Paroxetine-Induced Hyponatremia in Older Adults

A 12-Week Prospective Study

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Background: Older depressed patients are at high risk for development of hyponatremia after initiation of the selective serotonin reuptake inhibitor paroxetine, despite clinical monitoring and preventive management. The purposes of this study were to determine the incidence and etiology of paroxetine-induced hyponatremia in older patients and to identify patient characteristics that may account for variability in susceptibility to this adverse event.

Methods: This prospective, longitudinal study was conducted in a university-based ambulatory psychiatric research clinic from August 1999 through September 2001. Patients included 75 men and women aged 63 through 90 years (mean±SD age, 75.3±6.0 years) who received a diagnosis of a current Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, major depressive episode and were prescribed paroxetine. We monitored plasma sodium levels before initiating paroxetine therapy and after 1, 2, 4, 6, and 12 weeks of treatment. In a subset of individuals, we measured levels of antidiuretic hormone, glucose, serum urea nitrogen, and creatinine. Hyponatremia was defined as a plasma sodium level of less than 135 mEq/L after initiation of paroxetine therapy.

Results: Hyponatremia developed in 9 (12%) of the 75 patients after initiation of paroxetine treatment. Mean±SD time to development of hyponatremia was 9.3±4.7 days (median, 9 days; range, 1-14 days; n=8). In the multivariate regression, lower body mass index and lower baseline plasma sodium level (<138 mEq/L) were significant risk factors for the development of hyponatremia in these patients.

Conclusions: Hyponatremia is an underrecognized and potentially serious complication of paroxetine treatment in older patients. Our results provide a foundation for understanding the etiology and risk factors associated with paroxetine-induced hyponatremia.

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Major Depression is a common psychiatric disorder in older adults, affecting 10% to 20% of medically hospitalized elderly patients. It is reported that 10% to 34.5% of older persons living in the community also experience clinically significant depressive symptoms. Most depression in older patients is managed in the primary care setting. According to a recent report on national trends in outpatient treatment, depressed patients were 4.8 times more likely to receive treatment with an antidepressant in 1997 than in 1987. The marked increase in pharmacological treatment of this disorder is due in part to the introduction of a new class of highly effective antidepressant drugs known as the selective serotonin reuptake inhibitors (SSRIs). Owing to the relatively benign adverse effect profile of SSRIs, these agents are often prescribed as the first-line treatment of depression in older adults. Although these agents are reportedly safer than the tricyclic antidepressants, they are not without risk or adverse effects.

Since the introduction of SSRIs more than a decade ago, the medical literature is replete with isolated case reports of clinically significant hyponatremia in aged patients treated with these agents. In a case note review, Strachan and Shepherd reported hyponatremia in 5 (28%) of 18 elderly patients prescribed fluoxetine hydrochloride and 8 (22%) of 37 prescribed paroxetine, although an earlier retrospective case-control study of 845 patients documented that hyponatremia developed in 1 of 200 patients treated per year with these agents. More recently, Kirby et al recently reported a 39% incidence of hyponatremia in a retrospective analysis of 74 elderly inpatients who were receiving treatment with an SSRI or with venlafaxine hydrochloride. Despite the growing number of case and retrospective reports of SSRI-induced hyponatremia, prospective evaluation of the safety of these agents is lacking in individuals older than 65 years, the fastest growing segment of our population. Although severe hyponatremia can be fatal, symptoms associated with mild to moderate hyponatremia are nonspecific (eg,
nation.18 Medical burden was quantified by the Cumulative Ill-

tal Disorders, Fourth Edition,

Therefore, we included in the analysis 75 men and women aged

cause they failed to meet the baseline sodium inclusion criteria.

tion of paroxetine treatment. Two women were excluded be-

weeks of treatment. In one patient, development of symptoms

for initiating paroxetine therapy and after 1, 2, 4, 6, and 12

current medical conditions or were prescribed other medica-

None of the patients in whom hyponatremia developed had con-

within physiologic limits (60-110 mg/dL [3.3-6.0 mmol/L]).

This study was approved by the Institutional Review Board of

as part of a National

or incidence of falls) were documented at each visit and evalu-

ated at weekly clinical research meetings as part of a National

Clinical Diagnostics, Inc, Rochester, NY). The within-

or laboratory coefficients of variation were 0.9% for plasma so-

mEq/L at any assessment returned to the clinic to undergo ad-

Plasma paroxetine concentrations were measured to as-

 sess compliance and to determine whether the concentration

of paroxetine was a factor in the development of hyponatremia.

