Atrial Natriuretic Peptide Levels During and After Acute Cardiac Tamponade in Dogs

HARILAOS ZIORIS, MD, PANAYOTIS KARAYANNACOS, MD, CHERRY ZERVA, MD, VASSILIKI ALEVIZOU-TERZAKI, MD, FOTIS PAVLATOS, MD, GREGORY SKALKEAS, MD
Athens, Greece

The ability of the atrial wall to secrete atrial natriuretic peptide was studied in eight dogs during 2 h of cardiac tamponade and for 2 h after decompression of the pericardium. Cardiac tamponade was induced by instillation of 5% dextrose in water into the pericardial cavity until aortic systolic pressure was reduced by 30% to 35%. Heart rate, cardiac output and atrial, pericardial and aortic pressures were measured at 60 and 120 min of tamponade and at 5, 30, 60, 90 and 120 min after decompression. Blood samples were withdrawn at the same time for the determination of atrial natriuretic peptide and aldosterone levels.

Aortic pressure decreased significantly during tamponade and increased after decompression to near control levels. Right and left atrial pressures as well as intrapericardial pressure increased significantly during tamponade and returned to control levels after decompression. The effective transmural pressure, which was reduced during tamponade, was increased significantly at 5 min after decompression. Cardiac output was significantly reduced during tamponade and returned to pretamponade levels after decompression. Over the total experimental period, no significant changes in the levels of atrial natriuretic peptide were observed, whereas aldosterone increased significantly.

It is concluded that the increased atrial pressure observed during cardiac tamponade did not stimulate the secretion of atrial natriuretic peptide. Furthermore, atrial distension observed immediately after decompression was not sufficient or of long enough duration to induce measurable increases in atrial natriuretic peptide levels. Finally, the secondary hyperaldosteronism did not activate atrial natriuretic peptide secretion either during cardiac tamponade or after decompression.

(J Am Coll Cardiol 1989;13:936-40)

It is well known that, in the atrial wall, there are receptors sensitive to mechanical and chemical stimuli that respond with a greater or lesser neurohumoral discharge (1). An increase in the atrial pressure or distension of the atrial wall has been shown to cause natriuresis and diuresis (2–4), thus supporting the concept that changes in atrial pressure are important in the sequence of events regulating the circulating blood volume (5).

Recently, attention has been focused on the findings of de Bold et al. (2), who reported that mammalian atrial cells contain and secrete a potent natriuretic substance that was initially considered to be a 28 amino acid peptide (6,7). Further studies (8,9) support the fact that it is an atrial natriuretic peptide made up of 31 to 33 amino acid residues.

This atrial peptide has a natriuretic and vasodilative action and a suppressive effect on the renin-angiotensin-aldosterone axis (3,10–14). Although detailed knowledge of this peptide has been limited, it has been found to circulate in the blood of human subjects under normal and abnormal conditions (15–18) and to exist in increased concentrations in patients with paroxysmal supraventricular tachycardia, primary hyperaldosteronism, mitral valve stenosis, cor pulmonale, congestive heart failure, chronic renal failure with fluid retention and states with increased circulating blood volume (15,16,18–24).

Atrial dilation, which is the common denominator of all these conditions, probably results in excitation of stretch receptors and, thus, constitutes a secretory stimulus for atrial natriuretic peptide (20,21,25,26). The nature of this atrial stimulus is not yet completely clarified, but it is known that an increase in right and left atrial pressure beyond normal levels is capable of inducing atrial natriuretic peptide secretion (21). In cardiac tamponade of short duration (≤30 min), in which atrial pressure is increased without concur-
rent distension of the atrium, the atrial natriuretic peptide level is not increased (27,28). It was also reported (29) in one clinical case that plasma atrial natriuretic peptide levels increased after decompression of cardiac tamponade.

The present study attempted to answer the following questions: 1) Can atrial wall distension, observed at the time of decompression, cause the secretion of atrial natriuretic peptide? 2) Can the secondary hyperaldosteronism constitute a stimulus to atrial natriuretic peptide secretion during or after cardiac tamponade? 3) Does increased atrial pressure without dilation of the atrial wall during a 2 h period of cardiac tamponade raise plasma atrial natriuretic peptide levels?

Methods

Animal preparation. Eight healthy mongrel dogs of either sex, weighing between 12 and 15 kg, were studied. Thirty minutes before operation, the dogs were premedicated with acepromazine (0.5 mg/kg body weight) and atropine (0.05 mg/kg). Anesthesia was induced with sodium thiopental (20 mg/kg). An endotracheal tube was placed and connected to a volume-controlled respirator that supplied the dog with room air. To provide a stable anesthetic state, supplementary doses of thiopental were given throughout the experiment. Appropriate limb leads were attached to the dog for continuous electrocardiographic (ECG) monitoring. Corrections in ventilation and acid-base balance were made to keep homeostasis within normal limits.

