Glomerular Hemodynamics during Supraventricular Tachycardia

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SUMMARY

Supraventricular tachycardia (SVT) was induced in 7 patients by programmed cardiac stimulation via an esophageal lead. Blood pressure, renal function, and hormonal factors were measured before, during, and after SVT. The glomerular filtration rate increased during SVT, while renal blood flow did not change. The parameters of glomerular hemodynamics were calculated according to the method of Gomez. Glomerular pressure was 64 ± 3 (mean ± SE) mmHg before SVT, and rose significantly (p < 0.01) to 76 ± 5 during SVT. This rise in glomerular pressure was associated with a decrease in afferent vascular resistance (from 3355 ± 610 to 1770 ± 517 dynes sec/cm², p < 0.05) and an increase in efferent vascular resistance (from 3726 ± 758 to 4814 ± 780 dynes sec/cm², p < 0.05). Since atrial natriuretic peptide (ANP) increased during SVT (from 40 ± 15 to 208 ± 72 pg/ml, p < 0.01), these changes in glomerular hemodynamics may be attributed to the physiologic action of ANP. Despite the changes in glomerular hemodynamics during SVT, natriuresis appeared after SVT and not during SVT. This suggests that natriuresis accompanying SVT could not be attributed to the changes in glomerular hemodynamics. (Jpn Heart J 36: 429-437, 1995)

Key words: Supraventricular tachycardia Atrial natriuretic peptide Glomerular hemodynamics Natriuresis

POLYURIA is associated with supraventricular tachycardia (SVT) in about 50% of patients1) and is assumed to be due to reflex-mediated inhibition of the release of arginine vasopressin (AVP) via atrial distention.2,3) The discovery of atrial natriuretic peptide (ANP) and the elevation of its plasma level during SVT suggests that this peptide is also involved in the diuresis and natriuresis associated with SVT.4,5) In addition, ANP has unique vasoactive effects that include...
preglomerular vasodilatation and postglomerular vasoconstriction.\textsuperscript{6,7} These changes in glomerular hemodynamics have been reported only in animal studies. The present study was undertaken to examine whether the induction of SVT in humans modulates the glomerular hemodynamics in the same manner as ANP infusion. For this purpose, we used Gomez's equation,\textsuperscript{8} the principal portion of which was recently justified with several assumptions.\textsuperscript{9} Moreover, we examined whether such changes in glomerular hemodynamics can explain the natriuresis or diuresis associated with SVT.

**Patients and Methods**

SVT was induced in 12 patients by programmed cardiac stimulation through an esophageal lead. In order to minimize the effects of the systemic hemodynamic changes associated with SVT, we excluded 5 patients whose mean blood pressure decreased more than 10\% during SVT. The remaining seven patients (2 men and 5 women aged 22–47 years) were enrolled in this study. Organic heart disease was excluded by chest X-ray, electrocardiography and echocardiography. Serum creatinine levels and urinalysis were normal in all patients, suggesting the absence of renal disease. Electrophysiologic studies showed atrioventricular reentrant tachycardia (\(n = 5\)) or atrioventricular nodal reentrant tachycardia (\(n = 2\)). The examinations used in this study were performed as part of our protocol for selecting appropriate antiarrhythmic therapy to prevent recurrence of the tachycardia. Informed consent to participate in the study was obtained from each patient. None of them took any medications for at least 7 days before the examination. From 21:00 h on the day before investigation, 10\% p-aminohippuric acid (5 ml/h) and 0.9\% saline (95 ml/h) were infused via an antecubital vein. All experiments were started at 9:00 h after an overnight fast, and both water and food were withheld until the end of the study. At 9:00 h, the patients were asked to empty their bladders and then remain in a supine position except during urination. After a 60 min control period, tachycardia was induced by programmed cardiac stimulation and was terminated 60 min later by rapid atrial pacing through an esophageal lead. Blood pressure, heart rate, AVP and ANP levels, and renal function parameters were measured at 30 min intervals from 60 min before tachycardia to 60 min after tachycardia. The parameters of renal function included urine volume, urinary sodium excretion, and the clearance of creatinine and p-aminohippuric acid. Creatinine clearance was used as an indicator of the glomerular filtration rate (GFR), and p-aminohippuric acid clearance was used as an indicator of renal plasma flow (RPF). The renal blood flow (RBF) was determined by the following formula: \(RBF = RPF \left(100/\left(100 - \text{hematocrit}\right)\right)\).
The blood pressure was measured using a mercury sphygmomanometer, and the heart rate was monitored by electrocardiography. A 20 ml blood sample was taken every 30 min through a cannula inserted into an antecubital vein, beginning 30 min before the induction of tachycardia and ending 60 min after its termination. Urine was collected by free voiding at 30 min intervals. The levels of electrolytes, total protein and creatinine were measured by an autoanalyzer, and the p-aminohippuric acid concentration was determined by the method of Smith et al. The plasma levels of ANP, and plasma and urinary levels of AVP were measured by radioimmunoassay methods. Plasma renin activity (PRA) was measured by a commercial radioimmunoassay kit (Dianabo Co, Tokyo) and was expressed on the basis of the generation of angiotensin I. Catecholamine levels were measured by the fluorimetric method.