All reported symptoms (eg, confusion, anorexia, or fa-

tigue) or adverse events (eg, abrupt changes in mental status

or incidence of falls) were documented at each visit and evalu-

ated at weekly clinical research meetings as part of a National

of measuring levels of ADH, glucose, serum urea nitrogen (SUN),

and creatinine to investigate the potential etiology of hypona-

tramia in these patients.

Patients whose plasma sodium level was less than 135

mEq/L at any assessment returned to the clinic to undergo ad-

itional laboratory tests, including measurement of plasma so-

dium, ADH, glucose, SUN, and creatinine levels. A spot urine

sample was also collected for the measurement of the urine so-

dium level and osmolality in these individuals. We notified the

patient’s primary care physician of the development of hypo-

tramia and discussed a suggested plan for management.

Laboratory analyses, including levels of sodium, glucose, SUN,

and creatinine, were performed by the Clinical Chemistry Labo-

ratory at the University of Pittsburgh Medical Center using an

automated system (Vitros 950 Clinical Chemistry System; Ortho-

Clinical Diagnostics, Inc, Rochester, NY). The within-

laboratory coefficients of variation were 0.9% for plasma so-

dium level, 1.6% for urine sodium level, 1.6% for SUN level,

1.1% for creatinine level, and 1.0% for glucose level. Plasma

osmolality was calculated using the following formula20:

Plasma Osmolality = 2(Sodium) + (Glucose/20) + (SUN/3)

Urine osmolality was determined by means of freezing point de-

ression with a within-laboratory coefficient of variation of 1.4%.

Plasma ADH levels were determined by radioimmunoas-

say methods. Blood samples were obtained by direct venipunc-

ture into a 10-mL venous blood collection tube (Vacutainer; Bec-

ton, Dickinson and Co, Franklin Lakes, NJ) containing 143 US

Pharmacopeia units of heparin sodium. Blood was centrifuged

at 4°C at 1500g for 10 minutes. The plasma was separated, trans-

ferred into polypropylene storage tubes, and frozen at −80°C

until analyzed. The radioimmunoassay system used for determi-

ning ADH levels was based on methods previously described by

Robertson and colleagues24 and subsequently modified.25,26 The

intra-assay and interassay coefficients of variation range from 5% to

7% at each concentration of the standard curve (0.5-20 pg/mL

[0.5-18.5 pmol/L]).

Plasma paroxetine levels were determined using reverse-

phase high-performance liquid chromatography and UV detec-

tion.27 Blood samples were collected by venipuncture into a 10-mL

venous blood collection tube containing 13% menadione EDTA.

Blood was centrifuged at 4°C at 1500g for 10 minutes. The plasma

was separated, transferred into polypropylene storage tubes, and

frozen at −80°C until analyzed. The high-performance liquid chro-

matography column used for separation was an UltraspHERE 5µ

C18, 150 X 2.0-mm internal diameter (Phenomenex Inc, Tor-

rance, Calif). The mobile phase consisted of potassium phos-

phate and acetonitrile (62:38, vol/vol), with a pH of 2.4. The wave-

length used for UV detection was 205 nm, and the assay was linear,

from 5 to 500 ng/mL. Interassay variation for this assay was 1.4% for

250 ng/mL and 3.23% for 75 ng/mL. Commercially pur-

duced analytical paroxetine controls were analyzed in every assay.

METHODS

This study was approved by the Institutional Review Board of

the University of Pittsburgh, Pittsburgh, Pa, and was ancillary

to an ongoing Institutional Review Board–approved antidepres-

sant treatment protocol in which the US Food and Drug

Administration–approved SSRI paroxetine was prescribed. All

studies were conducted within the Intervention Research Cen-

ter for Late Life Mood Disorders at the University of Pitts-

burgh, Western Psychiatric Institute and Clinic.

SUBJECTS

From August 1999 through September 2001, 94 patients pro-

vided written informed consent to participate in this research

study. Only those patients who were determined to be non-

monotremic (plasma sodium level ≥135 mEq/L) at baseline and

who met criteria for inclusion in the antidepressant treatment

protocol were eligible for entry into the present study.11 Of these

94 patients, 17 men and women were excluded owing to the ab-

sence of a sodium level measurement at baseline or after initi-

tion of paroxetine treatment. Two women were excluded be-

cause they failed to meet the baseline sodium inclusion criteria.

