

Insufficient secretion of atrial natriuretic peptide at acute phase of myocardial infarction

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Maeda, Keiko, Takayoshi Tsutomoto, Atsuyuki Wada, Naoko Mabuchi, Masaru Hayashi, Tomoko Hisanaga, Takeshi Kamijo, and Masahiko Kinoshita. Insufficient secretion of atrial natriuretic peptide at acute phase of myocardial infarction. *J Appl Physiol* 89: 458–464, 2000.—To investigate the secretion of the plasma levels of atrial natriuretic peptide (ANP) in patients with acute myocardial infarction (AMI), we evaluated the relationship between plasma levels of ANP and pulmonary capillary wedge pressure (PCWP) in 45 consecutive patients during the acute phase of AMI (~12 h after the attack) (*group 1*) and compared data with those obtained after 1 mo (*group 2*). In both *groups 1* and *2*, plasma ANP levels significantly correlated with PCWP. The slope of the linear regression line between the PCWP and ANP in *group 1* was significantly lower, by about one-third, than that in *group 2*. In addition, we examined changes in ANP levels and left ventricular end-diastolic pressure (LVEDP) over 180 min after AMI induced by injection of microspheres into the left coronary arteries of three dogs. The LVEDP and ANP levels 30 min after AMI were significantly higher than those before; however, despite the persistent high LVEDP during the 180 min after AMI, ANP levels decreased gradually and significantly to 63% of the peak level at 150 min. These findings suggest that the secretion of ANP during the acute phase of myocardial infarction may be insufficient relative to the chronic phase.

cardiac natriuretic peptides; ischemia; pulmonary capillary wedge pressure; acute heart failure

BOTH ATRIAL NATRIURETIC PEPTIDE (ANP) and brain natriuretic peptide (BNP), produced and secreted mainly from the atria and ventricles, respectively, have biological effects such as natriuresis, diuresis, vasodilation, and inhibition of the renin-angiotensin-aldosterone system and sympathetic nervous system (2, 4, 5, 10, 14, 19, 25, 30). Plasma levels of ANP and BNP increase with the severity of heart failure (3, 11, 14, 23, 24). In patients with chronic congestive heart failure (CHF), a significant correlation between plasma levels of ANP and BNP and hemodynamic parameters such as pulmonary capillary wedge pressure (PCWP), left ventricular end-diastolic pressure (LVEDP), and left ventric-

ular ejection fraction has been reported (1, 11, 16, 19, 21, 23, 24, 30). ANP is stored in secretory granules, and its secretion is predominantly regulated by the stretching of the atria, whereas BNP is thought to be secreted in constitutive form, indicating that the release of BNP occurs just after the synthesis of the protein by mRNA. And, in vitro, stimulation of endothelin (ET)-1 and α_1 -adrenergic agent increases production of ANP and BNP in cardiomyocytes (8, 15).

In patients with acute myocardial infarction (AMI), a decrease in plasma ANP levels soon after AMI has been reported (20, 27). However, these investigators did not measure atrial pressure and plasma BNP levels at the same time as blood sampling for ANP. Therefore, the relationship between the hemodynamics and sufficiency of these cardiac natriuretic peptide secretions in patients with AMI remains controversial.

We evaluated the relationship between plasma cardiac natriuretic peptide levels and hemodynamics, such as atrial pressure, in patients during the acute phase of AMI and compared the results with those in patients during the subacute phase of AMI and attempted to clarify changes in plasma ANP and BNP levels and LVEDP after acute phase of myocardial infarction in a canine models.

METHODS

Study 1

Subjects. Forty-five consecutive patients with AMI who were admitted within 24 h after onset of symptoms and who underwent right heart catheterization, coronary angiography, and percutaneous transluminal coronary angioplasty (PTCA) were studied in our institution (*group 1*). The 37 men and 8 women ranged in age from 36 to 77 yr (mean age 58.1 ± 1.6 yr). The diagnosis of AMI was made on the basis of chest pain persisting for at least 30 min and ST-segment elevation of at least 0.1 mV in at least two contiguous leads. Twenty-three patients were diagnosed as having anteroseptal infarction, 16 as having inferior infarction, and 6 as having lateral infarction. There were no patients with previous myocardial infarction. The blood samples were taken after PTCA, and

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the average time of blood sampling after onset of symptoms was 12.5 ± 1.1 h (ranging from 2 to 24 h). Thirteen patients were treated with nitrates, two patients with calcium antagonists, and four patients by intra-aortic balloon pumping. Ten patients were treated with intravenous dopamine and/or dobutamine.

