Atrial natriuretic peptide in spontaneous tachycardias

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SUMMARY Because anecdotal reports suggest that concentrations of atrial natriuretic peptide are raised during tachycardias, plasma immunoreactive atrial natriuretic peptide concentrations were measured in 34 consecutive patients when tachycardia was diagnosed and again five and 15 minutes after conversion to sinus rhythm. Plasma atrial natriuretic peptide concentrations were raised in all but four patients, and were higher in patients with known heart disease than in those without. The concentrations were higher with ventricular tachycardia than with atrial fibrillation or supraventricular tachycardia, and in acute versus chronic tachycardia. There was only a weak positive relation between ventricular rate and atrial natriuretic peptide (r = 0·31); but there was a closer inverse correlation between atrial natriuretic peptide and systolic arterial pressure (r = -0·60). Conversion to sinus rhythm was associated with a definite fall in plasma atrial natriuretic peptide concentrations. Despite very high baseline concentrations of atrial natriuretic peptide only two patients reported polyuria. It is likely that atrial pressure rather than ventricular rate determines atrial natriuretic peptide release during tachycardia. Despite the absence of polyuria in all but two patients in this study atrial peptides could still contribute to, or cause, the polyuria of tachycardias.

Atrial natriuretic peptide is produced and stored by atrial myocytes,1–3 and is released into plasma. The major circulating form in man appears to be the 28 amino acid α human atrial natriuretic peptide.2 Animal experiments show that atrial natriuretic peptide secretion is increased by atrial stretch.3 4 Incremental cardiac pacing stimulates atrial natriuretic peptide release in man,5 and provisional reports suggest that atrial natriuretic peptide concentrations are increased during tachycardias.6–9 Exogenous α human atrial natriuretic peptide in high dose has widespread actions in man including hypotension, diuresis, natriuresis, and suppression of certain vasoactive hormones.10 11 Since tachycardias, particularly those of supraventricular origin, are not infrequently associated with a diuresis,6 12 13 there is speculation that the urinary response may be mediated, at least in part, by atrial natriuretic peptide.

To define the relation between atrial natriuretic peptide and arrhythmias we measured plasma immunoreactive atrial natriuretic peptide concentrations in 34 consecutive patients presenting with spontaneous tachycardias.

Patients and methods

We studied 34 consecutive patients (mean (SE) 60 (3), range 29–84 years; 25 men, 9 women) presenting with spontaneous tachycardias which were converted to sinus rhythm. In 24 patients the tachycardia was acute (less than three days' duration, range 0·5 to 24 h) and in 10 it was chronic (more than three days' duration, range 6–100 days). Twenty four had documented cardiac disease (ischaemic heart disease in 18, dilated cardiomyopathy in 4, hypertension in 1, and mitral valve disease in 1).
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Fourteen patients had congestive heart failure before the arrhythmia. The remaining nine patients had no evidence of heart disease. Medication at the time of presentation was frusemide in 13 patients, an angiotensin converting enzyme inhibitor in nine, digoxin in 11, and an antiarrhythmic agent in six. Fifteen patients were not taking medications.

The arrhythmia was atrial fibrillation in 22 patients, re-entrant supraventricular tachycardia in five, and ventricular tachycardia in seven. Conversion to sinus rhythm was effected by direct current cardioversion in 18 patients and by pharmacological cardioversion (intravenous verapamil, lignocaine, or flecainide) in 13 subjects; it was spontaneous in the remaining three. Peripheral venous samples for the measurement of atrial natriuretic peptide were drawn immediately before the termination of the tachycardia and again five and 15 minutes after conversion to sinus rhythm. Blood was taken into chilled tubes containing edetic acid and Trasylol, rapidly centrifuged at +4°C, and the plasma stored at −80°C. Plasma was extracted with SepPak C18 cartridges before radioimmunoassay as described elsewhere.14 The three samples for each patient were analysed in the same assay, but separate assays were used for samples from different patients. The intra-assay coefficient of variation was 10.1% and the inter-assay variability was 13.8%. We measured arterial pressure during the tachycardia with a standard mercury sphygmomanometer with the patient supine in bed.

Grouped data were compared by Student’s t test and relations between indices were assessed by Pearson’s product moment correlation coefficient. All results are given as mean (SEM).

Results

Ventricular rate during the tachycardia ranged from 70 to 220 beats/minute (mean 143 (7) beats/minute). The mean systolic arterial pressure was 116 (52) mm Hg (range 50–170 mm Hg). Plasma atrial natriuretic peptide concentrations before cardioversion were widely scattered between a minimum of 17 pmol/l and a maximum of 525 pmol/l (fig 1). In only four patients were baseline atrial natriuretic peptide concentrations within our normal range of 8–24 pmol/l. After conversion to sinus rhythm mean atrial natriuretic peptide concentrations fell to 116 (17) by five minutes and to 101 (19) pmol/l at 15 minutes (p < 0.01 and p < 0.02 respectively compared with initial concentrations). All but five patients had lower atrial natriuretic peptide concentrations 15 minutes after cardioversion than before. One patient showed a pronounced rise in atrial natriuretic peptide at 15 minutes after an initial decline (fig 1). There were no distinguishing clinical features to explain this anomalous response.

