Effect of Hospitalization on Urinary Catecholamine Excretion in Patients with Hand-Arm Vibration Syndrome

Mieko IWAMOTO1, Akira NAGAI2, Seiichiro TAKAHASHI1 and Noriaki HARADA1

1Department of Hygiene, Yamaguchi University School of Medicine and
2Nagai Clinic, Setoda, Hiroshima

Abstract: Effect of Hospitalization on Urinary Catecholamine Excretion in Patients with Hand-Arm Vibration Syndrome: Mieko IWAMOTO, et al. Department of Hygiene, Yamaguchi University School of Medicine—The purpose of this study was to investigate the effect of hospitalization for five weeks on the autonomic nervous activity of patients with hand-arm vibration syndrome (HAVS). Urine samples were collected from ten patients with HAVS before, during, and after hospitalization. Amounts of urinary free catecholamines (norepinephrine, epinephrine and dopamine) were measured. Urinary excretion of norepinephrine and dopamine during hospitalization was significantly lower than that before hospitalization. The effect of hospitalization continued for 10 days after hospitalization. The results of this study suggest that hospitalization is useful for the treatment of patients with HAVS to reduce the sympathetic hyperactivity. (J Occup Health 2001; 43: 70–74)

Key words: Hand-arm vibration syndrome, Sympathetic nervous activity, Urinary catecholamine

We have investigated the autonomic nervous function in patients with hand-arm vibration syndrome (HAVS) using blood chemical analysis and electrophysiological methods. Vibration-induced white finger (VWF) is the most characteristic symptom in HAVS. With regard to the pathogenesis of VWF, a local mechanism has been proposed, since VWF mainly appears on the skin of the fingers and hands directly exposed to vibration. It only rarely reaches the lower arms exposed to transmitted vibration in severe cases, therefore the role of the local mechanism is assumed to be large.

On the other hand, VWF is normally provoked by cold when the whole body is exposed to cold. Occasionally, a rapid change of atmospheric temperature provokes an attack of VWF. When exposed to whole body cooling, patients with VWF showed a significantly greater increase in plasma norepinephrine than age-matched healthy controls. These facts indicate that the sympathetic nervous system has a role in evoking VWF. Using responses of plasma norepinephrine and cyclic nucleotides to whole body cooling, we observed the differences in the autonomic function between patients with VWF and healthy controls1–3. It has been also pointed out that patients with VWF have higher complaint rates of subjective symptoms not localized in the upper limbs3. The aim of this study was to evaluate the effect of hospitalization on the sympathetic nervous activity in patients with HAVS.

Subjects and Methods

Ten patients with HAVS volunteered for this study and gave written informed consent. All patients were male with a mean age of 64.7 yr (SD 6.4, range 55 to 70 yr). Three of them had experienced attacks of VWF and seven had not. They had used vibratory tools such as grinders, rivet guns and hammers in a shipyard. Their average duration of operation of vibratory tools was 28.4 yr (SD 11.4, range 11 to 40 yr), and their mean exposure time (SD) was 22,720 h (10,728). Their average length (SD) of medical treatment for HAVS was 4.8 yr (2.8). The patients with VWF and those without VWF didn’t differ in age, duration of operation of vibratory tools (yr), exposure time (h) and duration of medical treatment (yr). Five patients had hypertension and two had diabetes mellitus. All patients had stopped being exposed to vibration and were under treatment for HAVS. The patients were hospitalized for five weeks. The patients were treated by the same treatment before, during, and after hospitalization except for during hospitalization when the patients received an intravenous drip of 20 µg of prostaglandin E1 (PGE1) in 500 ml 5% glucose solution (one drip per three d). Urine samples were collected three times.
times before, eight times during and three times after hospitalization. Urine volume was measured from the urine samples collected. Twenty milliliters of urine were transferred immediately into glass scintillation vials containing 150 µl of both 10% EDTA and 4% thioglycolic acid solutions which were stored at -70°C until analysis.

Urinary free catecholamines (norepinephrine, epinephrine and dopamine) were measured using high performance liquid chromatography with electrochemical detection. Urinary catecholamine levels are expressed in micrograms per day (µg/d) and in nanograms per milligram of creatinine (ng/mg creatinine). Urinary creatinine was measured by spectrophotometric technique according to the Folin-Wu method.