In *group 2*, 45 patients (all of *group 1*) who underwent follow-up coronary angiography and right heart catheterization 1 mo after myocardial infarction were studied. Eight patients were classified as New York Heart Association (NYHA) functional class I, 37 as NYHA II, and none as NYHA III or IV. Thirty-four patients had been treated with angiotensin-converting enzyme inhibitors, 4 with β -blockers, 39 with nitrates, 5 with calcium antagonists, and 3 with diuretics. All drugs were discontinued at least 24 h before this study.

Informed consent was obtained from all patients for participation in the study, according to a protocol approved by the Committee on Human Investigation at the Shiga University of Medical Science.

Study protocol. In patients with AMI, a 7 Fr Swan-Ganz catheter was inserted into the femoral vein before coronary angiography. The heart rate (HR) was monitored by electrocardiogram, and mean blood pressure (MBP) was measured by femoral arterial pressure. A Swan-Ganz catheter was inserted via the femoral vein into the right atrial and the main pulmonary artery, where the pressure was measured. The catheter was then inserted farther into the pulmonary artery, and PCWP was measured by inflating the balloon. Cardiac output was determined by the thermodilution method. Blood samples for measurements of plasma ANP and BNP levels were taken from the pulmonary artery after PTCA. In *group 2*, after 20 min of bed rest, with the patient supine and premedicated with diazepam (5 mg orally), right heart catheterization was performed and hemodynamics were measured as in *group 1*. Blood samples were taken from the pulmonary artery.

Measurements of plasma ANP and BNP levels. In the two groups, samples for the assay of plasma ANP and BNP levels were transferred to chilled disposable tubes containing aprotinin (500 kallikrein-inactivating units/ml) and EDTA (1 mg/ml). The blood samples were immediately placed on ice and centrifuged at 4°C , and aliquots of plasma were immediately stored at -30°C until the assay. Plasma ANP levels were measured with a specific immunoradiometric assay for human α -ANP by using a commercial kit (ANP kit, Shionoria, Osaka, Japan), and plasma BNP levels were measured with a specific immunoradiometric assay for human BNP by using a commercial kit (BNP kit, Shionoria), as previously reported (11, 24). In 25 age-matched normal subjects, the mean plasma ANP level was 12.7 ± 1.3 pg/ml and the mean plasma BNP level was 15.2 ± 2.8 pg/ml.

Plasma ET-1 levels were measured by radioimmunoassay as described (11). This antibody showed 100% cross-reactivity with ET-1, 7% with ET-2, 7% with ET-3, and 17% with BIG ET-1. However, it did not cross-react with angiotensin I or II, vasopressin, or human cardiac natriuretic peptides. The mean plasma ET-1 level was 1.5 ± 0.9 pg/ml in 20 age-matched normal control subjects, as we previously reported (11). Plasma norepinephrine (NE) levels were measured by high-performance liquid chromatography.

Study 2

Animal preparation and experimental protocol. Experiments were performed on three beagle dogs (CSK Research Park, Nagano, Japan), without regard to gender, weighing

10–12 kg. The animals were treated in accordance with Chugai Pharmaceutical's ethical guidelines for animal care, handling, and euthanasia. After an overnight fast, the animals were anesthetized with pentobarbital sodium (35 mg/kg), with supplemental doses of $6 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ administered throughout the experiments; intubated; and ventilated with room air in a tidal volume of 20 ml/kg at a rate of 10–15 breaths/min (Harvard Apparatus, South Natick, MA). The heart was exposed through a left thoracotomy incision at the fourth intercostal space. An electrical magnetic flow probe (Nihon Kohden, Tokyo, Japan) was then placed around the ascending aorta to measure aortic blood flow.