Therefore, we included in the analysis 75 men and women aged

63 through 90 years (mean ± SD age, 75.3 ± 6.0 years) who were
diagnosed as having a Diagnostic and Statistical Manual of Men-


ASSESSMENTS

A complete medical, psychiatric, and medication history was

obtained, and laboratory measures were assessed in all pa-

tients at the baseline visit. Patients underwent screening be-

fore entry into the study. All patients had a score of 15 or greater

on the 17-item Hamilton Rating Scale for Depression11 and a

score of 18 or higher on the Folstein Mini-Mental State Exam-

ination.18 Medical burden was quantified by the Cumulative Ill-

ness Rating Scale–Geriatric.18 Adrenal, renal, and thyroid func-

tion were determined to be normal, and glucose levels were

within physiologic limits (60-110 mg/dL [3.3-6.0 mmol/L]).

None of the patients in whom hyponatremia developed had con-

current medical conditions or were prescribed other medica-

tions known to cause hyponatremia.

Plasma concentrations of sodium were determined before

initiating paroxetine therapy and after 1, 2, 4, 6, and 12

weeks of treatment. In one patient, development of symptoms

of hyponatremia within 24 hours of initiating paroxetine therapy

necessitated the immediate measurement of the plasma so-

dium level. Patients with sodium levels near the lower limit of

the physiologic range before initiation of paroxetine therapy

were instructed to restrict daily fluid intake in an attempt to

minimize risk for development of hyponatremia. In a subset

of individuals, blood samples were collected for the purpose

of measuring levels of ADH, glucose, serum urea nitrogen (SUN),

and creatinine to investigate the potential etiology of hypona-

tramia in these patients.

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STATISTICAL ANALYSIS

Descriptive statistics were used to summarize demographic, clinical, and baseline laboratory variables. All data are expressed as mean ± SD.

At the completion of the study, patients were classified into 1 of the following 2 groups: patients with hyponatremia (sodium level, < 135 mEq/L on ≥ 1 occasions) or those who maintained normonatremia (sodium level, ≥ 135 mEq/L throughout the study). Univariate logistic regressions were performed to examine between-group differences in baseline demographic, clinical, and laboratory measures. We then performed a multivariate logistic regression using sex, medical burden, and all variables identified in the univariate logistic regression analyses that were significant at *P < .10*. The final model was obtained by a backward stepwise regression procedure (threshold removal set at *P < .10*).

Maximum change in plasma sodium concentration after initiation of paroxetine therapy was plotted according to baseline sodium concentration in all subjects. A receiver operating characteristics curve was calculated to show the sensitivity and specificity of determining a cutoff for baseline plasma sodium as a reliable screening measure to identify patients at risk for development of hyponatremia.

Plasma osmolality and ADH levels measured on the date closest to the initiation of paroxetine treatment were chosen for graphic presentation and correlation analyses. Plasma paroxetine and ADH levels were plotted and correlation analyses were performed to determine whether any relationship existed between them. Statistical analyses were performed using SAS software, version 8.2.25

RESULTS

Baseline demographic, clinical, and laboratory data for the 75 patients are displayed in Table 1. Hyponatremia developed in 9 (12%) of the 75 patients after initiation of paroxetine treatment and constitute the hyponatremic group, whereas 66 individuals constitute the normonatremic group. Mean time to development of hyponatremia after starting paroxetine therapy was 9.3 ± 4.7 days (median, 9 days; range, 1-14 days; n = 8). One subject started the study while receiving paroxetine and, consequently, the time to onset of hyponatremia was not determined. The mean dose of paroxetine at the time of hyponatremia was 12.5 ± 1.6 mg, with hyponatremia developing in 8 of the 9 patients while prescribed 10 mg of paroxetine. There were no correlations between plasma paroxetine concentrations and measures of plasma sodium or plasma ADH levels (data not shown).

