



Empagliflozin Raises Sodium in SIADH Patient, Enabling Timely Surgery

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Abstract

Empagliflozin, a selective sodium-glucose cotransporter 2 (SGLT2) inhibitor, induces osmotic diuresis via glucosuria and may represent a novel therapeutic approach for managing syndrome of inappropriate antidiuretic hormone secretion (SIADH). This case report details the successful use of empagliflozin to correct persistent hyponatremia in a 78-year-old man with SIADH, awaiting elective abdominal surgery for hernia repair over several months. The patient, who had a history of hypertension and multinodular thyroid goiter with normal thyroid function tests, continued to experience low serum sodium levels despite discontinuing enalapril, previously used for hypertension management. An extensive evaluation confirmed a diagnosis of SIADH, with sodium levels initially ranging between 124 and 128 mmol/L. Traditional management, including fluid restriction, failed to normalize his sodium levels, leading to repeated cancellations of his scheduled surgery due to persistent hyponatremia. In October 2023, treatment with empagliflozin was initiated, leading to a gradual increase in sodium levels. Within 3 weeks, his serum sodium had normalized to 134 mmol/L, accompanied by a rise in serum osmolality. As a result, the elective surgery was successfully performed without complications. These findings suggest that empagliflozin, in combination with fluid restriction, offers a promising treatment option for improving sodium levels in patients with SIADH, helping avoid unnecessary delays in elective surgical interventions.

Keywords

- ▶ empagliflozin
- ▶ SIADH
- ▶ hyponatremia
- ▶ SGLT2 inhibitor

Introduction

Syndrome of inappropriate antidiuretic hormone secretion (SIADH) is a predominant cause of hyponatremia, but the available treatment options are limited and often challenging. Management of SIADH involves correcting the hyponatremia and treating the underlying cause once identified. The cornerstone of treatment is fluid restriction, typically limiting intake to approximately 1,000 mL per day. In more severe

or symptomatic cases, hypertonic saline (3% NaCl) may be administered, particularly in acute hyponatremia, to rapidly and safely correct sodium levels.

Pharmacologic options include the use of vasopressin receptor antagonists (vaptans) such as tolvaptan, which directly counteracts the effects of excess antidiuretic hormone (ADH), promoting water excretion without significant loss of sodium. Tolvaptan has shown efficacy in treating

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hyponatremia due to SIADH, particularly in the cases where fluid restriction alone is insufficient. However, its use requires careful monitoring due to the risk of overcorrection, which can lead to osmotic demyelination syndrome.

Other treatments may include demeclocycline, which induces nephrogenic diabetes insipidus to increase water excretion, or loop diuretics combined with sodium chloride to enhance free water clearance. Despite these options, treatment remains challenging due to the potential complications associated with overcorrection, making careful monitoring essential.

Recently, the selective sodium-glucose cotransporter 2 inhibitor (SGLT2 inhibitor) empagliflozin has emerged as a potential treatment for hyponatremia in SIADH. Empagliflozin works by blocking the SGLT2 in the kidneys, reducing glucose reabsorption and promoting its excretion in the urine (glycosuria).¹ This process induces osmotic diuresis, leading to increased free water excretion, which can help correct hyponatremia.

Several case studies have suggested that SGLT2 inhibitors, including empagliflozin, may be effective in managing chronic SIADH-induced hyponatremia.^{2,3} Based on a search of recent literature, there have been approximately 10 published studies and clinical trials focusing on the use of empagliflozin in treating SIADH, indicating its growing interest as a novel treatment option. These studies highlight the potential of SGLT2 inhibitors as a novel therapeutic option, particularly in patients who are refractory to conventional treatments such as fluid restriction. However, further research is needed to fully establish the efficacy and safety profile of SGLT2 inhibitors in this setting. This case is particularly valuable as it demonstrates the practical use of empagliflozin in a real-world clinical setting, highlighting its effectiveness in preventing delays in surgery.

Case Description

A 78-year-old man with a history of hypertension and multinodular thyroid goiter with normal thyroid function tests presented to the clinic with persistent hyponatremia. His serum sodium levels had consistently ranged between 124 and 128 mmol/L since January 2023. Despite discontinuation of enalapril in September 2023, which he had been taking for hypertension, his sodium levels remained persistently chronically low.