A 6 Fr double-tipped, high-fidelity pressure catheter (Millar Instruments, Houston, TX) was placed in the left ventricle through the right femoral artery for the measurement of MBP and LVEDP. The right carotid artery was exposed, and a catheter was advanced into the left main coronary artery. Microspheres (mean 50 μm in diameter) were then injected to induce AMI. The microspheres were injected as a bolus of 1.0–1.5 ml (48,000 microspheres/ml), and injections were made 4–10 times until the LVEDP increased over 10 mmHg, as previously reported (9). The average dose of microspheres was 0.44 million (range 0.24–0.7 million). Measurements of hemodynamics and blood samples were performed before and 30, 60, 90, 120, 150, and 180 min after AMI. Blood samples were taken from the brachial artery.

Measurements of plasma ANP and BNP levels. In dogs with AMI, plasma ANP was measured by radioimmunoassay as previously described (9). Plasma BNP was measured by a radioimmunoassay specific to canine BNP (Peninsula Laboratories), using a method described by Grantham et al. (6), with some modification. BNP was extracted by using C_{18} Sep-Pak filter (Waters). Concentrated eluates were then assayed by using a canine-specific antibody. The minimum detectable concentration for the assay was 1 pg/tube with an interassay variation of 15% and intra-assay variation of 5%. This antibody has 100% cross-reactivity with canine BNP.

Statistical Analysis

Data are expressed as means \pm SE. The correlations of the plasma levels of ANP and BNP with hemodynamic parameters and plasma levels of ET-1 and NE were examined by using linear regression analysis. Stepwise multivariate regression analyses were used to detect independent predictors of plasma ANP and BNP among the seven variables in *groups 1* and *2*, as listed below. The difference in the slope of the linear regression line was tested by an analysis of covariance. The plasma levels of natriuretic peptides and LVEDP were compared over the time course in dogs with AMI by using ANOVA for repeated measures. A value of $P < 0.05$ was considered significant.

RESULTS

Study 1

Hemodynamic data and plasma neurohumoral factor levels in group 1 and group 2. Cardiac catheterization data and levels of plasma neurohumoral factors are shown in Table 1. HR, right atrial pressure (RAP), and PCWP were significantly higher in *group 1* than in *group 2*. There was no significant difference in MBP or cardiac index (CI) between the two groups.

The plasma ANP levels were significantly lower in *group 1* than in *group 2*, whereas the plasma BNP levels tended to be higher in *group 1* than in *group 2*.

Table 1. Hemodynamic data and plasma neurohumoral factors in consecutive patients with myocardial infarction

	Group 1 (<24 h)	Group 2 (1 mo)
HR, beats/min	81 ± 2.3†	70 ± 1.7
RAP, mmHg	6.4 ± 0.4†	2.2 ± 0.3
PCWP, mmHg	11.0 ± 0.7†	6.0 ± 0.4
MBP, mmHg	90 ± 2.1	89 ± 2.1
CI, l · min ⁻¹ · m ⁻²	2.95 ± 0.09	2.93 ± 0.09
ANP, pg/ml	33.9 ± 4.0*	59.8 ± 8.2
BNP, pg/ml	115 ± 21	94 ± 14
ET-1, pg/ml	3.55 ± 0.25†	2.32 ± 0.10
NE, pg/ml	499 ± 79*	255 ± 19

Values are means ± SE for 45 subjects. Group 1, acute myocardial infarction within 24 h after onset group; group 2, 1 mo after myocardial infarction group; ANP, atrial natriuretic peptide; BNP, brain natriuretic peptide; ET-1, endothelin-1; NE, norepinephrine; HR, heart rate; RAP, right atrial pressure; PCWP, pulmonary capillary wedge pressure; MBP, mean blood pressure; CI, cardiac index. * $P < 0.01$ vs. value in group 2 by paired t -test. † $P < 0.001$ vs. value in group 2 by paired t -test.

The plasma ET-1 and NE levels were significantly higher in group 1 than in group 2.

Correlation of plasma ANP and BNP levels with hemodynamic parameters and plasma ET-1 and NE levels. Correlation of plasma ANP and BNP levels with hemodynamic parameters and plasma ET-1 and NE levels are shown in Table 2. In group 1, there was a significant correlation of plasma ANP levels with PCWP and ET-1 and of plasma BNP levels with PCWP and MBP. In group 2, there was a significant correlation of plasma ANP levels with HR and PCWP and of plasma BNP levels with RAP and PCWP.

