Influence of Vasopressin Level on Osmotic Pressure and Sodium Concentration in Plasma and Cerebrospinal Fluid in Patients with Intracranial Lesions

Masaki MIURA, Shuichi TAKAGI, Yasuhiko MATSUKADO and Yukitaka USHIO

Department of Neurosurgery, Kumamoto University School of Medicine, Kumamoto

Abstract

To study the influence of the vasopressin level on osmotic pressure and sodium concentration in plasma and cerebrospinal fluid (CSF), plasma and CSF were sampled simultaneously in 27 patients with central nervous system lesions. A significant elevation of arginine vasopressin (AVP) levels in plasma and CSF and a significant increase in the osmotic pressure gradients of plasma and CSF were observed in hyponatremic patients. The significant increases in the osmotic pressure gradients may be attributable to hemodilution and CSF concentration resulting from the elevated AVP level, because the sodium concentration gradients of plasma and CSF did not significantly increase. The elevated AVP levels in plasma and CSF and the increased osmotic pressure gradients of plasma and CSF normalized in parallel with improvement of consciousness. These findings suggest that the increased osmotic pressure gradients of plasma and CSF, derived from increased AVP secretion into blood and CSF, exacerbates brain edema induced by the primary lesion and may contribute to the clinical deterioration of some patients with intracranial lesions.

Key words: vasopressin, osmotic pressure, sodium, plasma, cerebrospinal fluid

Introduction

Anesthesia9,10 and surgical stress11,12,19 stimulate arginine vasopressin (AVP) secretion from magnocellular neuroendocrine cells in the paraventricular and supraoptic nuclei, as do changes in plasma osmotic pressure and circulatory blood volume. There have been reports of increased AVP secretion during intracranial hypertension7,23 and of elevated plasma AVP levels in patients with stroke14 and subarachnoid hemorrhage (SAH).17,18 Vorherr et al.27 found that bleeding stimulated the release of AVP directly into the cerebrospinal fluid (CSF) and bloodstream. Dogterom et al.5 suggested that AVP detected in CSF might be released directly into the ventricular system after synthesis by the hypothalamic nuclei.

As the role of AVP in CSF remains unclear, we examined the AVP level, osmotic pressure, and sodium concentration in plasma and CSF of patients with central nervous system (CNS) lesions to better understand the influence of vasopressin on osmotic pressure and sodium concentration in plasma and CSF.

Materials and Methods

The study population consisted of 27 consecutively admitted patients with CNS lesions, including supratentorial tumors (2), infratentorial tumors (8), hydrocephalus (7), cerebrovascular disease (4), cervical spondylosis (3), meningitis (1), normal pressure hydrocephalus (1), and cerebral atrophy (1). Plasma and CSF samples were taken at least once, simultaneously, from each patient (30 samples in all) and AVP level, osmotic pressure, and sodium concentration were assayed. Osmotic pressure and sodium concentration in plasma and CSF were measured immediately after sampling. To determine AVP levels in plasma, the samples were placed in tubes containing chilled ethylenediaminetetra-acetic acid and separated immediately. Plasma and CSF were stored at -70°C until radioimmunoassay (RIA) with the Immuno Nuclear Vasopressin RIA Kit (Im-
munonuclear Corp., Stillwater, Minnesota). In patients with supra- and infratentorial tumors, ventricular CSF was obtained at surgery. In those with hydrocephalus, CSF was sampled during ventriculoperitoneal shunting procedures. In the remaining cases, CSF was obtained by lumbar puncture.

On the basis of AVP levels in plasma and CSF of normal controls, the upper limit of AVP in plasma and CSF was set at 10 pg/ml. The samples were first classified as either normonatremic or hyponatremic. The normonatremic samples were subdivided as follows: normal AVP levels in plasma and CSF (Group A), elevated AVP level in plasma only (Group B), elevated AVP level in CSF only (Group C), and elevated AVP levels in plasma and CSF (Group D). Group E was comprised of hyponatremic samples. Then, the effect of the AVP level on the osmotic pressure and sodium concentration gradients of plasma and CSF was examined.

The gradients were calculated by subtracting the plasma level from the CSF level. For statistical analysis we used Student’s t-test; p < 0.05 was considered significant.