Maximum change in sodium concentration from baseline is displayed in Figure 1 for all patients relative to their baseline sodium concentration. Although sodium concentrations decreased in most patients after initiation of paroxetine therapy, the greatest declines were observed in the 9 patients who met criteria for hyponatremia. Eight patients had at least an 8-point drop in sodium concentration, and 6 had more than 1 sodium level below the cutoff of 135 mEq/L. Most patients in whom

Table 1. Baseline Demographic, Clinical, and Laboratory Data for Normonatremic and Hyponatremic Patients

<table>
<thead>
<tr>
<th></th>
<th>Normonatremic Patients</th>
<th>Hyponatremic Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Patients</td>
<td>66</td>
<td>9</td>
</tr>
<tr>
<td>Findings a</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>75.2 ± 6.1 (63.0-90.0)</td>
<td>74.5 ± 6.1 (62.0-84.0)</td>
</tr>
<tr>
<td>No. (%) male</td>
<td>66</td>
<td>9</td>
</tr>
<tr>
<td>No. (%) white</td>
<td>66</td>
<td>9</td>
</tr>
<tr>
<td>BMI</td>
<td>28.2 ± 6.9 (16.8-56.5)</td>
<td>28.3 ± 6.9 (17.9-52.7)</td>
</tr>
<tr>
<td>CIRS-G score</td>
<td>9.6 ± 3.7 (2.0-19.0)</td>
<td>10.0 ± 3.7 (4.0-14.0)</td>
</tr>
<tr>
<td>17-Item Hamilton-D score</td>
<td>19.4 ± 3.9 (8.0-30.0)</td>
<td>19.0 ± 3.9 (15.0-22.0)</td>
</tr>
<tr>
<td>Folstein MMSE score</td>
<td>28.1 ± 2.0 (23.0-30.0)</td>
<td>29.0 ± 2.0 (21.0-29.0)</td>
</tr>
<tr>
<td>Sodium level, mEq/L</td>
<td>140.9 ± 2.3 (136.0-146.0)</td>
<td>141.0 ± 2.3 (135.0-142.0)</td>
</tr>
<tr>
<td>S, mg/dL</td>
<td>14.3 ± 4.8 (7.0-20.0)</td>
<td>14.5 ± 4.8 (7.0-20.0)</td>
</tr>
<tr>
<td>Creatinine level, mg/dL</td>
<td>1.0 ± 0.3 (0.6-2.3)</td>
<td>1.0 ± 0.3 (0.7-1.0)</td>
</tr>
<tr>
<td>ADH, pg/mL</td>
<td>2.1 ± 0.8 (1.0-4.9)</td>
<td>1.7 ± 0.5 (1.4-2.2)</td>
</tr>
<tr>
<td>Plasma osmality, mOsm/kg</td>
<td>293.3 ± 5.5 (281.4-307.5)</td>
<td>293.1 ± 5.5 (278.1-290.8)</td>
</tr>
</tbody>
</table>

Abbreviations: ADH, antidiuretic hormone; BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); CIRS-G, Cumulative Illness Rating Scale–Geriatrics; Hamilton-D, Hamilton Rating Scale for Depression; MMSE, Mini-Mental State Examination; NA, not applicable; SUN, serum urea nitrogen.

SI conversion factors: To convert ADH to picomoles per liter, multiply by 0.923; creatinine to micromoles per liter, multiply by 88.4; SUN to millimoles per liter, multiply by 0.357.

*Unless otherwise indicated, data are expressed as mean ± SD (range), with medians.

Figure 1. Maximum observed change from baseline sodium level compared with baseline sodium concentration for patients who became hyponatremic (n = 9) and those who remained normonatremic (n = 66). The dashed line represents no change from baseline sodium level. Duplicate values are represented by a single circle.
We identified a 12% incidence of hyponatremia that developed within 1 to 14 days after initiation of paroxetine therapy in this cohort of depressed older patients. The incidence described herein is a conservative one and is likely an underestimate, because the study by design included monitoring and preventive clinical management of plasma sodium levels. Early countermeasures may account for the transient nature of hyponatremia in some of our patients. To our knowledge, this is the first prospective evaluation of hyponatremia with the use of an SSRI, paroxetine, in elderly depressed patients.

Risk factors for the development of paroxetine-induced hyponatremia in these patients included lower baseline sodium levels and lower BMI. Although female sex was not a significant predictor of hyponatremia in

![Figure 2](www.archinternmed.com)

**Figure 2.** Plasma osmolality compared with plasma antidiuretic hormone (ADH) levels after initiation of paroxetine therapy for hyponatremic (n=5) and normonatremic (n=41) individuals. The ADH values were not available for all subjects. The vertical dashed line represents the osmotic threshold, whereas the horizontal dashed line represents the lower limit of detection of the ADH assay.