Predictor of plasma ANP and BNP in groups 1 and 2 by stepwise multivariate regression analysis. To investigate the independent predictors of ANP and BNP in groups 1 and 2, stepwise multivariate regression analysis was used with seven variables including HR, RAP, PCWP, MBP, CI, ET-1, and NE. Among these seven variables, in group 1, PCWP ($P = 0.013$) was an independent and significant predictor of ANP, and PCWP ($P = 0.0201$) and MBP ($P = 0.0054$) were independent and significant predictors of BNP. In group 2, PCWP ($P = 0.0001$) and HR ($P = 0.006$) were independent and

significant predictors of ANP, and PCWP ($P = 0.0009$) was an independent and significant predictor of BNP.

Comparison of the slopes of the linear regression lines between PCWP and plasma ANP and BNP levels in group 1 with those in group 2. The relationships between PCWP and plasma levels of ANP and BNP in the two groups are shown in Fig. 1. In the two groups, there were significant correlations between PCWP and plasma ANP levels. Almost all data from group 1 were localized on the right side of the linear regression line from those of group 2, and the slope of the linear regression line between the two parameters in group 1 was about one-third of that in group 2. This difference was significant ($P < 0.05$). These findings suggest that the secretion of ANP was not sufficient relative to the degree of PCWP increase during the acute phase of AMI.

On the other hand, there were also significant correlations between PCWP and plasma BNP levels in the two groups. However, the difference in the slopes of the linear regression line between the two parameters in groups 1 and 2 was not significant.

Study 2

Time course of hemodynamic data and plasma ANP and BNP levels after AMI in dogs. Hemodynamic data in dogs with AMI are shown in Table 3. MBP, HR, and RAP after AMI decreased significantly compared with those before AMI. The LVEDP and plasma ANP levels 30 min after AMI were significantly higher than those before AMI (LVEDP: 5 vs. 13 mmHg, ANP: 64 vs. 202 pg/ml; $P < 0.05$). However, despite the high LVEDP during the 180 min after AMI, plasma ANP levels at 150 and 180 min significantly decreased to 63 and 62% of the peak level at 30 min, respectively. However, plasma BNP levels did not change significantly compared with those before AMI, as shown in Fig. 2.

DISCUSSION

ANP is produced and stored in granules and secreted mainly from the atria, and the secretion of ANP is regulated by the stretching of the atria (17). In patients with chronic CHF, including old myocardial infarction, plasma ANP levels increase with the severity of heart

Table 2. Correlation of plasma levels of cardiac natriuretic peptide with hemodynamics and other neurohumoral factors in patients with myocardial infarction

	Group 1 (<24 h)				Group 2 (1 mo)			
	ANP		BNP		ANP		BNP	
	r	P	r	P	r	P	r	P
HR	0.07	NS	0.12	NS	0.32	0.031	0.20	NS
MBP	-0.18	NS	-0.45	0.002	0.06	NS	-0.14	NS
RAP	-0.02	NS	0.24	NS	0.19	NS	0.34	0.024
PCWP	0.46	0.0013	0.39	0.008	0.61	0.0001	0.53	0.0001
CI	-0.15	NS	-0.25	NS	0.08	NS	-0.07	NS
ET-1	0.34	0.024	0.35	0.019	-0.06	NS	0.11	NS
NE	0.22	NS	-0.13	NS	0.26	NS	-0.04	NS

r , Correlation coefficient; NS, not significant.