The parameters of glomerular hemodynamics were calculated using the following equations devised by Gomez:

1. Total renal resistance: \( R = (P_m - P_v) \times 1328/RBF \)
2. Mean glomerular pressure: \( P_G = h + H + GFR/\lambda \)
3. Afferent resistance: \( R_A = (P_m - P_G) \times 1328/RBF \)
4. Efferent resistance: \( R_E = GFR \times 1328/\lambda(RBF - GFR) \)

In these equations: the unit of resistance is dynes \( \times \) sec/cm\(^5\), that of pressure mm Hg and those of RBF and GFR ml/sec corrected to 1.73 m\(^2\) body surface area. The other abbreviations are as follows: \( P_m \) = mean arterial pressure, \( P_v \) = renal venous pressure, \( h \) = mean onotic pressure, \( H \) = interstitial pressure, and \( \lambda \) = a permeability coefficient.

For the application of these equations, we assumed that the permeability coefficient is 0.0812. Kimura et al showed its use gave reliable values for parameters of glomerular hemodynamics in hypertensive patients with normal renal function. In addition, it was assumed that the interstitial pressure and the renal venous pressure (Pv) were equal to 10 mmHg and did not change throughout the study. The mean onotic pressure, h, was calculated from the mean plasma protein concentration, \( C_m \), in the glomerular capillaries, which in turn was calculated from \( C_A \), the concentration in the afferent plasma and filtration fraction (FF): \( h = 5(C_m - 2) \), in which \( C_m = C_A/FF \ln(1/1-FF) \).

For evaluating the changes associated with SVT, the means of two values were calculated for the parameters before and during SVT. Since the urine volume after the termination of SVT demonstrated conflicting values between the initial and subsequent 30 min period, the parameters obtained after SVT were reported separately for the initial and later periods. The mean of two values before SVT was assigned to the control value and the results were analyzed by one-way ANOVA for overall significance. The difference from the control value was evaluated using Fisher’s PLSD test. \( p < 0.05 \) was considered to be statistically significant.
significant. Data are presented as mean ± standard error.

**RESULTS**

**Changes in heart rate, blood pressure, serum total protein, hematocrit, and hormonal factors during SVT (Table I):** Heart rate increased from 67 ± 3 beats/min to 162 ± 4 due to SVT induction. There were no significant changes in blood pressure throughout the protocol. Although both serum total protein and hematocrit were apt to increase during SVT, these changes were insignificant. Urinary AVP excretion decreased during SVT and increased in the 30–60 min period after SVT. Plasma levels of AVP did not change during SVT and