The statistical tests used were paired t-test and Pearson’s correlation coefficient test. The significance level was considered at p<0.05.

Results

Table 1 shows the inside and outside temperatures of patients homes and the hospital. The temperature inside the hospital was higher than that inside the patients homes. The walking steps of the patients per day at home tended to be larger than that at the hospital as shown in Table 2.

Figure 1 shows the average values for 24 h urinary catecholamines excretion before, during, and after hospitalization. The three measurements made before, and after hospitalization are denoted by A and E, respectively. During hospitalization, B, C and D represent the first three, middle two, and last three measurements of catecholamines, respectively. Urinary excretion of norepinephrine and dopamine during (B, C and D) hospitalization for five weeks was significantly lower than that before (A) hospitalization. The effect of hospitalization continued for about 10 d after (E) hospitalization. The excretion of epinephrine didn’t

<table>
<thead>
<tr>
<th>Table 1. Inside and outside temperatures (°C) at the patients homes and the hospital</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inside</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Patients homes</td>
</tr>
<tr>
<td>Hospital</td>
</tr>
</tbody>
</table>

*: Data are given as mean (range); #: Data are from single measurements.

<table>
<thead>
<tr>
<th>Table 2. Daily walking steps of the patients at home and the hospital</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steps per d (range)</td>
</tr>
<tr>
<td>Home</td>
</tr>
<tr>
<td>Hospital</td>
</tr>
</tbody>
</table>

Fig. 1. Comparison of urinary catecholamine concentration of the patients with hand-arm vibration syndrome before, during, and after hospitalization. NE, norepinephrine; EP, epinephrine; DA, dopamine; A, three measurements before hospitalization; B, first three measurements during hospitalization; C, middle two measurements during hospitalization; D, last three measurements during hospitalization; E, three measurements after hospitalization; *: p<0.05; **: p<0.01 compared with A (paired t-test). Data are average values for 24 h urinary catecholamine excretion.
change during and after hospitalization.

Figure 2 shows the correlations among daily excretion of catecholamines. A significant positive correlation was found only between daily urinary norepinephrine and dopamine levels (\(y=3.8x + 47.6, r=0.66, p<0.001\)).

Table 3 shows the ratios of urinary catecholamines and creatinine. The ratios of urinary norepinephrine and creatinine during (C and D) and after (E) hospitalization were significantly lower than that before (A) hospitalization (\(p<0.05\)). The ratio of urinary dopamine and creatinine during (D) hospitalization was significantly lower than that before (A) hospitalization (\(p<0.05\)). The ratio of urinary epinephrine and creatinine didn’t change significantly during and after hospitalization.

Discussion

It has been suggested that exposure to hand-arm vibration might affect the autonomic nervous function and it has been demonstrated on the basis of subjective symptoms complained of by patients with HAVS with higher prevalence rates than healthy controls\(^6\). When exposed to whole body cooling, patients with HAVS showed a significantly greater increase in plasma norepinephrine than age-matched healthy controls. The excess secretion of norepinephrine in blood reveals that the responsiveness of the sympathetic nervous system to cold exposure is enhanced in patients with HAVS.

Saito \textit{et al.}\(^7\) reported that the plasma norepinephrine and epinephrine concentrations tended to decrease in female patients with vibration syndrome after hospital treatment. They also reported that urinary norepinephrine and epinephrine showed no significant decrease, but that urinary dopamine decreased significantly in the patients after treatment. Takata \textit{et al.}\(^8\) didn’t observe any change in sympathetic activity during the early phase of hospitalization of patients with essential hypertension, but observed a hypotensive effect after 7 d of hospitalization.

