Effect of pericardiocentesis on circulating concentrations of atrial natriuretic hormone and arginine vasopressin in dogs with spontaneous pericardial effusion

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Factors regulating the secretion of atrial natriuretic hormone (ANH) and arginine vasopressin (AVP) have not been elucidated fully. In several studies the release of these peptides has been studied by inducing both increased atrial pressure and atrial distension. A few studies employ cardiac tamponade, allowing the effect of atrial pressure and atrial stretch to be studied separately. In eleven dogs with spontaneous cardiac tamponade the effect of pericardiocentesis on circulating concentrations of ANP and AVP was studied. Pericardiocentesis was followed by a prompt rise in (non-elevated) plasma ANH concentrations from 21.6 ± 7.3 to 65.4 ± 17.1 pmol/l (mean ± SEM). The initially slightly elevated AVP concentration of 5.5 ± 1.5 pmol/l declined following pericardiocentesis to 2.1 ± 0.5 pmol/l. In three dogs the systolic arterial pressure was measured indirectly and the central venous pressure was measured with a fluid-filled catheter. Before and after pericardiocentesis arterial pressure readings did not change significantly. Central venous pressure values showed an immediate very steep significant decrease after centesis. It is concluded that ANH release is primarily regulated by stretch and not by atrial pressure, that plasma AVP concentrations are moderately elevated in cardiac tamponade and that in cardiac tamponade pericardiocentesis causes a rapid decline in plasma AVP concentration.

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In heart failure, neuroendocrine activity is increased to maintain blood pressure. This is achieved primarily by augmented sympathetic drive to the heart and blood vessels, and additionally also by retention of salt and water. For the latter, the renin angiotensin–aldosterone system is activated and the release of the neurohypophysial hormone arginine vasopressin (AVP) is enhanced. As if to counterbalance these vasoconstrictor and retentive forces, natriuretic substances such as atrial natriuretic hormone (ANH) or atrial natriuretic peptide (ANP) are released (1).

For the regulation of the secretion of both ANH and AVP in low-output heart failure syndrome, signals arising in the atria seem to be the principal stimuli. Atrial natriuretic hormone, which is a peptide synthesized and stored in the myocardium, is released primarily in response to increases in atrial pressure or volume (2). The release of AVP under these conditions appears to be regulated primarily by non-osmotic factors, i.e. inhibitory influences from atrial baroreceptors (3) that are transmitted via neural pathways to hypothalamic vasopressin-producing neurones (4).

In studies designed to determine the nature of the signals involved in the regulation of the release of AVP and ANH, atrial pressure usually has been increased by volume loading and by inflating a balloon in the atrium (5). There has been one study in which the approach allowed an increase in atrial pressure without causing atrial stretch (6). In this model of experimentally induced cardiac tamponade there were no significant changes in plasma ANH during the tamponade or after its relief. In one reported clinical case, the ANH concentrations in plasma increased after decompression of the cardiac tamponade (7).

Here, we present our observations in dogs with spontaneous cardiac tamponade due to pericardial effusion. Plasma concentrations of ANH and AVP were measured before, during and after pericardiocentesis.

Animals and methods

The animals entering the protocol were two female and eight male dogs, all of larger breeds (four St Bernard dogs, a German pointer, a Newfoundland dog, an Old English Sheepdog, a Tatra dog, a Staffordshire bull terrier and a Great Dane) aged 2.6–10 years, the diagnosis of pericardial effusion was based upon the physical findings (weak or absent femoral pulse and apex beat), electrocardiography (low voltage, electrical...
alternans pattern), radiography (large globoid shape of cardiac silhouette) and echocardiography (echo-free space between parietal pericardium and epicardium). The Great Dane re-entered the protocol when it was presented 6 months after the first pericardiocentesis because of recurrence of the condition. The dogs were placed in metabolism cages and food and water were withheld for the 23 h of the protocol.

Pericardiocentesis was performed with the animal in right laterad recumbency, by introducing an 18-gauge needle or a “Pneumocath catheter” (Intra, Saarbrücken, Germany) in the ventral part of the left 6th intercostal space. A three-way stopcock and syringe were attached to the catheter. During centesis there was continuous electrocardiographic monitoring. The value of hemorrhagic fluid that was removed ranged from 40 to 1590 ml (mean 543 ml). The time required to complete the centesis was 5–45 min (mean 21 min).

Blood samples were collected for measurements of plasma AVP and ANH concentrations at 60, 30 and 15 min before and at 0, 5, 30, 60 and 120 min after completion of the pericardiocentesis. Three more samples were taken 5 h, 11 h and 22 h after completion of pericardiocentesis. The samples were collected in ice-chilled EDTA-coated tubes, to which 1000 KI u/l (Trasylol, Bayer, Leverkusen, Germany) had been added. Plasma ANH and AVP were measured by radioimmunoassay as reported and validated for the dog (8).

