Effects of water loading in schizophrenic patients with polydipsia–hyponatremia: an MRI pilot study

Ahmed M. Elkashefa*, Fuad Issaa, Antonette Gindrawa, Richard J. Wyatta, Darrell G. Kirchb

aNeuropsychiatry Branch, NIMH Neuroscience Center at St. Elizabeths, 2700 Martin Luther King Jr. Ave, S.E.
Washington, DC 20032, USA and bOffice of the Dean, School of Medicine, Medical College of Georgia, Augusta.
GA 30912-4750, USA

(Received 16 August 1993; revised 10 December 1993; accepted 19 December 1993)

Abstract

We conducted an MRI pilot study of three schizophrenic patients with the syndrome of polydipsia–hyponatremia. Paired MRI scans were obtained at baseline and in the water-loaded state to study the acute effects of water loading and accompanying changes in serum sodium and osmolality on brain structures. We report the pilot data on the observed individual MRI changes of reduced volume of the lateral ventricles in all three patients, and the third ventricles in two patients, in the water-loaded state. These changes were not statistically significant possibly because of small sample size.

Key words: Polydipsia; MRI; (Schizophrenia)

1. Introduction

Polydipsia, with increased water consumption reflected by increased urine output, was described in psychiatric patients long before the introduction of neuroleptic drugs to treat psychosis (Sleeper and Jellinek, 1936; Lawson et al., 1985). In many cases, psychiatric patients with polydipsia progress to develop chronic hyponatremia and episodes of water intoxication. The prevalence of polydipsia in schizophrenic patients has been estimated to be 6–17%, with an associated total morbidity and mortality of about 20% in these polydipsic patients (Jose and Perez-Cruet, 1936; Vieweg et al., 1985; Illowsky and Kirch, 1988). The neuropathology and pathophysiologic mechanisms underlying the syndrome of polydipsia–hyponatremia remain unclear (Goldman et al., 1988).

There are very few brain imaging studies in schizophrenic patients with the polydipsia–hyponatremia syndrome. One pneumoencephalographic study of a schizophrenic patient with polydipsia–hyponatremia reported increased size of the third and lateral ventricles (Peterson and Marshal, 1975). Kirch et al. (1985) reported an increased mean ventricular brain ratio (VBR) on computed tomographic (CT) brain scans in six patients with polydipsia compared with normal controls, however, group mean VBR did not differ significantly from schizophrenic controls. Lawson et al. (1991) performed a CT study of 18 schizophrenic patients in which the patients with hyponatremia were more likely than the other schizophrenic patients to show prefrontal cortical...
atrophy or increased VBR. Preclinical animal study (Vlajkovic et al., 1986) and few clinical case reports (Berginer et al., 1985; Trabert et al., 1987) suggest that acute water intoxication is accompanied by structural changes in total brain and ventricular size. We conducted the present pilot study using magnetic resonance imaging (MRI) to explore whether observed abnormalities in brain structures in polydipsia–hyponatremia are affected by water loading and acute changes in serum sodium and osmolality.

2. Materials and methods

Three inpatients, two males and one female with a mean (± SD) age of 39.3 ± 3.5 years, and an average duration of illness of 19.3 years, were studied after providing informed consent. All met DSM-III-R criteria for schizophrenia, chronic undifferentiated type, and were on constant standard dose of Haloperidol (0.4 mg/kg). All three patients were free of any significant medical problems especially those that can cause polydipsia–hyponatremia. All patients were confirmed to have polydipsia, polyuria, and hyponatremia documented by repeated low serum sodium concentrations and osmolality accompanying diurnal weight increases. Patient weight was checked four times daily and serum electrolyte concentrations were determined if the patient exceeded a threshold weight determined to be associated with hyponatremia.

The MRI scans were obtained using a 0.3 Tesla scanner (Fonar, Melville, NY) using a double echo pulse sequence to obtain both a proton density and a T2 weighted image (TE 30 and 85, TR 2000). Images were acquired in the coronal and the transaxial planes, with contiguous slices 7 mm thick. The baseline normonatremic scan was obtained immediately following a 12 h period of overnight fluid restriction. The second scan was obtained after patients spontaneously became water loaded as manifested by an acute weight increase at or above the set weight limit and/or drop in serum concentration sodium below 130 mEq/l.

Volumetric measurements of the lateral ventricles and the third ventricle were obtained from the coronal slices. All measurements were done by a rater (AME) who was blind to the fluid status of the patient’s MRIs using the Loats image analysis system (Loats, Westminster, MD). Paired t-tests were used to compare the means of the differences for the paired sets.

