Recognizing Medical Complications of Psychiatric Treatment: A Case of Antipsychotic-Induced SIADH

Kyra Colston, Maggie Sutton, Mia Trueblood, Carli Cahill, Lia Hiestand
Indiana University School of Medicine, Indianapolis Indiana

INDIANA UNIVERSITY SCHOOL OF MEDICINE

BACKGROUND

Hyponatremia is a serious electrolyte disturbance requiring prompt recognition and treatment. It is defined as:

- Serum sodium level <135 mmol/L
- Severe at serum sodium levels at <125 mmol/L

Consequences of hyponatremia range from mild symptoms such as dizziness, nausea, vomiting, and headache to serious signs such as delirium, seizure, encephalopathy, and coma.

Patients with psychiatric conditions like schizophrenia are at an increased risk for hyponatremia due to psychogenic polydipsia and medication-induced syndrome of inappropriate antidiuretic hormone secretion (SIADH).

Hyponatremia is estimated to affect 4% of patients with schizophrenia not treated with antipsychotic medications and 10% of patients with schizophrenia treated with antipsychotic medications.

Women > 60 years old are at the highest risk for developing antipsychotic-induced hyponatremia.

Hyponatremia has been reported to increase risk of mortality in psychiatric patients by 55% and substantially increase healthcare costs.

CASE REPORT

68-year-old female with schizoaffective disorder depressive type was admitted to psychiatric care with worsening auditory and visual hallucinations (AH/VH) due to medication noncompliance.

Paliperidone palmitate injections were restarted.
Clozapine was restarted at 50 mg and slowly titrated biweekly with a plan to reach her previous dose of 300 mg daily.

Although AH/VH improved over several weeks, when clozapine dose reached 150 mg BID, she began experiencing:

- Extreme polydipsia – Drinking from sink while on fluid restriction
- Extreme polyphagia - Finding extra food in the trash, 25-pound weight gain since admission
- Repeat vomiting - Due to speed of eating and drinking

Labs were repeated due to concern for psychogenic polydipsia:

- **Serum sodium = 106 mmol/L**

At this time, **mental status was unchanged** and pt denied:

- headaches, dizziness, nausea, abdominal pain, muscle cramping

She was promptly transferred to the ER for electrolyte repletion via 1g sodium chloride TID

- **Urine osmolarity was high - consistent with SIADH**

Pt was still exhibiting increased appetite and thirst. Clozapine was reduced to 100mg BID with clinical improvement, so titration continued to 50 mg BID, 50mg QHS, then stopped entirely.

After clozapine reduction, serum sodium = 138 mmol/L

HYPONATREMIA IN PYSCHIATRIC DISORDERS

Normal physiology of antidiuretic hormone (ADH):

Development of hyperosmolar or hypovolemic state → Posterior pituitary releases ADH → ADH binds principal cells in the late distal tubules and collecting ducts of the kidneys, increasing aquaporin insertion into the apical membrane → Increased resorption of water by the kidney corrects hyperosmolarity or hypovolemia → ADH secretion is downregulated

Normal physiology of thirst:

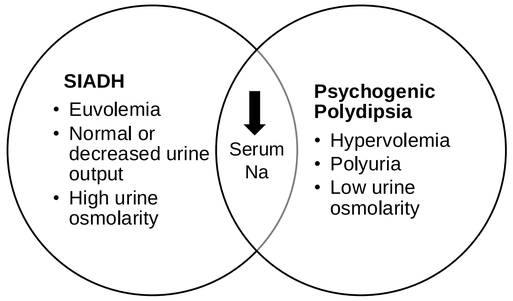
Intracellular or extracellular dehydration → Forebrain detects changes in osmolarity via subfornical organ and organum vasculosum of the lamina terminalis + Hypovolemic detected by macula densa and various baroreceptors, activating RAAS → Activation of lamina terminalis triggers activation of SNS, release of ADH, and generation of thirst → Drinking behavior is increased, brain terminates thirst

Syndrome of Inappropriate ADH Secretion (SIADH)

- ADH is released in excessive unregulated quantities due to various causes (such as effects of antipsychotic medication)
- Excess water resorption by the kidney creates a dilutional hyponatremia

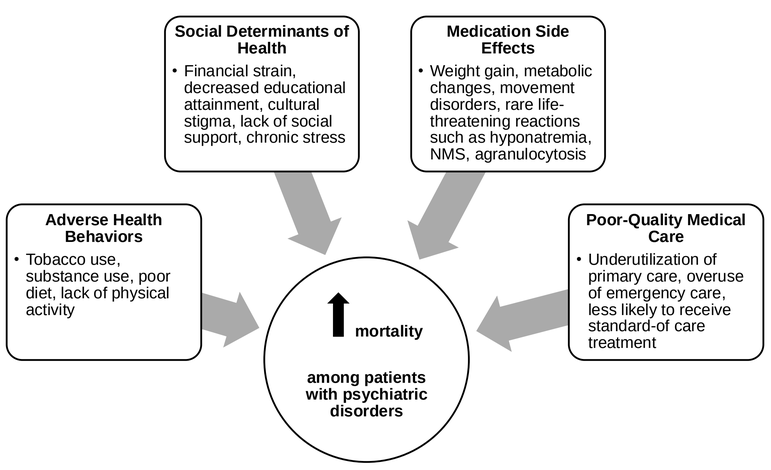
Psychogenic Polydipsia

- Imbalance of neurotransmitters due to psychiatric condition cause dysregulation of thirst center
- Excessive water intake exceeds the excretory capacity of the kidneys and creates dilutional hyponatremia

