Atrial natriuretic peptide in childhood nephrotic syndrome

Sir,

Atrial natriuretic peptide (ANP) is released in response to extracellular volume expansion and has well-defined effects on sodium and water homeostases. The mechanisms causing sodium and water retention in nephrotic syndrome are not fully clarified. Sodium retention has been traditionally attributed to hypovolaemia [1], but a primary renal disturbance is also suggested [2,3]. Insensitivity to ANP is another hypothesis [4], but the exact role of ANP in the pathophysiology of oedema and sodium retention in nephrotic syndrome is still controversial. We have previously shown that plasma ANP was significantly increased in acute poststreptococcal glomerulonephritis and suggested that despite the sodium retention, increased ANP was compatible with unresponsiveness of the kidneys to ANP [5].

We have evaluated plasma ANP in 12 patients with nephrotic syndrome (three girls and nine boys) plus 11 controls (five girls and six boys) in order to elucidate the possible role of ANP in these nephrotic states. The mean age of the patients and controls were 10.0 and 9.2, respectively. None of the patients had received diuretics in the beginning of the study at the time of sampling and at the time of measurement of total blood volumes.

Group means were compared by Student’s t-test for independent samples. Spearman correlation analysis was used to determine correlation between variables. Results were expressed as mean ± standard deviation (SD). Statistical significance was assigned to values less than 0.05.

Total blood volumes of the patients were found to be slightly reduced (normal ranges: 60–74 ml/kg) (Table 1). Mean plasma ANP in the control group was 16.5 ± 7.4 pg whereas the mean for the nephrotic children was 8.7 ± 8.7 pg/ml (P = 0.031) (Table 1). No significant correlation was found between ANP and age, gender, fractional excretion of sodium (FE\textsubscript{Na}), blood volume or the severity of proteinuria. There was also no significant correlation between proteinuria (evaluated as the protein/creatinine ratio) and FE\textsubscript{Na}. The role of ANP in the pathogenesis of nephrotic syndrome is uncertain. In experimental studies, increased ANP and blunted response to exogenous ANP have been demonstrated [6]. In clinical trials ANP has been found to be elevated, normal or diminished in nephrotic syndrome [3,4,7,8]. In our study, ANP was lower in nephrotic state, suggesting that this might contribute to the sodium and water retention in these patients. However, the mechanism(s) underlying in the pathogenesis of sodium retention and oedema in nephrotic syndrome seems to be different from unresponsiveness to ANP alone.

Vande Walle et al. [3] have recently studied 63 MCNS patients. Measurements were made in 33 children during remission and 30 (nine with incipient proteinuria, 13 nephrotic syndrome patients with hypovolaemic symptoms and eight nephrotic children without hypovolaemic symptoms) during relapse. Mean ANP was found to be slightly lower (albeit statistically nonsignificant) from normal in children with hypovolaemic symptoms. Blood volume measurements did not discriminate patients with or without hypovolaemic symptoms. Thus they proposed that sodium retention in nephrotic children also has a primary renal component. Since we have failed to show correlations of ANP with FE\textsubscript{Na} and blood volumes, we are unable to comment on the pathophysiology of the low values of ANP, other mechanisms might be operative in childhood nephrotic syndrome.

Table 1. Clinical and laboratory data of the patients and the controls

<table>
<thead>
<tr>
<th>Group</th>
<th>Blood pressure (mmHg)</th>
<th>Serum albumin (g/dl)</th>
<th>Urine protein/creatinine ratio</th>
<th>GFR*</th>
<th>Fractional sodium excretion (%)</th>
<th>Blood volume (ml/kg)*</th>
<th>ANP* (pg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Systolic</td>
<td>Diastolic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nephrotic S.</td>
<td>107.9 ± 13.7</td>
<td>71.7 ± 10.3</td>
<td>1.8 ± 0.8*</td>
<td>25.7 ± 13.1</td>
<td>77.5 ± 31.7</td>
<td>0.8 ± 0.6</td>
<td>59.5 ± 13.6</td>
</tr>
<tr>
<td>Controls</td>
<td>100.9 ± 12.2</td>
<td>70.5 ± 9.2</td>
<td>4.1 ± 0.5</td>
<td>25.7 ± 13.1</td>
<td>77.5 ± 31.7</td>
<td>0.8 ± 0.6</td>
<td>59.5 ± 13.6</td>
</tr>
</tbody>
</table>

* Glomerular filtration rate (ml/min/1.73 m\textsuperscript{2}); b Normal ranges = 60–74 ml/kg; c Atrial natriuretic peptide; d Significantly different from the control group (P < 0.001); e Significantly different from the control group (P = 0.031).

2. Brown EA, Markandu ND, Sagnella GA et al. Evidence that some mechanism other than the renin system causes sodium retention in nephrotic syndrome. Lancet 1982; ii: 1237–1241