ORIGINAL ARTICLE

The Association between Hyponatremia and Psychotropic: An Observational Study in Chronic Forensic Rehabilitation Ward at Mental Health Hospital, Taif, Saudi Arabia

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Abstract

Background: Hyponatremia is the most common electrolyte imbalance experienced in psychiatric clinical practice, both in hospital and outpatient settings, in patients taking psychotropic medications. It is a multifactorial clinical condition characterized by a plasma sodium level of less than 130 millimoles per liter. In psychiatric patients, this is mostly ignored and untreated, which can lead to increased mortality.[1]

Aims and objectives: The main objectives of this study are:

- To evaluate the socio-demographic profile.
- To evaluate the severity of hyponatremia in patients using psychotropic.
- To evaluate the association between hyponatremia and psychotropic.

Materials and methods: This was an observational study performed in the forensic psychiatric rehabilitation wards of the Mental Health Hospital, Taif, Saudi Arabia. Study participants were patients admitted to the inpatient ward ($n = 73$) between 2018 and 2022. Descriptive statistical analysis was explored and presented as categorical variables such as frequencies and percentages. We also explored the relationship between hyponatremia and psychotropics.

Results: An observational study was conducted over a period of 5 years. The majority of patients (34.48%) were in the age group of 46 to 55 years, and the total number of hyponatremia patients was ($n = 29$; 39.72%). The maximum number of patients was 44.82% with mild hyponatremia (130–134 mmol/L), 37.93% with moderate (125–130 mmol/L), and 17.24% with severe hyponatremia (<120 mmol/L). Hyponatremia was found in 4.10% of antidepressant patients, 20.54% of patients on antipsychotics, and 9.58% of patients on mood stabilizers.

Conclusions: In our study, hyponatremia was most prevalent among patients between 45 and 55 years of age. Haloperidol was the most likely antipsychotic to cause hyponatremia. Among atypical antipsychotics, aripiprazole was most commonly associated with hyponatremia, followed by risperidone and amisulpride, whereas quetiapine had a minimal number. Among mood stabilizers, valproic acid was associated with hyponatremia, whereas lithium and carbamazepine were less likely to be associated.

Keywords: Antidepressant, Antipsychotic, Hyponatremia, Mood stabilizer.

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Introduction

The term hyponatremia is most commonly used in psychiatry and other clinical areas to describe an electrolyte abnormality that can lead to a variety of health complications. The condition is widespread and potentially dangerous, resulting in neurological and psychiatric symptoms, and is triggered by drugs such as psychotropics.[2–4] Psychogenic polydipsia and inappropriate antidiuretic hormone (ADH) secretion can cause hyponatremia in psychiatric patients.[5] Hyponatremia occurs when the kidneys are unable to excrete enough fluid, or when too much fluid is consumed. The increase in osmolality induces thirst and increases fluid consumption. The osmoreceptors in the hypothalamus, which release antidiuretic hormones, detect this increase in osmolality. The syndrome of inappropriate antidiuretic hormone (SIADH) results from persistent ADH stimulation.[6]

Hyponatremia usually presents with restlessness, drowsiness, myoclonic jerks, and convulsions, which can progress to confusion, coma, and death if the symptoms are not treated. This condition occurs frequently among hospitalized patients and in routine (outpatient) psychiatric clinical care, and it has been associated with a 55% mortality risk.[7,8] There is ample evidence

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Ethical approval: The research work started after it was approved by the Ethical Committee of Research, and Studies Department, Directorate of Health Affairs, Taif, Saudi Arabia.

that hyponatremia can be caused by various psychotropic drugs. The most common types include diuretics, antidepressants, antipsychotics, mood stabilizers, and antiepileptics.[9] Drug-induced hyponatremia can be asymptomatic as well and is incidentally diagnosed by blood tests. Mild cases can be treated by careful observation.[10]