**Table I. Changes in Heart Rate, Blood Pressure, Serum Total Protein, Hematocrit, and Hormonal Factors during SVT**

<table>
<thead>
<tr>
<th></th>
<th>before SVT</th>
<th>during SVT</th>
<th>0–30 min after SVT</th>
<th>30–60 min after SVT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate, beats/min</td>
<td>67 ± 3</td>
<td>162 ± 4**</td>
<td>82 ± 3</td>
<td>80 ± 3</td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>122 ± 4</td>
<td>113 ± 7</td>
<td>117 ± 3</td>
<td>114 ± 4</td>
</tr>
<tr>
<td>MBP, mmHg</td>
<td>92 ± 3</td>
<td>92 ± 3</td>
<td>90 ± 3</td>
<td>88 ± 4</td>
</tr>
<tr>
<td>DBP, mmHg</td>
<td>76 ± 4</td>
<td>80 ± 4</td>
<td>77 ± 3</td>
<td>75 ± 4</td>
</tr>
<tr>
<td>TP, g/l</td>
<td>67.4 ± 1.2</td>
<td>68.7 ± 1.0</td>
<td>67.4 ± 0.8</td>
<td>66.0 ± 1.3</td>
</tr>
<tr>
<td>Hematocrit, %</td>
<td>38.1 ± 1.0</td>
<td>38.9 ± 0.9</td>
<td>37.9 ± 1.1</td>
<td>37.7 ± 1.1</td>
</tr>
<tr>
<td>PRA, ng/ml/h</td>
<td>1.62 ± .55</td>
<td>2.02 ± .91</td>
<td>1.37 ± .49</td>
<td>1.32 ± .38</td>
</tr>
<tr>
<td>Norepinephrine, pg/ml</td>
<td>291 ± 47</td>
<td>355 ± 74</td>
<td>324 ± 62</td>
<td>322 ± 65</td>
</tr>
<tr>
<td>Epinephrine, pg/ml</td>
<td>26.9 ± 9</td>
<td>33 ± 11</td>
<td>28 ± 7</td>
<td>27 ± 7</td>
</tr>
<tr>
<td>p-AVP, pg/ml</td>
<td>2.8 ± .7</td>
<td>2.7 ± .7</td>
<td>4.0 ± 1.1*</td>
<td>3.5 ± 1.1</td>
</tr>
<tr>
<td>u-AVP, pg/min</td>
<td>42 ± 14</td>
<td>18 ± 6*</td>
<td>74 ± 18</td>
<td>112 ± 44**</td>
</tr>
<tr>
<td>ANP, pg/ml</td>
<td>40 ± 15</td>
<td>208** ± 72</td>
<td>107 ± 30</td>
<td>65 ± 23</td>
</tr>
</tbody>
</table>

ANP = atrial natriuretic peptide; DBP = diastolic blood pressure; MBP = mean blood pressure; p-AVP = plasma levels of arginine vasopressin; PRA = plasma renin activity; SBP = systolic blood pressure; TP = serum total protein; u-AVP = urinary excretion of arginine vasopressin, *p < 0.05, **p < 0.01 (vs. before).

**Table II. Changes in Renal Function during Supraventricular Tachycardia (SVT)**

<table>
<thead>
<tr>
<th></th>
<th>before SVT</th>
<th>during SVT</th>
<th>0–30 min after SVT</th>
<th>30–60 min after SVT</th>
</tr>
</thead>
<tbody>
<tr>
<td>UV, ml/min</td>
<td>1.84 ± .38</td>
<td>4.44* ± .65</td>
<td>4.14* ± .87</td>
<td>1.36 ± .16</td>
</tr>
<tr>
<td>UNaV, mEq/min</td>
<td>220 ± 29</td>
<td>289 ± 65</td>
<td>378* ± .66</td>
<td>259 ± 44</td>
</tr>
<tr>
<td>RBF, ml/min/1.73 m²</td>
<td>692 ± 76</td>
<td>744 ± 87</td>
<td>746 ± 73</td>
<td>734 ± 98</td>
</tr>
<tr>
<td>GFR, ml/min/1.73 m²</td>
<td>126 ± 14</td>
<td>170* ± 23</td>
<td>131 ± 14</td>
<td>112 ± 12</td>
</tr>
<tr>
<td>FF</td>
<td>.30 ± .04</td>
<td>.39* ± .04</td>
<td>.28 ± .02</td>
<td>.26 ± .03</td>
</tr>
<tr>
<td>FE Na, %</td>
<td>1.40 ± .14</td>
<td>1.31 ± .25</td>
<td>2.08* ± .31</td>
<td>2.07* ± .29</td>
</tr>
<tr>
<td>R, dynes sec/cm²</td>
<td>5994 ± 1006</td>
<td>9292 ± 825</td>
<td>9123 ± 947</td>
<td>8323 ± 1396</td>
</tr>
</tbody>
</table>

