rats swim for more than 30 minutes, plasma ANP concentration decreases to below the resting level.

Keywords : ANP, BNP, CNP, hypertension, exercise

Introduction

NP comprises a family of peptides that includes atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP) and C-type natriuretic peptide (CNP). NP causes diuresis, natriuresis and vasodilation. ANP and BNP also have lipolytic effects in humans. ANP is released mainly from the heart atria, and although stretching of the myocardium is the main stimulus for its release, several factors are considered to stimulate ANP release. BNP is released predominantly from the heart ventricles, and the main stimulus is also stretching of the myocardium such as volume expansion and pressure overload. BNP is often used for heart failure diagnosis because plasma BNP concentration reaches very high levels in subjects with heart failure. CNP exists in a wide variety of tissues and works as a paracrine or autocrine.

NP during exercise

Plasma ANP and BNP increase during exercise1,2). The increased pressure in the heart during exercise stimulates the release of these natriuretic peptides. NPs cause vasodilation, diuresis and natriuresis. Increased NPs play a counter-regulatory role to increased blood pressure during exercise and make it lower.

In humans, plasma ANP increases immediately after starting bicycle exercise, even at low workloads. This response is different from other exercise-related plasma concentrations of substances such as lactate. So ANP release is stimulated mainly by the stretching of the myocardium during exercise2). In fact the right atrial plasma ANP correlated with the right atrial pressure during bicycle ergometry, and reduced venous return by bilateral thigh-cuff occlusion, decreased right atrial ANP concentration3). Exercise similarly raised plasma BNP with concomitant increases in systolic blood pressure (SBP), heart rate (HR) and so on. SBP and norepinephrine is correlated to plasma BNP concentration3).

We measured rat plasma ANP concentration after three hours of swimming. The plasma ANP concentration also increased in rats similar to humans4). To identify the source of the plasma ANP increment during exercise, ANP content in the myocardium was analyzed. ANP content in the right atria significantly decreased in the rats and recovered to the basal level one day after swimming, suggesting the right atrium is the main source of ANP secretion during exercise (Fig. 1). Another study reported that rat ANP content in the ventricles decreased after 30 minutes of swimming, suggesting ANP seems to be released from the ventricles5). So the source of ANP released during exercise seems to depend upon the rat and exercise conditions.

There are three types of receptors for these peptides: A-type receptor, B-type receptor and C-type receptor. A-type and B-type receptors have guanylate cyclase activity, but the C-type receptor does not. cGMP, made from GTP by guanylate cyclase, functions as a second messenger, and cGTP invokes certain cell functions.

To examine the effect of exercise training on the NP receptors, we measured the number and the affinity of NP receptors and guanylate cyclase activity in the lungs, the adrenals and the kidneys of the rats. The number of adrenal NP receptors significantly increased after exercise training. Guanylate cyclase activity in the kidney, stimulated by CNP, was significantly lower in the exer-
cise-trained group). These findings are consistent with exercise-induced hypervolemia, but not with the anti-hypertensive role of exercise-training.

One of the effects of NP on the adrenals is the inhibition of aldosterone release. We reported the effects of exercise on ANP action on the adrenals. After two hours of treadmill running, the adrenals were excised and aldosterone release was stimulated with angiotensine II and inhibited with ANP. NP receptors in the crude membrane of the adrenals were also stimulated with ANP, and cGMP was measured. cGMP accumulation significantly increased in the membrane of rats in the exercise group. But aldosterone release was not inhibited. These results suggest that exercise may blunt the inhibitory effect of ANP on angiotensine II induced aldosterone release, and affect receptor-mediated intracellular signal transduction events in the adrenals.

NP and exercise in a hypertensive state

Exercise is recommended for moderately hypertensive patients. Plasma ANP and BNP concentration is higher in patients with essential hypertension at rest, because it increases intra-heart pressure. How do these peptide concentrations change during exercise? In humans, plasma ANP and BNP concentrations increase during bicycle ergometer exercise in essential hypertensive patients. These changes were correlated to heart rate. When spontaneously hypertensive rats (SHR) swam, plasma concentration of ANP and mean arterial pressure (MAP) increased and peaked at ten minutes, and then both plasma ANP concentration and MAP declined to a level below the resting level at 30 minutes of exercise. We used DOCA-salt hypertensive rats, hypertensive model rats. Plasma ANP concentration at rest was significantly higher in the hypertensive group compared to the normotensive group. And plasma ANP concentration decreased after three hours of swimming in the hypertensive rats, although plasma ANP increased in normotensive rats. ANP content in the right atria decreased after swimming in the normotensive group, but there was no difference in the hypertensive group. These results suggest that the ANP release reaction to exercise is different in the hypertensive group than the normotensive group.

The relationship between exercise and NPs is reported from other aspects. Hypertension as well as chronic exercise induces hypertrophy in the heart. One of the features of exercise-induced hypertrophy is less BNP expression compared to hypertension-induced hypertrophy. A previous microarray study suggests that the beneficial effects of exercise-training on aortic stiffness are related to CNP as well as other factors.

References