Surgical procedure. A right thoracotomy was performed through the fifth intercostal space. A Foley catheter was inserted into the pericardium and secured by a double pursestring suture. For continuous monitoring of central aortic and right and left atrial pressures, catheters were placed through the carotid artery, the azygos vein and a branch of a right pulmonary vein. Cardiac output was measured by the thermodilution technique with use of a Swan-Ganz catheter inserted through the jugular vein into the pulmonary artery. Blood samples were taken from the catheter in the right atrium for determination of atrial natriuretic peptide and aldosterone.

Tamponade. Cardiac tamponade was induced by the instillation of a solution of dextrose in water at 37°C into the pericardial sac over 5 min until aortic systolic pressure was reduced by 30% to 35%. The tamponade was maintained for 2 h, adding more dextrose to maintain the same level of aortic pressure. The pericardium was then released by rapid drainage of the fluid.

Measurements and blood sampling. All hemodynamic variables were recorded before, at 60 and 120 min of tamponade and at 5, 30, 60, 90 and 120 min after the release of tamponade. Blood samples were simultaneously taken from the right atrium for natriuretic peptide and aldosterone determinations. An equal volume of 5% dextrose was infused to replace the volume of blood sampled. Atrial natriuretic peptide was measured in plasma with the Amersham radioassay kit and aldosterone levels with a Sorin Aldoctk assay kit.

Statistics. Statistical analysis of all data was performed with use of the Student's t test for paired data. Values are presented as mean ± SEM.

The study with the experimental animals conformed to the position of the American Heart Association on research animal use.

Results

Detailed results of all measured variables during the different phases of the study are presented in Table I.

Hemodynamic variables. Aortic systolic pressure decreased significantly during the 2 h of tamponade. After decompression of the pericardial sac, a significant increase in aortic pressure was observed. However, arterial pressure remained at significantly lower levels compared with control values.

Mean right atrial pressure increased significantly during tamponade and returned to control levels with decompression. Similar changes in mean left atrial pressure were observed, although absolute values were higher than those for the right atrium.

Effective transmural pressure of the atria, calculated as the difference between mean atrial and pericardial pressures, decreased significantly during tamponade and increased to the pretamponade level after decompression of the pericardium.

During tamponade, a significant decrease in cardiac index was observed. After the removal of fluid from the pericardium, the cardiac index initially increased and then gradually declined to levels significantly lower than control.

Heart rate showed a continuous decrease with the onset of tamponade, which became significant after 120 min.

Hormone levels. Right atrial aldosterone concentration increased by almost 400% during tamponade. In the period after removal of pericardial fluid, aldosterone concentration decreased gradually, although values remained significantly higher than control values. Changes in atrial natriuretic peptide levels were not significant during tamponade and after decompression of the pericardium.

Discussion

Atrial natriuretic peptide and atrial pressure. Mammalian atrial cells contain granules resembling those of endocrine organs (12,30,31). The number of these granules is directly proportional to salt load and blood volume (32). Although the muscle cells of both the right and the left atrium contain natriuretic peptide-secreting granules, these are found in twice the concentration in the tissue of the right atrium.
Table 1. Results of Measured Variables (mean ± SEM) in Eight Dogs

<table>
<thead>
<tr>
<th>Tamponade (min)</th>
<th>Decompression (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before 60 120 60 90 120 60 90 120</td>
</tr>
<tr>
<td><strong>Systolic aortic pressure (mm Hg)</strong></td>
<td>151.50 ± 4.17 101.50 ± 2.58* 104.00 ± 3.96* 140.00 ± 8.01** 135.25 ± 4.63* 131.62 ± 6.63* 130.62 ± 7.65* 129.50 ± 6.70*</td>
</tr>
<tr>
<td><strong>Mean right atrial pressure (mm Hg)</strong></td>
<td>3.32 ± 0.47 10.05 ± 1.02* 9.06 ± 0.93* 3.81 ± 0.72† 2.97 ± 0.57 2.83 ± 0.50 2.88 ± 0.57 2.62 ± 0.47</td>
</tr>
<tr>
<td><strong>Mean left atrial pressure (mm Hg)</strong></td>
<td>4.87 ± 0.71 10.14 ± 1.06* 9.76 ± 0.97* 5.11 ± 0.62‡ 4.80 ± 0.51 4.75 ± 0.52 4.91 ± 0.45 4.31 ± 0.49‡</td>
</tr>
<tr>
<td><strong>Pericardial pressure (mm Hg)</strong></td>
<td>0 9.08 ± 0.95 7.89 ± 0.73 0 0 0 0 0</td>
</tr>
<tr>
<td><strong>Cardiac output index (ml/min per kg)</strong></td>
<td>120 ± 9 60 ± 10* 60 ± 7* 130 ± 9* 120 ± 8 110 ± 10 90 ± 7* 90 ± 8*</td>
</tr>
<tr>
<td><strong>Heart rate (beats/min)</strong></td>
<td>151.25 ± 5.57 148.53 ± 5.10 126.00 ± 8.51** 110.25 ± 7.1111 115.83 ± 10.67* 114.57 ± 11.10* 115.50 ± 10.91* 109.12 ± 10.24*</td>
</tr>
<tr>
<td><strong>Aldosterone (pmol/ml)</strong></td>
<td>84.50 ± 22.98 333.25 ± 77.81* 281.37 ± 58.53* 234.75 ± 57.75* 176.00 ± 42.14** 165.50 ± 35.78* 155.62 ± 37.13* 157.25 ± 35.57*</td>
</tr>
<tr>
<td><strong>ANP (fmol/ml)</strong></td>
<td>18.30 ± 4.58 26.41 ± 6.24 23.83 ± 5.78 26.10 ± 5.71 28.41 ± 6.06 20.49 ± 4.45 17.81 ± 5.45 18.52 ± 4.76</td>
</tr>
</tbody>
</table>