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR (95% CI)</th>
<th>$\chi^2$ Test Statistic</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multivariate model</td>
<td>30.30 (0.59 to &gt;99)</td>
<td>34.38*</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Sex</td>
<td>3.73 (0.44 to 31.81)</td>
<td>1.45</td>
<td>.23</td>
</tr>
<tr>
<td>BMI</td>
<td>0.79 (0.66 to 0.95)</td>
<td>6.60</td>
<td>.01</td>
</tr>
<tr>
<td>Total CIRS-G score</td>
<td>0.90 (0.73 to 1.10)</td>
<td>1.10</td>
<td>.29</td>
</tr>
<tr>
<td>17-Item Hamilton-D score</td>
<td>1.00 (0.82 to 1.20)</td>
<td>0.003</td>
<td>.95</td>
</tr>
<tr>
<td>Folstein MMSE score</td>
<td>0.73 (0.61 to 0.88)</td>
<td>1.94</td>
<td>.15</td>
</tr>
<tr>
<td>Sodium level</td>
<td>0.90 (0.77 to 1.06)</td>
<td>1.67</td>
<td>.20</td>
</tr>
<tr>
<td>Creatinine level</td>
<td>0.63 (0.33 to 0.84)</td>
<td>9.72</td>
<td>.022</td>
</tr>
</tbody>
</table>

**Table 3. Multivariate Logistic Regression Analyses for Presence or Absence of Hyponatremia as a Function of Each Potential Risk Factor at Baseline**

Abbreviations: BMI, body mass index; CI, confidence interval; CIRS-G, Cumulative Illness Rating Scale–Geriatrics; MMSE, Mini-Mental State Examination; OR, odds ratio; SUN, serum urea nitrogen.

**Comment**

The incidence described herein is a conservative one and is likely an underestimate, because the study by design included monitoring and preventive clinical management of plasma sodium levels. Early countermeasures may account for the transient nature of hyponatremia in some of our patients. To our knowledge, this is the first prospective evaluation of hyponatremia with the use of an SSRI, paroxetine, in elderly depressed patients.

Risk factors for the development of paroxetine-induced hyponatremia in these patients included lower baseline sodium levels and lower BMI. Although female sex was not a significant predictor of hyponatremia in...
In general, the incidence of hyponatremia is higher among older patients, possibly due to age-related physiological changes in water and electrolyte handling; however, the extent of these physiological changes is highly variable. Examples of age-related physiological changes in water and osmotic homeostasis include a reduction in total body water level and/or diminished renal blood flow and glomerular filtration; increased ADH secretion or lack of ADH suppression in response to osmolar or pharmacological stimuli, and decreased renal response to ADH. Despite these factors, whether age is an independent risk factor is difficult to discern owing to the presence of comorbid medical conditions or concomitant prescribed medications that are known to cause hyponatremia or alter ADH secretion.

As shown in Figure 1, sodium concentrations declined in most patients in the normonatremic and hyponatremic groups after initiating paroxetine therapy. However, the development of hyponatremia does not appear to be dose related, as plasma paroxetine concentrations were not associated with risk for development of hyponatremia. A 10-mg dose of paroxetine was prescribed for 8 of the 9 patients when the episode of hyponatremia was detected. On detection, paroxetine therapy was held or discontinued, and patients were instructed to restrict daily fluid intake to 1000 mL or less until the plasma sodium level normalized (eg, sodium level, ≥135 mEq/L).

The maintenance of water homeostasis and physiologic serum sodium levels is highly dependent on ADH. This nonapeptide is synthesized within the hypothalamus and transported to, stored in, and released from the posterior lobe of the pituitary gland in response to physiologic stimuli. By binding to ADH receptors in the renal tubules or collecting ducts of the kidney promoting reabsorption of water, ADH exerts the major control over osmolality in the body. Antidiuresis leads to a decrease in plasma osmolality and an increase in urine osmolality.