Baseline plasma atrial natriuretic peptide concentrations during tachycardia were higher in the 25 patients with heart disease (170 (28) pmol/l) than in the nine patients without heart disease (59 (21) pmol/l, p < 0.05; fig 2). Those with acute tachycardias had higher concentrations than patients with chronic tachycardias (163 (30) pmol/l and 88 (14) pmol/l respectively); however, the difference was
not statistically significant (fig 2). Ventricular tachycardia was associated with greater increase in atrial natriuretic peptide (332 (58) pmol/l) than atrial fibrillation (85 (11) pmol/l, p < 0·05), or supraventricular tachycardia (120 (39) pmol/l, NS; fig 2). There was a positive, though weak, relation between the baseline ventricular rate and plasma atrial natriuretic peptide concentrations (r = 0·31, NS). However, there was a statistically significant inverse correlation between plasma atrial natriuretic peptide concentrations and systolic arterial pressure before cardioversion (r = 0·60, p < 0·001; fig 3). Only two patients had a diuresis during the tachycardia; neither had cardiac disease or gross increases in plasma atrial natriuretic peptide (48 and 32 pmol/l). One of these patients presented with acute supraventricular tachycardia and the other with acute atrial fibrillation.

Discussion

This study confirms that plasma atrial natriuretic peptide concentrations are often raised in patients with spontaneous tachycardias. Despite the clear association between tachycardia and increased atrial natriuretic peptide concentrations, however, we observed only a weak statistical relation between atrial natriuretic peptide and ventricular rate before cardioversion. It seems unlikely, therefore, that ventricular rate itself is the proximate cause of atrial natriuretic peptide release. More likely, atrial natriuretic peptide release is mediated by associated haemodynamic changes and, in particular, the increase in atrial pressure. This is supported by the inverse correlation between baseline atrial natriuretic peptide concentrations and systolic arterial pressure, the latter being a crude index of haemodynamic derangements during the tachycardia. Further, patients with prior heart disease, many of whom have raised atrial natriuretic peptide concentrations, would be expected to show greater increases in atrial pressure during tachycardia than patients with normal hearts, and indeed we found higher atrial natriuretic peptide concentrations in the patients with previous heart disease. Finally, ventricular tachycardias are likely to result in very high atrial pressures with canon waves, and this group of patients had higher atrial natriuretic peptide concentrations than those with supraventricular tachycardias in whom atrial pressures would probably be lower. The suggestion that atrial pressure or atrial stretch is the stimulus to

![Fig 2](image-url) **Fig 2** Immunoreactive atrial natriuretic peptide (IR–ANP) concentrations in patients presenting with tachycardia. Results are shown for individuals and as mean (SEM). *p < 0·05: AF, atrial fibrillation; SVT, supraventricular tachycardia; VT, ventricular tachycardia.
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Fig 3  Immunoreactive atrial natriuretic peptide (IR-ANP) concentrations and systolic arterial pressure in 33 patients presenting with tachycardia. □, ventricular tachycardia; ○, supraventricular tachycardia; Δ, atrial fibrillation. An additional patient did not have blood pressure recorded. (r = -0.60, p < 0.001.)

atrial natriuretic peptide release during tachycardia is supported by the observations by Weil et al who reported a close positive association between right atrial pressure and plasma atrial natriuretic peptide concentrations during intracardiac pacing in man.21 This is also consistent with animal data indicating that atrial stretch is an important, and perhaps the dominant stimulus, to release of atrial natriuretic peptide.3 4 Although increased cardiac secretion of atrial natriuretic peptide may account in full for the high atrial natriuretic peptide concentrations we found during tachycardia it is possible that clearance of the peptide from plasma is delayed under these circumstances and that this too may contribute to the higher concentrations. This would be especially so when cardiac output falls sharply during the arrhythmia and blood flow to the kidneys and liver, organs where atrial natriuretic peptide is cleared,5 6 is likely to decline precipitously. Little is known about the factors that regulate the clearance of atrial natriuretic peptide from plasma in man.

The half life of atrial natriuretic peptide, as determined from human atrial natriuretic peptide infusion studies in healthy volunteers which used venous sampling, is approximately three minutes.22 In the present study the fall in plasma atrial natriuretic peptide concentrations after cardioversion was slow, with an estimated half life well beyond three minutes. The probable explanation is that atrial pressures do not necessarily return to normal immediately after sinus rhythm is restored.23 In addition, some of our patients had cardiac failure before the onset of tachycardia, and atrial natriuretic peptide concentrations would not be expected to fall into the normal range. Finally, it is possible that the plasma clearance rate of atrial natriuretic peptide is reduced for some time after sinus rhythm is achieved.

There has been speculation that atrial peptides might account for the well-known association of diuresis with tachycardia.6 7 None the less, all but five of our patients had high plasma atrial natriuretic peptide concentrations, yet only two noted polyuria. Further, plasma atrial natriuretic peptide concentrations in these two patients were not grossly increased. Superficially, this might be taken as evidence against a role for atrial peptides in the polyuria of tachycardias. Much more information is needed, however, on the factors which modify the urinary response to atrial natriuretic peptide before firm conclusions can be reached. Already it is known that the arterial pressure,24–26 dietary sodium intake,27 activity of pressor systems,28 and the presence of heart failure29 can modify the renal actions of administered atrial natriuretic peptide. It is possible, therefore, that a minor rise in plasma atrial natriuretic peptide concentrations during tachycardia in a patient whose arterial pressure is maintained will induce an appreciable diuresis. On the contrary, a much higher atrial natriuretic peptide concentration may fail to increase urine output in a patient with cardiac failure in whom ventricular tachycardia has induced profound hypotension.

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