FE Na = fractional excretion of sodium; FF = filtration fraction; GFR = glomerular filtration rate; R = renal vascular resistance; RBF = renal blood flow; UV = urine volume, UNaV = urinary sodium excretion, *p < 0.05, (vs. before).
Changes in glomerular pressure (P_G) (upper panel) and the afferent (R_A) and efferent (R_E) renal vascular resistance (lower panel) during supraventricular tachycardia (SVT). P_G increased during SVT, along with a significant decrease in R_A and a significant increase in R_E. a p<0.05, b p<0.01 (vs. before).

Figure. Changes in glomerular pressure (P_G) (upper panel) and the afferent (R_A) and efferent (R_E) renal vascular resistance (lower panel) during supraventricular tachycardia (SVT). P_G increased during SVT, along with a significant decrease in R_A and a significant increase in R_E. a p<0.05, b p<0.01 (vs. before).

increased after SVT. There were insignificant changes in plasma levels of norepinephrine and epinephrine. Plasma levels of ANP increased during SVT and returned to the control levels after SVT.

**Changes in renal function during SVT (Table II):** Urine volume increased during SVT as well as after SVT, while urinary sodium excretion increased only after SVT. The fractional excretion of sodium did not change during SVT and increased after SVT. Although RBF and R did not change significantly, GFR and FF increased during SVT.

**Changes in glomerular hemodynamics (Figure):** The P_G was 64 ± 3 mmHg before SVT, increased to 76 ± 5 mmHg during SVT and then decreased to 60 ± 2 after SVT. R_A was 3355 ± 610 dynes × sec/cm^5 before SVT. It decreased to 1770 ± 517 dynes × sec/cm^5 during SVT and then returned to the control level after SVT. R_E increased from 3726 ± 758 to 4814 ± 780 dynes × sec/cm^5
with the induction of SVT, and then returned to the control level after SVT.

**Discussion**

Our previous report\(^1\) showed that SVT was accompanied by hypotension in half the patients. Patients in whom SVT was accompanied by hypotension had greater heart rates than patients without hypotension.\(^1\) The greater heart rate seemed to lead to hypotension through inadequate diastolic ventricular filling. The patients with hypotension showed appreciable increases in PRA and catecholamines as compensatory mechanisms to the hypotension. The enrollment of only patients without hypotension made it possible to exclude the effects of these vasoactive substances on glomerular hemodynamics. Previous reports\(^4,5\) have already shown a marked rise in plasma levels of ANP and an increase in GFR after the induction of SVT. In the present study, glomerular hemodynamics were assessed using the equations devised by Gomez.\(^6\) We found a decrease in \(R_A\) and an increase in \(R_E\) during SVT, changes which were associated with a rise in \(P_G\). These findings are consistent with those seen following ANP infusion in animal experiments using an intravital videoscope and the micropuncture technique.\(^6,7\) Brenner et al\(^6\) found the decrease in preglomerular resistance along with the increase in postglomerular resistance in a micropuncture study using the Münch-Wistar rat. Further, Marin-Grez et al\(^7\) used intravital microscopy to demonstrate that ANP causes postglomerular vasoconstriction accompanied by preglomerular vasodilatation, thereby leading to an increase in glomerular pressure. Thus, the changes in glomerular hemodynamics during SVT can be attributed to the action of ANP released during the episode of tachycardia.

Various vasoactive substances other than ANP affect glomerular hemodynamics. For instance, angiotensin II\(^4\) and norepinephrine\(^5\) increase both \(R_A\) and \(R_E\). Because PRA and plasma levels of norepinephrine did not change significantly during SVT, the effects of these vasoactive substances will be eliminated in our study. We have previously reported significant increases in PRA and catecholamines\(^16\) which were attributed to the hypotension occurring during SVT. In the present study, we excluded those patients in whom SVT was accompanied by hypotension, so that insignificant changes in these vasoactive factors ensued. Ichikawa et al\(^17\) reported that the infusion of \(d(CH_2)_5 VdAVP\), a specific antagonist of the pressor effects of AVP, increased the glomerular ultrafiltration coefficient, \(K_f\), values but had no effects on \(R_A\) and \(R_E\). This finding excluded the possibility that the decrease in AVP during SVT affected \(R_A\) and \(R_E\).