Plasma norepinephrine is mainly released from the sympathetic nerve endings. Epinephrine is secreted primarily by the adrenal medulla and the control of its release is not the same as the control for norepinephrine release\(^9\). Norepinephrine and dopamine are sensitive sympathetic indexes\(^10,11\) and epinephrine is an emotional stress index\(^12\). The amount of urinary norepinephrine and dopamine is expected to be an accumulated indicator of sympathetic nervous activity. In the present study, daily urinary excretion of norepinephrine and dopamine during hospitalization was significantly lower than that before hospitalization, and the effect continued after discharge. The ratios of urinary catecholamines and creatinine during hospitalization were also lower than

---

**Table 3.** Ratios of urinary catecholamines to creatinine before, during, and after hospitalization

<table>
<thead>
<tr>
<th>Hospitalization</th>
<th>NE/Cr (ng/mg)</th>
<th>EP/Cr (ng/mg)</th>
<th>DA/Cr (ng/mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before (A)</td>
<td>66.2 ± 14.8</td>
<td>16.6 ± 4.1</td>
<td>335.7 ± 103.0</td>
</tr>
<tr>
<td>During (B)</td>
<td>40.1 ± 5.9</td>
<td>17.8 ± 4.3</td>
<td>203.6 ± 34.1</td>
</tr>
<tr>
<td>(C)</td>
<td>32.0 ± 5.4*</td>
<td>13.3 ± 2.7</td>
<td>183.0 ± 32.7</td>
</tr>
<tr>
<td>(D)</td>
<td>26.8 ± 2.8*</td>
<td>12.9 ± 3.0</td>
<td>171.9 ± 44.9*</td>
</tr>
<tr>
<td>After (E)</td>
<td>40.7 ± 6.5*</td>
<td>14.5 ± 4.3</td>
<td>165.6 ± 24.1</td>
</tr>
</tbody>
</table>

Data are given as mean ± SE. *: \(p<0.05\) compared with A (paired t-test). Cr, creatinine; other abbreviations as in Fig. 1.
those before hospitalization. When correlation analyses were done using all measurements of urinary catecholamines, the correlation between norepinephrine and dopamine was positively significant; however, epinephrine was not correlated significantly with norepinephrine or dopamine. The effect of hospitalization on epinephrine excretion was different from norepinephrine, and dopamine. The effect of hospitalization was not different between patients with and without VWF. In this study, hospital room temperature was moderately higher than outdoor atmospheric temperature as well as the temperature inside the patients' homes, and hospitalized patients were not so physically active. We assume that these conditions might effect the results of this study, however, other reasons could also be considered.

The patients in the present study received intravenous infusions of PGE, during hospitalization. PGE, acts on vasodilatation and inhibition of platelet aggregation11. The clinical usefulness of prostaglandin derivatives was reviewed for the treatment of peripheral vascular disease such as arteriosclerosis obliterans, Buerger’s disease, Raynaud’s disease, and collagen disease etc. Some reports14–17 have indicated that PGE, may affect the functional state of contraction of vascular tissue relaxing the smooth muscle cells and inhibiting the sympathetic neuromuscular transmission. On the other hand, Okuda et al.28 did not observe significant differences in respect to catecholamines, stress hormones, lactate level and blood sugar between a group who received PGE, and a group not receiving PGE, during elective prolonged surgery over 12 h.

The results of the present study suggest that decreases in urinary norepinephrine and dopamine during hospitalization are due to higher room temperature, lighter physical activity and intravenous infusion of PGE,.

We assume that urinary excretion of norepinephrine during and after hospitalization might be lower than that of before hospitalization in healthy persons or other patients. Harada et al. reported that the patients with HAVS indicated a high level of urinary norepinephrine at rest compared with healthy controls, and the patients had a larger percent increase in plasma norepinephrine than healthy controls exposed to different stressors19–21. Therefore, it is presumed that the decrease in norepinephrine in patients with HAVS might be larger than in healthy persons in the case of hospitalization. The decrease in norepinephrine during hospitalization is related to the withdrawal of sympathetic activity20.

There is no drastic medical treatment for patients with HAVS at the present time. Therefore, higher room temperature, light physical activity, and PGE, infusion during hospitalization are useful for treating of patients with HAVS to reduce sympathetic hyperactivity.

References

16) Messina EJ, Weiner R, Kaley G. Inhibition of bradykinin vasodilation and potentiation of norepinephrine and angiotensin vasoconstriction by

Mieko Inawasoro, et al.: Hospitalization and Urinary Catecholamine Excretion