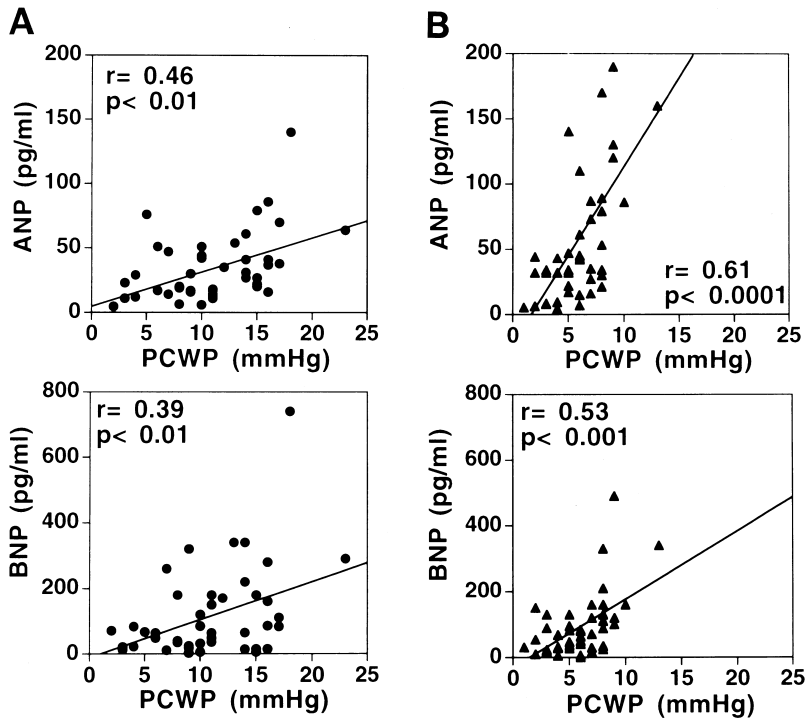


Fig. 1. Correlations of pulmonary capillary wedge pressure (PCWP) with plasma levels of atrial natriuretic peptide (ANP; top) and brain natriuretic peptide (BNP; bottom) in patients in group 1 (A; ●) and group 2 (B; ▲). Group 1, acute myocardial infarction group; group 2, 1 mo after myocardial infarction group.

failure (3, 11, 14, 23, 24). Although there have been a number of reports of a significant correlation between plasma ANP levels and PCWP or LVEDP (1, 11, 16, 19, 21, 23, 24, 30) in chronic CHF, including old myocardial infarction, the relationship between the hemodynamics and the sufficiency of ANP secretion in patients with AMI remains controversial.

In the present study, we measured plasma ANP levels and hemodynamic parameters in 45 consecutive patients with AMI both on admission (group 1) and at 1 mo after myocardial infarction (group 2). There was significant correlation between PCWP and plasma ANP levels in both groups 1 and 2. Furthermore, by stepwise multivariate analysis, PCWP was an independent and significant predictor of high levels of ANP and BNP. Therefore, we examined the relationship PCWP and cardiac natriuretic peptide in group 1 and group 2. Although PCWP, which is an important stimulator of ANP secretion, was significantly higher in group 1 than in group 2, plasma ANP levels were significantly lower in the former than in the latter, and

the slope of the linear regression line between the PCWP and ANP in group 1 was one-third of that in group 2, suggesting that the secretion of ANP was not sufficient relative to the degree of PCWP increase during the acute phase of AMI, probably because of the decrease in secretory granules. Insufficient endogenous ANP during AMI may worsen the hemodynamics and promote left ventricular remodeling. Our laboratory previously reported that, in a patient with mitral stenosis and very low plasma levels of ANP because of remarkable fibrosis in the atrium despite severe pulmonary hypertension, low-dose infusion ($0.025 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) of exogenous ANP was very effective in improving the pulmonary hypertension (12).

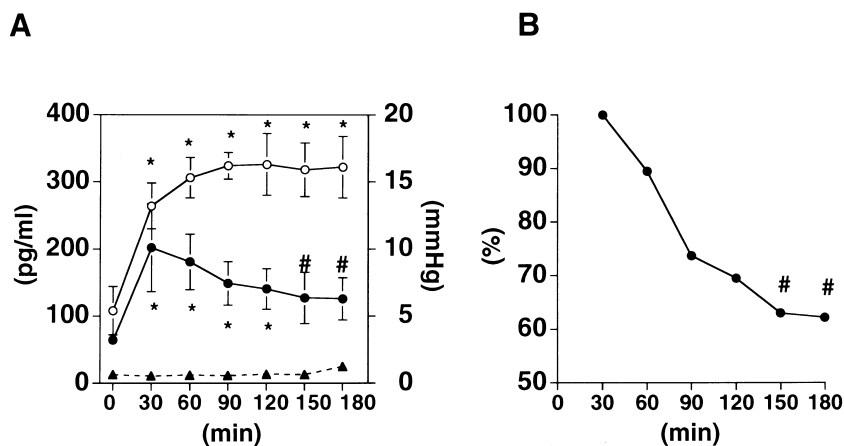
Although plasma ET-1 and NE levels were significantly higher in group 1 patients than in group 2, plasma ANP levels were significantly lower in group 1 patients than in group 2 patients. ET-1 and α -adrenergic agents directly increase ANP release in cardiocytes in vitro (8, 15). Also, our laboratory previously reported that, in patients with left ventricular dysfunc-