There are many studies on hyponatremia with antidepressants, but very few studies have examined hyponatremia with antipsychotics, mood stabilizers, or antiepileptics. The available data is mostly in the form of case reports and observational studies.[11,12] There are several risk factors associated with hyponatremia due to psychotropics. These include demographic factors such as age and gender,[13] environmental factors such as the summer season,[14] physical characteristics such as a low body weight,[15,16] and psychiatric illness variables. There are other risk factors such as comorbid hypertension, hypothyroidism, diabetes mellitus, chronic obstructive pulmonary disease (COPD), heart failure, head injuries, strokes, liver cirrhosis,[17,18] and a history of hyponatremia. Co-prescribed medications such as antihypertensives, antidiabetics, diuretics, proton-pump inhibitors, antibiotics, antiepileptics, and non-steroidal anti-inflammatory drugs may also contribute to the risk of hyponatremia.[19–21]

Materials and Methods

Participants

The study included male inpatients from the rehabilitation and forensic psychiatry wards at the Mental Health Hospital in Taif, Saudi Arabia. The participants were all on psychotropics for 5 years, between January 2018 and March 2022.

Parameters

In this study, we evaluated the socio-demographic profile and hyponatremia severity in patients using psychotropic medications such as antidepressants, antipsychotics, and mood stabilizers, and we evaluated the association between hyponatremia and psychotropic medications. Moreover, we collected data on the hyponatremia symptoms through interviews with patients using psychotropics. Over the past 5 years, we also conducted physical examinations and collected data from available laboratory investigations.

Inclusion Criteria

- A group of diagnosed psychiatric cases based on the International Classification of Diseases-10 diagnostic criteria, in which adult patients received psychotropic medications such as antidepressants, antipsychotics, and mood stabilizers.
- Patients who have participated in the study are from the chronic forensic rehabilitation unit.
- All participants who took psychotropic during the past 5 years were included in the study.

Exclusive Criteria

- Female patients.
- Age range of participants below 30 years.
- Patients who discontinued treatment before the study was completed.

Sampling Technique

Researchers used a purposeful sampling strategy to select participants from the Mental Health Hospital in Taif, Saudi Arabia.

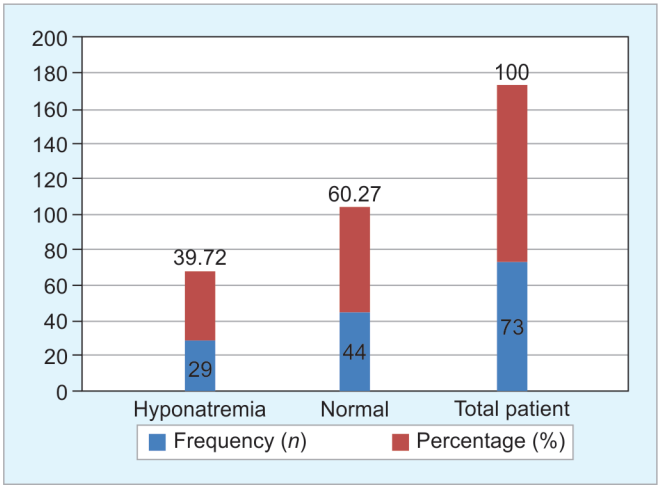

Fig.1: Number of cases of hyponatremia

The sample size was $N = 73$, which included only male participants. The following three groups were studied separately:

1. Antidepressant are taken by patients.
2. Antipsychotics taken by patients.
3. Mood stabilizers taken by patients.

The assessment of serum sodium levels collected over the last 5 years. The study included all inpatients meeting the inclusion criteria who were diagnosed with a psychiatric illness and receiving antidepressants, antipsychotics, mood stabilizers, or a combination of these psychiatric medications.

Research Instrument

An objective of this study was to determine the socio-demographic profile and pattern of hyponatremia among the study population in conjunction with psychotropic drugs such as antidepressants, antipsychotics, and mood stabilizers, as well as combinations of these drugs. Researchers filled out these forms while observing and evaluating hyponatremia patients receiving psychotropic medications. The researcher categorizes the symptoms into mild, moderate, and severe.

Data Analysis

The categorical variables were observed as percentages and numbers. After obtaining written informed consent, all patients age 30–75 who were taking psychotropic medications were interviewed. Consent was obtained in Arabic, which the patient understood, and they were free to accept or reject the study. In a study of 73 patients taking psychotropic medications, 29 had hyponatremia, while 44 displayed normal laboratory findings.