### Results

Table 1 shows the CSF and plasma AVP levels in normonatremic and hyponatremic samples. The AVP levels of the latter were significantly elevated compared to those of Group A (normonatremic; normal CSF and plasma AVP levels).

Comparison of the osmotic pressure gradients of plasma and CSF of normonatremic and hyponatremic samples revealed no significant differences among the four normonatremic groups. On the other hand, there was a significant difference between Groups E (hyponatremic) and A (Table 2).

### Table 1 AVP levels in plasma and CSF of normonatremic and hyponatremic samples

<table>
<thead>
<tr>
<th>Group</th>
<th>AVP (pg/ml)</th>
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<tbody>
<tr>
<td></td>
<td>Plasma</td>
<td>CSF</td>
<td></td>
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<tr>
<td>Normonatremic:</td>
<td></td>
<td></td>
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<tr>
<td>A (n = 5)</td>
<td>5.38± 3.06</td>
<td>3.42± 2.75</td>
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<tr>
<td>B (n = 4)</td>
<td>32.08±18.24*</td>
<td>4.44± 2.09</td>
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</tr>
<tr>
<td>C (n = 5)</td>
<td>6.01± 2.83</td>
<td>30.22±13.39**</td>
<td></td>
</tr>
<tr>
<td>D (n = 8)</td>
<td>19.41±10.24**</td>
<td>17.30± 9.84**</td>
<td></td>
</tr>
<tr>
<td>Hyponatremic:</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>E (n = 8)</td>
<td>15.96±10.95*</td>
<td>11.56± 8.82*</td>
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</tbody>
</table>

*p<0.05, **p<0.01 vs. Group A. Values are means ± SD.

As shown in Table 3, there was no significant difference in the sodium concentration gradients of plasma and CSF among any of the groups.

Four of the 27 patients manifested disturbance of consciousness. One patient had a cerebellar metastatic tumor, another had a giant pituitary adenoma, and two had had SAH from an anterior communicating artery aneurysm. Three of these patients showed mild hyponatremia (124, 128, and 134 mEq/l). The osmotic pressure and sodium concentration gradients of plasma and CSF tended to increase as CSF and plasma AVP levels rose (Fig. 1).

Figure 2 shows the transitional changes observed in the AVP level, osmotic pressure, and sodium concentration in plasma and CSF in one of the patients with SAH. This patient’s improvement in consciousness was accompanied by normalization of the CSF and plasma AVP levels and by a decrease in the osmotic pressure and sodium concentration gradients of plasma and CSF.
Fig. 1  AVP level, osmotic pressure, and sodium concentration in plasma (○) and CSF (●) of four patients with impaired consciousness. The osmotic pressure and sodium concentration gradients of plasma and CSF tended to increase as AVP levels in plasma and CSF rose. Case 1: cerebellar metastatic tumor, Case 2: giant pituitary adenoma, Cases 3 and 4: SAH due to rupture of an anterior communicating artery aneurysm.

Fig. 2  Changes in the AVP level, osmotic pressure, and sodium concentration in plasma (○) and CSF (●) of a patient with SAH. This patient's AVP levels in plasma and CSF and the osmotic pressure and sodium concentration gradients of plasma and CSF normalized as the consciousness disturbance improved. The abscissa indicates the number of days from onset of SAH. Consciousness was assessed by the Japan Coma Scale.211

Discussion

Elevated plasma AVP levels have been reported in association with intracranial hypertension,7,23 stroke,14 and SAH.17,18 In patients with intracranial tumors, hydrocephalus, and intracranial hemorrhage, Sorensen et al.25 noted a significant relationship between intracranial pressure and the CSF, but not the plasma, vasopressin concentration. These investigators suggested that an increase in intracranial pressure may stimulate the central release of vasopressin. In our study, the AVP level in plasma and/or CSF was elevated in 23 of 27 samples from 24 patients with CNS lesions other than cervical spondylosis: AVP level was elevated in plasma only in seven samples, in CSF only in six, and in both CSF
and plasma in 10. This indicates that in such intracranial disorders as brain tumor, hydrocephalus, and cerebrovascular disease, there is a high incidence of increased AVP release into blood and CSF.