Table 3. Time course of hemodynamic data and plasma cardiac natriuretic peptides levels after AMI in dogs

	Time, min						
	0	30	60	90	120	150	180
HR, beats/min	124 ± 16	157 ± 9*	151 ± 6*	148 ± 9*	150 ± 13*	154 ± 16*	156 ± 14*
MBP, mmHg	147 ± 4	131 ± 7*	127 ± 7*	133 ± 6*	135 ± 8*	139 ± 8*	137 ± 4*
RAP, mmHg	3.7 ± 0.2	4.6 ± 0.1*	4.6 ± 0.3*	4.5 ± 0.3*	4.4 ± 0.3*	4.5 ± 0.3*	4.6 ± 0.3*
LVEDP, mmHg	5.4 ± 1.8	13.2 ± 1.7*	15.3 ± 1.5*	16.2 ± 1.0*	16.3 ± 1.0*	15.9 ± 2.0*	16.1 ± 2.3*
ANP, pg/ml	64 ± 9.5	202 ± 65*	181 ± 41*	140 ± 30*	149 ± 32*	127 ± 38†	126 ± 31†
BNP, pg/ml	12.6 ± 7.2	10.7 ± 0.3	12.1 ± 0.3	11.2 ± 2.3	13.5 ± 3.6	12.9 ± 3.7	24.9 ± 3.7

Values are means ± SE for 3 dogs. 0 min, before acute myocardial infarction (AMI); LVEDP, left ventricular end-diastolic pressure. * $P < 0.05$ vs. value at 0 min by ANOVA. † $P < 0.05$ vs. value at 30 min by ANOVA.

Fig. 2. A: time course of plasma ANP (●) and BNP (▲) levels and left ventricular end-diastolic pressure (○) before and after acute myocardial infarction in dogs. * $P < 0.05$ vs. 0 min by ANOVA. # $P < 0.05$ vs. 30 min by ANOVA. B: time course of plasma ANP levels is expressed as a percentage of that at 30 min set at 100%. # $P < 0.05$ vs. 30 min by ANOVA.



tion, a high LVEDP and plasma ET-1 level are predictors of high ANP levels (11). Although these factors stimulating ANP secretion increase during the acute phase of AMI, plasma ANP levels were significantly lower in *group 1* patients than those in *group 2* patients.

Moreover, in dogs, the LVEDP and plasma ANP levels 30 min after AMI were significantly higher than those before AMI. However, despite the persistent high LVEDP during the 180 min after AMI, plasma ANP levels decreased significantly at 150 and 180 min compared with those at 30 min. There are no previous studies that have reported the results of measuring LVEDP and plasma ANP levels during the 3 h after AMI. Previous studies reported that plasma ANP levels were immediately and significantly increased by rapid atrial pacing in dogs and then tended to decrease within 60 min during pacing (6, 9, 26, 28), suggesting an acute decrease of stored ANP granules.

These findings demonstrate that a sudden rise in LVEDP due to infarction releases ANP. Once increased, plasma ANP levels and ANP secretion are predominantly regulated by the stretching of the atria, with an increase of ANP mRNA required for at least 24 h after stimulation, and, soon thereafter, ANP is reduced as a result of the release of stored ANP. The time course of plasma ANP levels in dogs with AMI in this study suggests that it would be difficult to determine the transient increase in plasma ANP levels in patients with AMI, because most patients are hospitalized several hours after onset. These results are in agreement with the results of *study 1*.

BNP is secreted mainly from the ventricle, and previous studies reported that the secretion of BNP is regulated by blood pressure and fluid volume (14, 18, 19, 30). In patients with CHF, reports showed that plasma BNP levels correlated with PCWP and LVEDP and, consequently, that plasma BNP levels reflect the degree of left ventricular overload (11, 19, 24, 30). Plasma BNP levels are elevated in patients with AMI because of stimulation by myocardial necrosis and local mechanical stress on ventricular cardiocytes (13). The time course of plasma BNP levels in patients with AMI is classified into two patterns: monophasic and bipha-

sic. Both patterns show a first peak at ~20 h after AMI, but the biphasic pattern shows a second peak 5 days after AMI, suggesting a relationship with infarct expansion and subsequent ventricular remodeling (13).