Results

This study was conducted on the chronic rehabilitation ward of the forensic psychiatric department. All the patients were male. Figure 1 shows the total number of psychiatric patients monitored was 73, of which 29 patients had hyponatremia (39.72%) and 44 patients were normal. Table 1 shows that 34.48% of our study population was between the ages of 46 and 55, followed by 27.58% between 30 and 45 years and 56 and 65 years. In our study, even though hyponatremia was seen in 29 patients, most of them were taking more than one psychotropic. Tables 3 to 6 show

Table 1: Age distribution of hyponatremia patients

Age groups in years	*Frequency (n)*	*Percentage (%)*
30–45	8	27.58
46–55	10	34.48
56–65	8	27.58
66–75	2	6.89
>76	1	3.44
Total	29	100.00

Table 2: Types of hyponatremia

Types of hyponatremia	*Frequency (n)*	*Percentage (%)*
Mild hyponatremia 130–134 mmol/L	13	44.82
Moderate hyponatremia 125–130 mmol/L	11	37.93
Severe hyponatremia <125 mmol/L	5	17.24

Table 3: Frequency of antidepressant intake

Antidepressant	*Frequency (n)*	*Percentage (%)*
Escitalopram	4	5.47
Mirtazapine	1	1.36
Total	5	6.84

Table 4: Frequency of various antipsychotics intake

Antipsychotics	*Frequency (n)*	*Percentage (%)*
Haloperidol	15	20.54
Aripiprazole	7	9.58
Risperidone	4	5.47
Amisulpride	4	5.47
Chlorpromazine	4	5.47
Olanzapine	3	4.10
Paliperidone	3	4.10
Quetiapine	1	1.36
Total antipsychotics	41	56.16

Table 5: Frequency of various mood stabilizer intake

Mood stabilizer (antiepileptic)	*Frequency (n)*	*Percentage (%)*
Valproic acid	6	8.21
Phenytoin sodium	2	2.73
Lithium	1	1.36
Carbamazepine	1	1.36
Total	10	13.69

Table 6: Frequency of both antidepressant and antipsychotics intake

Combination of antidepressant with antipsychotics	*Frequency (n)*	*Percentage (%)*
Escitalopram + haloperidol	2	2.73
Escitalopram + haloperidol + chlorpromazine	2	2.73
Mirtazapine + paliperidone + haloperidol	1	1.36
Total	5	6.84

Table 7: Frequency of hyponatremia in psychotropic

Psychotropic	*Total number*	*Percentage (%)*
Antidepressant	3	4.10
Antipsychotics	15	20.54
Mood stabilizer	7	9.58
Both antidepressants and antipsychotics	4	5.47
Total *N* = 73	29	39.72

Table 8: Symptoms of hyponatremia

Symptoms of hyponatremia	*Frequency (n)*	*Percentage (%)*
Asymptomatic	18	62.06
Loss of energy, drowsiness, and fatigue	8	27.58
Epileptic fit	2	8.89
Delirium or unconsciousness	1	3.44

hyponatremia detected in patients taking psychotropics based on frequency.

Of the 29 hyponatremia patients, 13 patients (44.82%) had mild hyponatremia (130–134 mmol/L), 11 patients (37.93%) had moderate hyponatremia, and 5 patients (17.24%) had severe hyponatremia (<125 mmol/L). It is depicted in Table 2. According to Table 3, the total number of patients taking antidepressants with the highest frequency was 5, with 6.84% of them taking escitalopram, which had the highest number at 5.47%. Total antipsychotics were taken by 41 patients (56.16%), with haloperidol taken by 15 (20.54%), aripiprazole taken by 7 (9.58%), and risperidone, amisulpride, and chlorpromazine taken by 4 patients (5.57%), as shown in Table 4.

There were ten mood stabilizers in total, with a frequency of 13.69%. As shown in Table 5, the maximum percentage was 6 (8.21%), all of whom were taking valproic acid. Table 6 shows that the most common treatment combinations of antidepressants and antipsychotics with the highest frequency were escitalopram, haloperidol, or chlorpromazine (2.73%). A combination of antidepressants and antipsychotics did not result in a significant increase in hyponatremia risk. Total antidepressant use is 4.10%, 20.54% on antipsychotics, 9.58% on mood stabilizers, and 5.47% on a combination of antidepressants and antipsychotics developing hyponatremia, as shown in Table 7. Table 8 shows symptoms of hyponatremia. Most of the hyponatremia patients were asymptomatic. The majority of the patients have experienced symptoms such as fatigue, drowsiness, and loss of energy. There was an epileptic fit in two patients and unconsciousness in one.