Our results were derived from Gomez’s equations with several assumptions. The principal assumptions were that the permeability coefficient of the glomerulus, \(\lambda\), remained constant and that \(P_v\) was not altered by SVT. Since serial data
were obtained from the same subject, the inter-individual differences in $\lambda$ among subjects can be ignored. Although an in vitro study has suggested that ANP increases $\lambda$ \cite{18}, this was not supported by other work.\cite{6} Angiotensin II, the most important vasoactive substance which decreases $\lambda$, did not seem to affect glomerular hemodynamics because the PRA showed no significant changes during SVT. Since AVP has the ability to decrease $\lambda$,\cite{17} the increase in GFR during SVT may be caused by the suppression in AVP. However, the actual decrease in AVP release was too small to be reflected in plasma levels of AVP. The effect of AVP in reducing $\lambda$ is mediated through V1a (vascular subtype) receptors on glomerular mesangial cells.\cite{19} Since much higher levels of AVP were required to activate the vascular receptor than to affect the V2 (tubular subtype) receptor,\cite{20} the glomerular actions of AVP seem to be trivial as inferred from the small changes in plasma levels of AVP.

$P_v$ is altered in conjunction with right atrial pressure during SVT. Tsai et al\cite{5} examined the hemodynamic changes during SVT and found a rise of 3 mmHg in right atrial pressure. Even if this were taken into consideration, it would not give different results. The $P_G$ would rise concomitantly with the interstitial pressure, $H$ (see equation (2) in Methods), driven by the increase in $P_v$. When applying Gomez’s equations, the rise in $P_G$ would lead to a greater decrease in $R_A$ and an increase in $R_E$. Thus, the glomerular hemodynamic results will be preserved, even if $P_v$ were taken into account.

SVT was associated with natriuresis and diuresis, which have been attributed to the release of ANP and/or the reflex suppression of AVP through the rise in atrial pressure during tachycardia.\cite{2,3} Natriuresis due to ANP has been repeatedly confirmed, and two renal mechanisms for this natriuresis have been proposed by animal experiments. One is the increase in GFR\cite{21} and the other is the inhibition of sodium reabsorption at the inner medullary collecting duct.\cite{22} Despite the significant increase in the plasma ANP level, urinary sodium excretion did not increase during SVT, whereas glomerular hemodynamics showed changes attributable to ANP. These findings indicate that the natriuretic effect of ANP can be dissociated from its effect on glomerular hemodynamics. The mechanism of the natriuresis induced by ANP must be related to factors other than changes in glomerular hemodynamics. The increase in natriuresis and fractional excretion of sodium after SVT can be attributed to a delayed action of ANP on the inner medullary collecting duct\cite{22} or a rise in prostaglandin E2 after termination of SVT.\cite{16} The lack of natriuresis during SVT means that the tubular action of ANP needs a longer time for its manifestation than does the glomerular action. The natriuresis after SVT might also be explained by renal prostaglandin E2 which was stimulated by increased AVP after termination of SVT.\cite{16}

The occurrence of polyuria without natriuresis during SVT has been ex-
plained by the reflex suppression of AVP release. The decrease in urinary excretion of AVP supports this assumption. Since higher levels of AVP are required for the glomerular action than for the tubular action, the small decreases in AVP levels will induce diuresis unaccompanied by the glomerular action. Alternatively, polyuria may be explained by ANP antagonizing the hydro-osmotic action of AVP in the collecting duct. The inability to detect the fall in plasma levels of AVP may be related to the inadequate sensitivity of AVP measurement.

In conclusion, SVT led to a rise in glomerular pressure, associated with a decrease in afferent vascular resistance and an increase in efferent vascular resistance. Since ANP increased during SVT, these changes in glomerular hemodynamics may be attributed to the physiologic action of ANP. Despite the changes in glomerular hemodynamics during SVT, natriuresis appeared after SVT and not during SVT. This suggests that natriuresis accompanying SVT could not be attributed to changes in glomerular hemodynamics.

REFERENCES