Further evaluation of the patient's hyponatremia revealed that he met the criteria for SIADH, which had been diagnosed at another hospital when he presented with hyponatremia during a routine workup for an incisional hernia, including a short Synacthen test. The criteria typically used to diagnose SIADH include the following:

- Hyponatremia: Serum sodium concentration is usually less than 135 mmol/L.
- Hypo-osmolality: Serum osmolality less than 275 mOsm/kg.
- Inappropriately concentrated urine: Urine osmolality is typically greater than 100 mOsm/kg, which is inappropriate given the low serum osmolality.
- Increased urine sodium: Urine sodium concentration is often greater than 40 mmol/L, indicating that the kidneys are excreting sodium normally despite low serum sodium levels.
- Euvolemia: Absence of clinical signs of volume depletion or overload.
- Absence of adrenal and thyroid disease: Normal adrenal and thyroid function, as determined by appropriate testing.

The patient was not taking any other medications that could contribute to his persistent hyponatremia. The patient's medication history included enalapril 20 mg daily for hypertension, which was initiated in 2002 and discontinued in September 2023. Rivaroxaban 20 mg was taken for atrial fibrillation since June 2014, while atorvastatin 20 mg was started in July 2019. Additionally, the patient had been on diltiazem 240 mg for hypertension since 2002.

On September 20, 2023, his laboratory results showed a serum sodium level of 128 mmol/L, urine sodium of 124 mmol/L, urine osmolality of 439 mOsm/kg, and serum osmolality of 259 mOsm/kg. A computed tomography (CT) scan of the chest and abdomen performed in May 2022 was normal. Despite fluid restriction, his sodium levels remained low. The patient reported no symptoms such as nausea, vomiting, polydipsia, polyuria, or weight gain. His random cortisol level was 300 nmol/L (sample taken after 11,00 hours), indicating no evidence of adrenal insufficiency considering that a previous short Synacthen test was done in another hospital. Thyroid function tests, including serum thyroid-stimulating hormone (TSH) at 1.2 mIU/L (normal reference range: 0.27–4.2 mIU/L) and free thyroxine (FT4) at 15 pmol/L (normal reference range: 12–22 pmol/L), were within normal limits.

The patient's mobility was limited due to hip osteoarthritis and an incisional hernia, for which he was awaiting surgery. Unfortunately, his surgery was postponed due to persistent hyponatremia. At his clinic visit, his weight was 87.9 kg, with a body mass index (BMI) of 26, and his blood pressure was 157/78 mm Hg. When measured at home, he was able to maintain a blood pressure within target range, averaging 130/70 mm Hg without the use of antihypertensive medication.

After discussing his condition in the clinic, we decided to initiate treatment with empagliflozin 10 mg once daily on October 26, 2023 (day 1). At the time of initiation, his serum sodium level was 126 mmol/L, with normal renal function. Frequent monitoring of his blood tests was performed to assess the effect of this intervention. Three days following the initiation of treatment, serum sodium levels increased to 129 mmol/L. Repeat tests on November 22, 2023 (day 27) showed that his sodium levels had normalized at 134 mmol/L (► Fig. 1). The patient tolerated the medication well with no reported side effects.