The relationship between the hemodynamics and plasma BNP, in addition to ANP levels, in patients with AMI remains controversial. A previous study showed that there was no correlation between plasma BNP levels and PCWP within 2 days after onset and that there was a significant correlation between plasma BNP levels and PCWP in the first month after onset (13), but the difference in the relationship between the acute and chronic phase of myocardial infarction was not examined. In the present study, there was a significant but rough correlation between PCWP and plasma BNP levels; however, there was no difference in the slopes of the linear regression lines between the two parameters in *groups 1* and *2*.

In dogs, after AMI, plasma BNP levels did not significantly increase for 3 h compared with levels before AMI. Also, a previous study reported that plasma BNP levels did not increase for 45 min in dogs that underwent rapid left ventricular pacing to induce acute heart failure (6) or for 1 h from onset of AMI in dogs (9). Hama et al. (7) reported that, in rats with AMI induced by coronary artery ligation, BNP concentration increased at as early as ~12 h and that BNP mRNA expression was augmented as early as 4 h postinfarction in both the infarcted region and noninfarcted region of the ventricle. Our findings suggest that, during the acute phase of myocardial infarction, BNP is secreted just after the synthesis of protein by mRNA, which proceeds rapidly but requires at least several hours, and that in 24 h BNP may be sufficiently secreted.

Limitations

We measured plasma cardiac natriuretic peptide in the pulmonary artery to assess cardiac secretion of ANP and BNP because we could not obtain informed consent for blood sampling at the coronary sinus and the ascending aorta in all patients with AMI. In this study, plasma ANP and BNP levels at the coronary

sinus and the ascending aorta could be measured in only 15 patients with AMI. There was significant correlation of PCWP with the increase in the plasma ANP and BNP levels between the aortic root and the coronary sinus 1 mo after myocardial infarction, and almost all data from AMI patients were localized on the right side of the linear regression line compared with those obtained 1 mo after myocardial infarction (data not shown). These findings were in agreement with the results of *study 1*.

In the present study, coronary revascularization, such as PTCA, is performed in all AMI patients within 24 h after onset, and it would be unethical to follow AMI patients without coronary revascularization (PTCA). However, in 13 AMI patients we could measure PCWP and plasma ANP levels at, before, and after PTCA, and there was no difference in plasma ANP levels and PCWP or in the slopes of the linear regression line between PCWP and plasma ANP levels between before and after PTCA. Therefore, there were no important effects of PTCA on PCWP and ANP in this study.

During the acute phase of AMI, the influences of pain, stress, and tachycardia cannot be negated completely. However, in this study they were not main factors for the ANP secretion in AMI, because most patients were free of chest pain after PTCA and because NE and HR are not predictors of ANP in AMI.

Because we cannot rule out changes in the clearance of these peptides between AMI and 1 mo after myocardial infarction, we measured plasma ANP at the pulmonary capillary wedge region, femoral artery, and femoral vein to evaluate the degradation of ANP in the vascular beds, as previously reported (22, 23). There was no change in the degradation of these peptides between AMI and old myocardial infarction (data not shown).

Clinical Implications

At the acute phase in patients with AMI, levels of cardiac natriuretic peptides, such as ANP, may be insufficient relative to those in patients in the subacute phase. In patients with AMI, augmentation of the cardiac natriuretic peptide system, such as by exogenous administration of ANP, may be a useful supplementary therapy for preventing left ventricular remodeling due to cardioprotective actions of ANP (29) such as suppression of the renin-angiotensin-aldosterone system.

Conclusion

In patients with AMI (~12 h after attack), ANP secretion is insufficient relative to the chronic phase (1 mo after attack). In dogs with AMI, peak of plasma ANP was after 30 min and gradually decreased to 62% of the peak level after 180 min. These findings suggest that the secretion of ANP during the acute phase of myocardial infarction may be insufficient relative to the chronic phase.

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