In rats, Buijs et al.2) histochemically traced oxytocin- and vasopressin-containing pathways from the paraventricular nucleus to the lateral ventricle, stria terminalis, and stria medullaris. Using the immunoperoxidase technique, Robinson and Zimmerman2) detected neurophysin, a carrier protein associated with vasopressin and oxytocin, not only in the supraoptic and paraventricular nuclei, their tracts, and the posterior pituitary, but also in the specialized ependymal tanyocytes of the infundibular recess of the third ventricle and in the external layer of the median eminence. Vorherr et al.3) and Dogterom et al.5) posited that AVP present in CSF might be released directly into the ventricular system after synthesis by the hypothalamic nuclei.

It has been suggested that AVP in CSF may regulate brain water permeability and that increased AVP in CSF may play a role in edema formation.4,13,22) On the other hand, Hammer et al.6,20) and Sørensen et al.26) proposed that elevated AVP levels secondary to intracranial hypertension may increase CSF water absorption and/or reduce CSF formation and thus lead to a decrease in intracranial hypertension. Brownfield and Kozlowski11) demonstrated the presence of vasopressin-like activity in CSF and choroid plexus extracts and proposed a process involving vasopressin-mediated transchoroidal CSF absorption. Vorherr et al.27) suggested that AVP secreted into CSF might play a role in the maintenance of the ionic concentrations of CSF and extracellular brain fluid. We found that elevated AVP levels in plasma and CSF resulted in significantly increased osmotic pressure gradients of plasma and CSF in hyponatremic patients, while the sodium concentration gradients of plasma and CSF were not significantly increased in these patients. This indicates that the increase in the osmotic pressure gradients of plasma and CSF was not a consequence of the increased sodium concentration gradients ascribable to hyponatremia. Fishman6) found that in experimental hyponatremia, the CSF sodium concentration varied in accordance with the plasma concentration, although there was a delay in equilibration between the two compartments. This suggests that the increased osmotic pressure gradients of plasma and CSF may be attributable to hemodilution and the concentration of CSF derived from increased AVP in plasma and CSF. In our normonatremic patients, elevation of AVP levels in plasma and/or CSF did not bring about a significant increase in the osmotic pressure gradients of plasma and CSF. In these patients, the duration of increased AVP secretion into the blood and CSF may not have been long enough to result in an increased osmotic pressure gradient through the action of AVP on the kidneys, on the organ for CSF absorption (arachnoid villi), and on the tissue for CSF production (choroid plexus).

In our study, in the four patients with impaired consciousness the osmotic pressure and sodium concentration gradients of plasma and CSF increased in proportion to the elevation of AVP levels in plasma and CSF. In a patient with SAH due to a ruptured anterior communicating artery aneurysm, the elevated AVP levels in plasma and CSF and the increased osmotic pressure and sodium concentration gradients of plasma and CSF normalized in parallel with the improvement of the consciousness disturbance. Jenkins et al.13) and Mather et al.17) suggested that increased AVP secretion into CSF might contribute to clinical deterioration in some patients with SAH. Dóczi et al.19) speculated that increased secretion of AVP into CSF in patients with SAH or intracranial hypertension of various origins may play a role in edema formation. An increase in the osmotic pressure gradients of plasma and CSF has also been observed in patients with disequilibrium syndrome during hemodialysis.15,16) The increase in the osmotic pressure gradients of the two compartments due to hemodialysis results in an increase in the volume of water in CSF and the extracellular fluid of the brain, and may bring about headache and confusion.

We conclude that the increased secretion of AVP into blood and CSF results in hemodilution and concentration of CSF via the effects of AVP on renal function, CSF production, and CSF absorption. The increase in osmotic pressure gradients of plasma and CSF resulting from hemodilution and CSF concentration may exacerbate the brain edema induced by the primary lesion and thereby contribute to the clinical deterioration of some patients with intracranial pathology, including brain tumors, hydrocephalus, and cerebrovascular disease.

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Address reprint requests to: M. Miura, M.D., Department of Neurosurgery, Kumamoto University School of Medicine, 1-1-1 Honjo, Kumamoto 860, Japan.