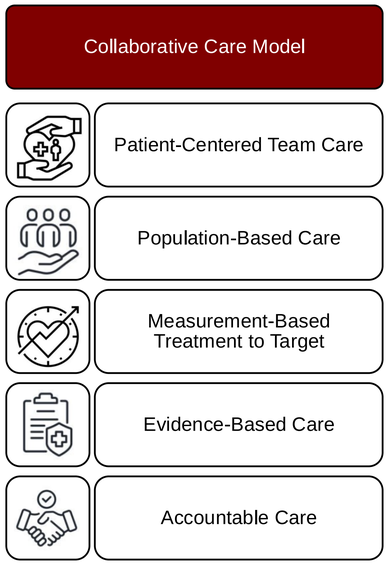


MENTAL AND PHYSICAL HEALTH

Patients with psychiatric conditions are estimated to die 25 years earlier than the general population, at least in part due to higher-than-average rates of general medical illness. Druss et al. summarizes factors that may contribute to increased mortality:



Integration of behavioral health and general medical services has been shown to improve patient outcomes. The American Psychiatric Association supports the evidence-based Collaborative Care Model.



DISCUSSION

This case illustrates the **importance of high quality and consistent care for patients with psychiatric disorders**, as their complex needs can mask hidden medical issues. SIADH caused by antipsychotics like clozapine is just one example of serious complications that could go unrecognized without thorough monitoring. **Integrated care models** that address mental and physical health are vital to ensure comprehensive assessment, prevent oversight of critical medical concerns, and improve overall outcomes.

This case also illustrates the importance of **maintaining a broad differential** for hyponatremia in the setting of a psychiatric disorder while also ensuring **prompt correction of electrolyte abnormalities**. A patient with a psychiatric condition should not be assumed to have psychogenic polydipsia. This patient likely had long-standing hyponatremia, as evidenced by her mild symptoms despite a serum sodium level of 106 mmol/L. Implementation of coordinated psychiatric and medical care through a Collaborative Care Model may have resulted in earlier correction of this patient's hyponatremia and reduced healthcare costs.

CONCLUSIONS

- Hyponatremia is a serious electrolyte disturbance requiring prompt recognition and treatment, affecting 10% of patients with schizophrenia receiving treatment with antipsychotic medication
- SIADH secondary to clozapine is a rare and easily overlooked cause of hyponatremia in patients receiving psychiatric treatment
- It is crucial that patients with symptoms of hyponatremia, especially women > 60, are not assumed to have psychogenic polydipsia, which is more often associated with psychiatric disorders
- Many patients with psychiatrics disorders do not receive adequate, standard-of-care treatment for general medical conditions
- Behavioral health and general medicine should be integrated to improve outcomes for patients with psychiatric conditions

REFERENCES

1. Ali SN, Bazzano LA. Hyponatremia in Association With Second-Generation Antipsychotics: A Systematic Review of Case Reports. Ochsner J. 2018 Fall;18(3):230-235. doi: 10.31486/toj.17.0059. PMID: 30275787; PMCID: PMC6162139.
2. American Psychiatric Association. Learn About the Collaborative Care Model [Internet]. [cited 2025 Feb 24]. Available from: https://www.psychiatry.org/psychiatrists/practice/professional-interests/integrated-care/learn
3. Cuzzo B, Padala SA, Lappin SL. Physiology, Vasopressin. [Updated 2023 Aug 14]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK526069/
4. Druss, B. G., Chwastiak, L., Kern, J., Parks, J. J., Ward, M. C., & Raney, L. E. (2018). Psychiatry's Role in Improving the Physical Health of Patients With Serious Mental Illness: A Report From the American Psychiatric Association. *Psychiatric services (Washington, D.C.)*, *69*(3), 254–256. https://doi.org/10.1176/appi.ps.201700359
5. Kotagiri R, Kutti Sridharan G. Primary Polydipsia. [Updated 2023 Jul 24]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK562251/
6. Leib DE, Zimmerman CA, Knight ZA. Thirst. Curr Biol. 2016 Dec 19;26(24):R1260-R1265. doi: 10.1016/j.cub.2016.11.019. PMID: 27997832; PMCID: PMC5957508.
7. Mazhar F, Battini V, Pozzi M, Invernizzi E, Mosini G, Gringeri M, Capuano A, Scavone C, Radice S, Clementi E, Carnovale C. Hyponatremia Following Antipsychotic Treatment: In Silico Pharmacodynamics Analysis of Spontaneous Reports From the US Food and Drug Administration Adverse Event Reporting System Database and an Updated Systematic Review. Int J Neuropsychopharmacol. 2021 Jul 14;24(6):477-489. doi: 10.1093/ijnp/pyab005. PMID: 33575781; PMCID: PMC8278799.
8. Pliquett RU, Obermüller N. Endocrine Testing for the Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH) [Updated 2022 Dec 22]. In: Feingold KR, Anawalt B, Blackman MR, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK279055/