In euvolemic, normonatremic healthy individuals, circulating levels of ADH are 1 to 2 pg/mL (0.9-1.8 pmol/L). Secretion of ADH is triggered appropriately in response to physiological stimuli such as high plasma osmolality or hypovolemia. Conversely, ADH secretion should be suppressed when plasma osmolality falls below the osmotic threshold (<280 mOsm/kg) and intravascular volume is replete. Secretion of ADH, despite low plasma sodium level or osmolality (as in the patients in whom hyponatremia developed in this study) is inappropriate and indicates the presence of a nonsmotic stimulus for ADH release. Some examples of nonsmotic stimuli of ADH secretion include ADH production of malignancies, pulmonary disorders, central nervous system disorders (eg, stroke, trauma, and infection), and certain pharmacological agents (eg, thiazide diuretics, antipsychotics, antiidiuretics, and nonsteroidal anti-inflammatory drugs).27,28,31

Experimental studies in rats suggest that serotonin is a potential stimulator of ADH secretion. The SSRIs, including paroxetine, are known to block the reuptake of serotonin in the central nervous system. Thus, inappropriate secretion or enhanced action of ADH as a result of enhanced serotonergic tone may contribute to the development of SSRI-induced hyponatremia in older patients, provided water intake is sufficient. Even if SSRIs stimulate ADH secretion, hyponatremia will not occur until patients ingest or are infused with excess fluids. A criterion for the diagnosis of the syndrome of inappropriate ADH secretion is that individuals be volume replete. Consequently, the effect of an SSRI to induce hyponatremia may not become manifest until the patient enters a phase of increased fluid ingestion. In this study, several patients in whom hyponatremia developed had temporally associated complaints of urinary tract infections and constipation, and many of these patients were encouraged to drink fluids to alleviate these conditions. Patients with normal kidney function are capable of excreting large volumes of hypotonic urine daily. However, transient periods of intense drinking may exceed the hourly capacity for free water excretion, and transient hyponatremia may develop in such instances, especially in patients prescribed psychotropic medications that enhance the release or action of ADH.

Recent improvements in detection and diagnosis of depressive disorders in the elderly along with use of SSRIs for treatment of anxiety disorders has resulted in an increased number of older patients being prescribed SSRIs. As such, a greater number of individuals are at risk for development of SSRI-induced hyponatremia. Patients with SSRI-induced hyponatremia may be asymptomatic, and therefore routine monitoring of sodium concentrations in elderly patients prescribed an SSRI is essential. Failure to detect and manage mild hyponatremia may result in progression to moderate or severe hyponatremia that can lead to seizures, coma, or death. Thus, early detection, appropriate monitoring, and treatment of hyponatremia in older patients who are prescribed an SSRI will have a significant public health impact by reduction of health care costs associated with preventable adverse medical events.

Hyponatremia is an underrecognized and potentially serious complication of paroxetine treatment in older patients. Hyponatremia associated with SSRIs has been postulated to be due to the syndrome of inappropriate ADH secretion. In this prospective study, we provide evidence in support of a mechanism mediated by the syndrome of inappropriate ADH secretion for paroxetine-induced hyponatremia in these older individuals. Plasma sodium concentrations decreased in nearly all of the older depressed patients prescribed paroxetine in this study. However, the risk for development of hyponatremia was highest in women with a low BMI who had sodium concentrations near the lower end of the physiologic range before initiating treatment. The risk for development of hyponatremia was highest in the first 2 weeks of paroxetine treatment and was not related to paroxetine concentrations. Therefore, we recommend monitoring sodium and SUN levels before initiating treatment with paroxetine or other SSRIs and at 1 and 2 weeks after initiation of treatment. This is especially important for patients who present with additional risk factors such as female sex, low BMI, and a baseline plasma sodium level of 138 mEq/L or less. At minimum, a sodium level should be measured in all elderly patients who exhibit abrupt...
changes in mental status (eg, lethargy or confusion) any time during treatment with an SSRI. If hyponatremia develops and continuation of SSRI therapy is desired, long-term restriction of daily fluid intake (eg, 800-1000 mL) has been somewhat successful, although patient compliance is often poor. Failure to respond to fluid restriction warrants discontinuation of the causative medication until sodium levels normalize.

CONCLUSIONS

The results obtained from this prospective study provide a foundation for understanding the etiology and risk factors associated with paroxetine-induced hyponatremia. Development and implementation of a rational plan for prescribing and safety monitoring of SSRIs in the aged should be based on an increased understanding of this common adverse event.

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REFERENCES