Discussion

The increasing prevalence and incidence of mental illnesses has resulted in the widespread use of psychotropic drugs. The purpose of this study was to monitor hyponatremia in patients treated with psychotropic drugs. Polypharmacy and combination therapy have become common treatment strategies among clinicians. In all age

groups, use of these psychotropic medications is variable, and there are various side effects. Such adverse reactions can lead to poor adherence to treatment and eventual failure. Antidepressants and antipsychotics have been associated with hyponatremia among psychiatric patients in several studies. The current study clearly illustrates how hyponatremia manifests in a target population based on demographics, type of drug used, and age of the patient.

There are many psychotropic drugs that can lead to hyponatremia, such as antidepressants and antiepileptics. It is most common to induce SIADH through this mechanism. There have been a variety of antipsychotic medications linked to SIADH, both typical and atypical. There is no clear mechanism by which antipsychotics cause SIADH. This hypothesis includes long-term blockage of the D2 receptor, resulting in enhanced D2 receptor sensitivity, which releases ADH.[22,23]

The incidence of hyponatremia in psychiatry patients, particularly those taking antidepressants like serotonin specific reuptake inhibitors (SSRIs), ranges between 0.5 and 25%,[24] even though it is not clear if any single SSRI has a higher risk of hyponatremia than the others.[25] It has been found that citalopram and escitalopram are the most commonly prescribed SSRIs for hyponatremia. In our study, we also found that elderly patients taking escitalopram had a greater risk of developing hyponatremia by about 5.47%. Other studies have also suggested that elderly SSRIs taken by psychiatric patients lead to hyponatremia.[26]

The role of antipsychotic drugs (APDs) in inducing hyponatremia is less conclusive than that of other psychotropics. In the 1970s, the first case of hyponatremia was reported under treatment with APDs. Among APDs, haloperidol impairs free water excretion by the patient.[27] Hyponatremia can be caused by both polypharmacy and individual antipsychotics. Initially, individual antipsychotics are the cause of hyponatremia; however, after the patient's psychotic symptoms and further evaluation, polypharmacy becomes the cause. In our study, hyponatremia developed in the majority of haloperidol-taking patients 15 (20.54%). Hyponatremia is more likely to occur in patients receiving typical antipsychotics than in those receiving atypical antipsychotics.[28] A recent case-control study found that the use of typical antipsychotics was more likely to lead to hospitalization due to hyponatremia than atypical antipsychotics.[29] Several studies have documented rechallenges and subsequent reoccurrences of hyponatremia due to APDs such as haloperidol, quetiapine, and aripiprazole.[30]

The study's limitations are as follows:

- The dose of medications was not mentioned in this study.
- Psychiatric diagnoses were not mentioned in this study.
- Female participants were not included in this study, as the study was done on the male chronic rehabilitation ward.
- We did not analyze diet, infection, water intake, exercise, diarrhea, vomiting, or injury, all of which are factors that could influence serum sodium levels.
- The duration of psychotropic medications was not assessed. It was reported that sodium levels were affected within 6 weeks of starting psychotropic medications.

Conclusion

In the present study, hyponatremia was identified as a potential adverse drug reaction associated with antidepressants and antipsychotic medications. The condition most commonly occurs during the first few weeks of treatment but can persist for several months. Hyponatremia is largely unrecognized and overlooked, due to which it is not treated properly in psychiatric patients. Antipsychotic drugs should be prescribed with awareness of adverse side effects, signs, and symptoms. Many psychiatric patients are asymptomatic, but some develop potentially life-threatening symptoms like seizures, coma, and delirium. We recommend that psychotropics be prescribed at the lowest effective dose, serum sodium levels should be monitored regularly, and the signs and symptoms of hyponatremia should be monitored throughout treatment.

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