In the first eight dogs entering the protocol, the urinary bladder was emptied at the time of completion of pericardiocentesis (t = 0). Recatheterization was performed after 2 h and at the end of the protocol. Creatinine, osmolality (U_{osm}) and sodium content were measured in the respective samples.

In the last three dogs entering the protocol, the arterial pressure and the central venous pressure were measured at the AVP and ANH sampling times. Measurements were made with the dog in right lateral recumbency. The systolic arterial pressure was measured using an inflatable cuff around the left frontlimb just below the elbow joint. The appearance of peripheral arterial pulsations following deflation of the cuff was detected using an ultrasonic Doppler flow detector (Parks Medical, Aloha, OR, USA). The pressure (mmHg) measured inside the cuff at the moment of the reappearing pulsations was considered as the systolic arterial pressure. The central venous pressure was measured with a 14-gauge 30.4-cm long fluid-filled catheter (Bardi-Cath, CR Bard International Ltd, Sunderland, UK), introduced through the jugular vein and positioned with its tip in the cranial caval vein. Measurements were made in cmH2O. Both the arterial and central venous pressure results were converted to kPa.

Statistics

The AVP and ANH results are expressed as means ± SEM and evaluated statistically by a two-tailed signed rank test; p < 0.05 was considered significant.

Results

Despite the withholding of food and water, the dogs produced considerable amounts of urine. In the first 2 h following the centesis, there was a high sodium excretion associated with low urinary creatinine concentrations (Table 1). Routine blood chemistry before and 22 h after pericardiocentesis revealed changes compatible with improved renal blood flow and loss of extracellular fluid (Table 2).

The ANH concentrations in plasma prior to pericardiocentesis (21.6 ± 7.3 pmol/l) were within the reference range (Table 2). Pericardial drainage resulted in a sudden and statistically significant rise to 65.4 ± 17.1 pmol/l, followed by a decline within a few hours to the initial values (Fig. 1). After 22 h the ANH concentrations (28.5 ± 4.9 pmol/l) were not significantly different from those obtained before drainage.

The initial plasma AVP concentrations were just above the upper limit of the reference range (Table 2 and Fig. 1). Pericardiocentesis caused a significant decrease in comparison with the first four concentrations measured at t = −60, −30, −15 and 0, leading to an AVP concentration at t = 30 of 2.2 ± 0.8 pmol/l (Fig. 1).

The central venous pressure measured in three dogs decreased sharply after centesis, without significant changes in the arterial systolic pressure (Fig. 2).

Table 1. Volume, osmolality, concentrations of creatinine and sodium and sodium excretion in urine collected before (U_0), 2 h after (U_2) and 22 h after (U_22) pericardiocentesis in dogs with spontaneous pericardial effusion (mean ± SEM).

<table>
<thead>
<tr>
<th></th>
<th>U_0</th>
<th>U_2</th>
<th>U_22</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine (ml·kg^-1·h^-1)</td>
<td>5.0 ± 1.9</td>
<td>1.4 ± 0.4</td>
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<td>8</td>
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<tr>
<td>Osmolality</td>
<td>947 ± 173</td>
<td>599 ± 133</td>
<td>676 ± 126</td>
<td>8</td>
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<tr>
<td>Creatinine (mmol/l)</td>
<td>13.9 ± 3</td>
<td>6.3 ± 2.1</td>
<td>10.6 ± 3.3</td>
<td>8</td>
</tr>
<tr>
<td>Na (mmol/l)</td>
<td>44 ± 24</td>
<td>56 ± 26</td>
<td>92 ± 27</td>
<td>7</td>
</tr>
<tr>
<td>Na (mmol·kg^-1·h^-1)</td>
<td>250 ± 167</td>
<td>135 ± 63</td>
<td></td>
<td>7</td>
</tr>
</tbody>
</table>

*Significantly different from values prior to pericardiocentesis.
Table 2. Blood chemistry values (mean ± SEM) 1 h before and 22 h after pericardiocentesis in eight dogs with spontaneous pericardial effusion.