3. Results

There was a weight increase in the water-loaded state for all three patients, which was accompanied by lower serum sodium concentration and osmolality. The mean weight increase was 8 lbs and serum sodium and osmolality fell 9 mEq/l and 20 mOsm/kg, respectively, in the water-loaded state. There was a reduction in the volume of the lateral ventricles in all three patients, and the third ventricles in two patients, in the water-loaded state. These changes were not statistically significant. There were no correlations between the biochemical and the MRI data found. A summary of the individual results is presented in Table 1.

Clinically, two of the three patients showed changes in mental status with water loading. One

<table>
<thead>
<tr>
<th>ID</th>
<th>Age</th>
<th>Sex</th>
<th>BNa+ (mEq/l)</th>
<th>WNa+ (mEq/l)</th>
<th>Bwt (lbs)</th>
<th>Wwt (lbs)</th>
<th>Bosm (mOsm/kg)</th>
<th>Wosm (mOsm/kg)</th>
<th>BLV (ml)</th>
<th>WLV (ml)</th>
<th>B3V (ml)</th>
<th>W3V (ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>39</td>
<td>F</td>
<td>140</td>
<td>125</td>
<td>203</td>
<td>212</td>
<td>291</td>
<td>260</td>
<td>14.3</td>
<td>13.7</td>
<td>1.7</td>
<td>1.9</td>
</tr>
<tr>
<td>2</td>
<td>43</td>
<td>M</td>
<td>137</td>
<td>136</td>
<td>189</td>
<td>200</td>
<td>286</td>
<td>786</td>
<td>17.5</td>
<td>15.4</td>
<td>7.0</td>
<td>1.3</td>
</tr>
<tr>
<td>3</td>
<td>36</td>
<td>M</td>
<td>136</td>
<td>124</td>
<td>144</td>
<td>148</td>
<td>287</td>
<td>266</td>
<td>61.3</td>
<td>42.1</td>
<td>4.4</td>
<td>2.8</td>
</tr>
</tbody>
</table>

Na+, serum sodium (mEq/l); wt, weight (lbs); Osm, serum osmolality (mOsm/kg); LV, lateral ventricles (ml); 3V, third ventricle (ml); VBR, ventricular brain ratio.
patient (No. 2) became confused and despondent, with increased latency of response to verbal commands. The other patient (No. 1) became euphoric, singing loudly, with inappropriate sexual remarks. Both regained their baseline mental status after water restriction.

4. Discussion

The small number of subjects in this pilot study obviously makes any conclusions exceedingly tentative. While the data show no statistically significant difference between states possibly because of small sample size, there was a reduction in size of the lateral ventricles in three out of three patients and in the third ventricles in two out of three patients after water loading compared with baseline. Thus, there very well may be state-related structural changes in the brain in polydipsia–hyponatremia. Some degree of brain edema may occur which subsequently leads to compression of the ventricular space. This edema may be pathophysiologically involved in the mental status alterations observed with water intoxication.

These results are consistent with preclinical data regarding water intoxication in animals. In one study dogs were intravenously infused with sterile water at a rate of 5 ml/min while monitoring their central arterial and venous pressures as well as cerebrospinal fluid (CSF) pressure (Vlajkovic et al., 1986). MRI brain scans were obtained at baseline and at 8 min intervals throughout the experiment. The study showed a progressive increase in CSF pressure. Brain water content was assessed by measuring the signal intensity on the MRI scans in different gray matter as well as white matter regions. Edema started in the gray matter of cerebral cortex, and gradually progressed to all parts of the brain. Death ensued with transtentorial and tranforaminal herniation leading to respiratory arrest after infusion of a water volume corresponding to 10–14% of body weight.

Few case reports have documented the acute effects on brain structure of water intoxication in humans. Berginer et al. (1985) described CT changes in a 52 year old hypertensive female with iatrogenic water intoxication, including narrowing of the 3rd ventricle and smaller lateral ventricles. This diffuse brain edema had resolved on a post recovery CT scan. In another case, Trabert et al. (1987) also found decreased size of the lateral and the third ventricles in the water intoxicated state compared with baseline in a 48 year old female patient with presenile dementia.

Based on the findings presented here, we are conducting a larger MRI study designed to examine brain changes in the acute water loaded state in chronic schizophrenic patients with polydipsia–hyponatremia. In addition, this pilot study illustrates the need for MRI structural brain studies of schizophrenic patients to address the hydration status of subjects, especially the subgroup of patients with polydipsia–hyponatremia. It appears that key measurements may vary depending on recent water consumption and brain water content.

References

Sleeper, F.H., Jellinek, E.M. (1936) A comparative physiologic,

Trabert, W., Huber, G., Bellaire, W., Thielen, T. (1987) klinische und computertomographische Verlaufsun-