*p < 0.05 compared with control; †p < 0.05 compared with preceding phase. ANP = atrial natriuretic peptide.

Also, in addition to its own secretion, the right atrium receives from the left atrium, natriuretic peptide, returning through the coronary sinus (18).

In an isolated heart model, Lang et al. (20) showed that for each 1 mm Hg increase in right atrial pressure, the level of atrial natriuretic peptide in plasma increased by 38%. Also, in a clinical study, Raine et al. (21) showed that when right atrial pressure was increased by 1 mm Hg above the level of 4 mm Hg, the concentration of atrial natriuretic peptide in plasma increased by 36%. Rapid infusion of either sodium chloride solution or whole blood produced an increase in the plasma level of atrial natriuretic peptide. However, the peak concentration of the secreted hormone occurred much earlier when expansion was obtained with sodium chloride than with whole blood (20,35). Also hemodynamic studies in healthy humans (73) and patients with congestive heart failure (21) showed a linear relation between atrial natriuretic peptide concentration and atrial pressure.

Atrial natriuretic peptide during cardiac tamponade. Our present results confirm findings of other workers, cast light on some of the existing questions and leave open some topics that could stimulate further research. During the first 2 h of tamponade, there was no significant increase in atrial natriuretic peptide (Fig. 1). It seems that the increase in atrial pressure by itself is not sufficient to stimulate secretion of the peptide and that dilation caused by a pressure gradient across the atrial wall is also necessary (20–23,26–28). This hypothesis is supported by our finding that the effective transmural pressure was significantly reduced in both atria during tamponade (Fig. 2).

The secondary hyperaldosteronism we observed during the period of tamponade does not seem to be a potent stimulus for secretion of atrial natriuretic peptide (Fig. 3). We postulate that this stimulus of 2 h of tamponade is of...
However, plasma atrial natriuretic peptide failed to increase significantly above the control and tamponade levels. A possible explanation might be that, although after decompression atrial pressures returned to levels slightly above control levels, the difference in pressure between the two phases of the experiment was not greater than 1 mm Hg (20,21). On the other hand, if it is accepted that, immediately after decompression, pressure in the atria had increased for <5 min when the first pressure recording was made, this duration might be insufficient to stimulate secretion of the peptide (20,21,25,26). Finally, another explanation for the unresponsiveness of the receptors might be the loss of their sensitivity or activity, or both, which occurred during tamponade.

The increase in venous return that resulted in an augmented stroke volume and cardiac output did not constitute a secreting stimulus for the atrial natriuretic peptide. These changes, however, were not statistically significant except for stroke volume, which was increased by 39% and 26% at 5 and 30 min, respectively. Perhaps a prerequisite for the release of atrial natriuretic peptide might be a significant increase in circulating blood volume in the atria beyond the pretamponade values (20,21). It is also possible that the 2 h duration of tamponade is too short to allow the atrial receptors to become reset to the new hemodynamic conditions (1,29). Finally, it is apparent that aldosterone, although significantly increased, was not able to stimulate a similar secretion of atrial natriuretic peptide in plasma.

Conclusions. Cardiac tamponade of 2 h duration does not significantly increase atrial natriuretic peptide levels in blood. This finding might be explained by the absence of an elevated effective transmural pressure, which seems to be a prerequisite for the activation of stretch receptors. After decompression of the pericardial sac, no increase in the atrial natriuretic peptide level occurred despite the increase in the effective transmural pressure because either the increase was not much greater than the control level or it lasted for a very short period of time. It is also postulated that the duration of cardiac tamponade may not have been sufficient for the stretch receptors to become readjusted to the new conditions. It seems also that the elevated plasma levels of aldosterone are not a potent stimulus for the secretion of atrial natriuretic peptide either during acute tamponade or after decompression of the pericardial sac.

References


ATRIAL NATRIURETIC PEPTIDE IN TAMPONADE