<table>
<thead>
<tr>
<th>Plasma</th>
<th>t = -1 h</th>
<th>t = 22 h</th>
<th>References</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium (mmol/l)</td>
<td>142 ± 4</td>
<td>147 ± 2</td>
<td>141–149</td>
<td>8</td>
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<tr>
<td>Potassium (mmol/l)</td>
<td>4.7 ± 0.1</td>
<td>3.9 ± 0.1a</td>
<td>3.6–5.0</td>
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<tr>
<td>Urea (mmol/l)</td>
<td>11.1 ± 1.9</td>
<td>5.9 ± 0.8b</td>
<td>3–6.5</td>
<td>8</td>
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<tr>
<td>Creatinin (mmol/l)</td>
<td>123 ± 13</td>
<td>103 ± 11</td>
<td>50 ± 1 (kg^-1 body wt)</td>
<td>8</td>
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<tr>
<td>Total protein (g/l)</td>
<td>52 ± 2</td>
<td>56 ± 2a</td>
<td>54–70</td>
<td>8</td>
</tr>
<tr>
<td>Albumin (g/l)</td>
<td>28 ± 2</td>
<td>29 ± 2</td>
<td>25–34</td>
<td>8</td>
</tr>
<tr>
<td>Osmolality</td>
<td>305 ± 4</td>
<td>307 ± 3</td>
<td>295–320</td>
<td>8</td>
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<tr>
<td>ANH (pmol/l)</td>
<td>16.3 ± 6.2</td>
<td>27.3 ± 5.2</td>
<td>23.7 ± 8.5b</td>
<td>11</td>
</tr>
<tr>
<td>AVP (pmol/l)</td>
<td>6.6 ± 2.2</td>
<td>1.7 ± 0.6</td>
<td>4.1 ± 0.8b</td>
<td>11</td>
</tr>
</tbody>
</table>

*a Significantly different from initial values.

*b Mean ± sd; n = 12 (Ref. 8).

Discussion

In these dogs with pericardial disease there was a state of chronically increased pericardial pressure. In such conditions the rises in pericardial pressure and atrial pressure are directly proportional and very similar in magnitude (9). This leads to impaired ventricular filling and consequently decreased stroke volumes. The latter resulted in physical and laboratory abnormalities compatible with decreased renal blood flow and fluid retention. Pericardiocentesis resulted in rapid restoration of the circulation, reflected in normalization of the central venous pressure and associated with increased diuresis and natriuresis.

Prior to the pericardiocentesis the ANH concentrations in plasma were within the previously published reference range (8) and were in agreement with the values reported by others (10–12). Thus, apparently, the chronically increased pressure on the receptors of the cardiocytes did not cause an increased release of ANH. In contrast, the atrial stretch following pericardiocentesis caused an immediate and sharp rise in circulating ANH concentration, indicating that excitation of stretch (and not pressure) receptors is required for ANH release. The increase in ANH release can explain the observed natriuresis.

Fig. 1. Plasma ANH and AVP concentrations (mean ± SEM) in 11 dogs before and after treatment for pericardial effusion by pericardiocentesis. *Significantly different from values prior to pericardiocentesis.

Fig. 2. Representation of indirectly measured systolic arterial pressure (SAP) readings (○) and central venous pressure (CVP) values measured with a fluid-filled catheter in the cranial caval vein in three dogs with spontaneous pericardial effusion before and following pericardiocentesis (●). The values (mean ± so, N = 3) were measured in mmHg and cmH₂O respectively, and have been converted to kPa.
These observations are in agreement with the findings in a human case of cardiac tamponade (7), in which pericardial decompression also caused a rise in circulating ANH. In an experimental study in dogs, cardiac tamponade was induced by injecting fluid into the pericardial cavity (6). As we observed, increased atrial pressure without concurrent atrial distention did not result in increased ANH release. However, in that experiment, decompression did not cause a measurable increase in ANH levels. The authors postulated that the duration of the cardiac tamponade had not been sufficient for the stretch receptors to become readjusted to the new conditions.

In the dogs described here the initial AVP concentrations in plasma just exceeded previously reported reference values (13). To explain this, the factors influencing vasopressin secretion have to be considered, namely, plasma osmolality and afferent signals arising from sinoaortic (high pressure) and cardiopulmonary (low pressure) baroreceptors (14, 3). Because there was no plasma hypertonicity and certainly no hypernatremia, and we did not measure arterial systolic hypotension, the explanation for the slightly elevated AVP concentrations has to be found elsewhere. In line with experimental work of Lee et al. (3), it is proposed that a stronger AVP rise was prevented by the simultaneous inhibition of vasopressin release by baroreceptors in the left heart, triggered by the cardiac tamponade.

The immediate decline in plasma AVP concentrations might have been caused by the sudden relief of the cardiac tamponade. In addition, the rise in ANH concentration might have played a role, as it has been demonstrated that ANH can inhibit AVP release (15, 3). This decline in AVP might have contributed to the increased diuresis.

The results of this study indicate that:
(i) the primary denominator for ANH release is stretch of the atrial wall and not atrial pressure;
(ii) plasma AVP concentration is moderately elevated in cardiac tamponade;
(iii) pericardiocentesis causes a rapid decline in plasma AVP concentration, which might be partially ANH induced.

References

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