Sodium level, Blood

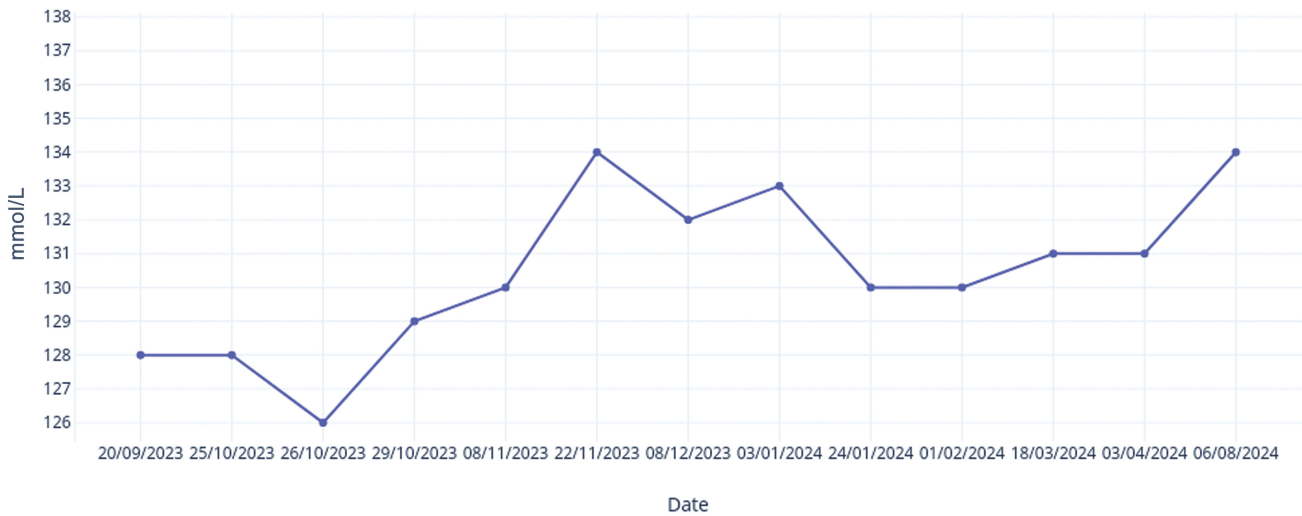


Fig. 1 Illustration of the changes in blood sodium levels over time.

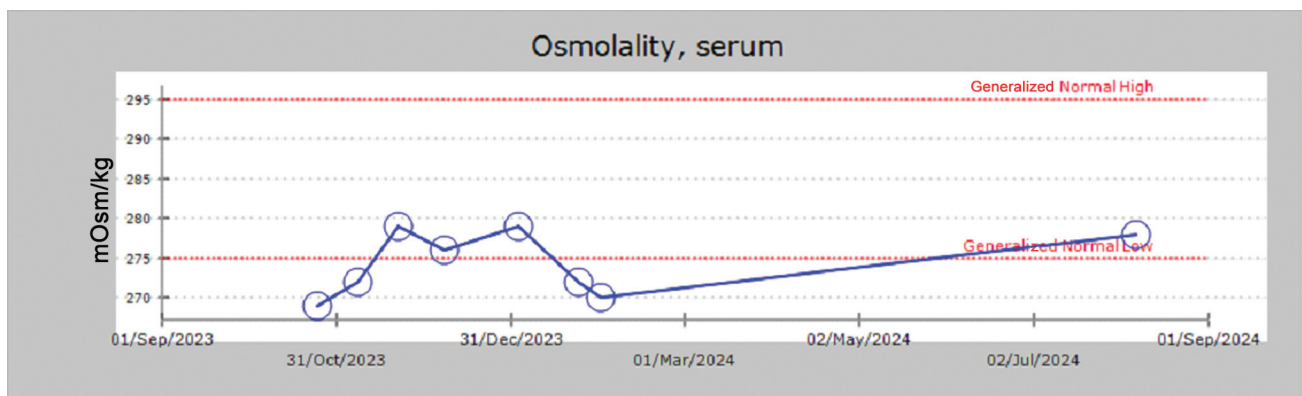


Fig. 2 Illustration of the changes in serum osmolality over time.

Empagliflozin was briefly discontinued after sodium levels normalized, but follow-up testing showed a subsequent decrease in serum sodium, suggesting that continued therapy was necessary to maintain normal sodium levels.

Follow-up blood tests in August 2024 showed normalization of his serum sodium to 134 mmol/L, an increase in serum osmolality to 278 mOsm/kg (► **Fig. 2**), and a rise in urine osmolality to 621 mOsm/kg, with the remainder of his blood tests remaining within normal ranges.

Discussion

While previous studies have demonstrated the efficacy of empagliflozin in increasing serum sodium levels in patients with both acute and chronic SIADH, this case adds value by documenting the use of empagliflozin to stabilize sodium levels in a patient awaiting elective surgery, a context not commonly emphasized. In line with previous findings, empagliflozin induced a significant increase in sodium levels over a short period, resolving hyponatremia and allowing the

patient to undergo surgery without complications. This case is particularly valuable as it highlights the practical application of empagliflozin in a real-world clinical scenario, showing its benefit in avoiding surgery delays, something not explicitly covered in prior trials.

Conclusion

This case illustrates the successful use of empagliflozin in treating persistent hyponatremia secondary to SIADH in a patient with limited mobility awaiting surgery. The patient's sodium levels normalized with empagliflozin therapy, allowing for the possibility of proceeding with the delayed surgery. This case adds to the growing body of evidence supporting the use of SGLT2 inhibitors in managing hyponatremia associated with SIADH.

Ethical Statement

No ethical approval is required for single case report.

Authors' Contributions

Both authors drafted and/or critically revised the report. K. A. treated the patient in the clinic and gathered the data and M.G. performed the literature review. Both the authors read and approved the final version of the manuscript.

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None.

Conflict of Interest

None declared.

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