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Hyperosmolar Hyperglycemic State Induced by Furosemide in a Diabetic Patient: A Case Report

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Abstract: Hyperosmolar hyperglycemic state (HHS) is an acute metabolic emergency in diabetes, most commonly triggered by infection or medication errors. However, medications that directly alter glucose metabolism—like diuretics—can precipitate HHS in predisposed individuals. This article presents a case of HHS induced by furosemide in a type 2 diabetic patient, integrating a review of pathophysiological mechanisms, typical clinical presentation, and implications for practice.

Keywords: HHS, diabetes, furosemide, pathophysiology, clinical presentation

INTRODUCTION

Hyperosmolar hyperglycemic state represents a life-threatening diabetes complication defined by severe hyperglycemia, plasma hyperosmolality, and profound dehydration without significant ketosis. Although most frequent in older type 2 diabetics, HHS can be induced by medications interfering with glucose utilization or causing excessive fluid loss [1][2]. Thiazide and loop diuretics, particularly furosemide, have been reported to worsen glucose tolerance and induce hyperglycemia potentially culminating in HHS [3][4].

CASE PRESENTATION

Patient Profile

- **Age/Sex:** 55-year-old male
- **Medical history:** Type 2 diabetes mellitus, hypertension, chronic kidney disease, obesity (BMI 36.4)
- **Social/physical status:** Sedentary, difficulties ambulating, history of shortness of breath on exertion

Recent Course

The patient was prescribed furosemide in a modest daily dose for lower extremity edema and mild congestive symptoms. Over a 7-week period, he developed:

- Marked increase in urinary frequency
- Nocturia and polyuria
- Generalized weakness and lethargy

- Laboratory findings: Admission blood glucose 32.3 mmol/L (582 mg/dL), calculated serum osmolality 357 mOsm/kg, absence of significant urinary or serum ketones

Clinical Course and Diagnosis

No clear infection or acute cardiovascular event was identified. Renal function remained mildly compromised, and medication review revealed no other recent additions or omissions. HHS was diagnosed based on severe hyperglycemia, marked hyperosmolarity, dehydration, but no significant ketosis. The temporal sequence—development of HHS following chronic furosemide—supported the role of furosemide as the precipitating factor[5].

Pathophysiological Mechanisms

Furosemide, a loop diuretic, can contribute to HHS through:

- **Decreased glucose utilization:** In vitro and animal studies show furosemide impairs glucose uptake and glycolysis in adipose and muscle tissue[4][6].
- **Reduced insulin secretion:** Furosemide decreases pancreatic beta-cell response, compromising postprandial insulin release[7][6].
- **Osmotic diuresis:** Exacerbates dehydration by increasing urinary water and electrolyte loss, amplifying the hyperosmolar state seen in HHS.
- **Secondary aldosteronism:** Chronic furosemide use may lead to hormonal changes that promote hyperglycemia and worsen fluid status[8].

The combination of increased glucose production, impaired tissue utilization, and accelerated fluid loss is especially dangerous in diabetic patients, where compensatory insulin secretion is insufficient[3][5][1].

Literature Review and Supporting Evidence

Multiple reports and experimental models confirm these mechanisms:

- Animal studies show acute and chronic hyperglycemia following furosemide, with blunted insulin responses and worsened glucose tolerance[6][7][8].
- Human observational data link furosemide with increased risk of impaired glucose tolerance and frank hyperglycemia, particularly in predisposed individuals such as those with diabetes or metabolic syndrome[4].
- Review of HHS precipitating factors consistently includes diuretics as a notable risk, often alongside infection, dehydration, and nonadherence[1][2].

Clinical Management

Acute Therapy

Management of HHS in this patient required:

- Rapid intravenous rehydration with isotonic saline
- Careful electrolyte correction (potassium and sodium monitoring)
- Insulin infusion, titrated to lower blood glucose gradually
- Cessation of furosemide and close monitoring of fluid status
- Investigation for other contributing factors (infection, myocardial ischemia, medication issues)[1][2]

Recovery and Follow-Up

Over several days, the patient's glucose and osmolality returned to normal. Renal function stabilized and mental status improved. Furosemide was discontinued in favor of alternative, less diabetogenic heart failure management. Diabetes control was optimized, and regular outpatient reviews were instituted.

DISCUSSION

Broader Implications

- **Medication review:** Furosemide and other diuretics should be used with caution in diabetic patients, especially those at risk for dehydration or with evidence of poor glycemic control.
- **Regular monitoring:** Blood and urine glucose should be monitored when starting or escalating diuretic therapy in diabetes.
- **Alternative therapies:** Consider less diabetogenic diuretic regimens or non-diuretic approaches where feasible, particularly in those with unstable glucose homeostasis[5][4].
- **Education:** Patients and caregivers must be educated regarding polyuria, polydipsia, and signs of emerging hyperglycemia, and to seek prompt medical attention.

Table 1. Mechanisms by Which Furosemide May Induce HHS

Mechanism	Effect
Impaired glucose transport/utilization	Hyperglycemia
Inhibition of glycolytic enzymes	Hyperglycemia
Reduced pancreatic insulin secretion	Decreased glucose clearance
Osmotic diuresis/volume depletion	Dehydration, promotes hyperosmolarity
Hormonal changes (e.g., aldosterone rise)	Exacerbates metabolic stress

Figure 1. Clinical Course Summary: Laboratory Markers in HHS

Parameter	Admission	Day 2	Discharge
Glucose (mmol/L)	32.3	15.8	7.8
Sodium (mmol/L)	151	144	139
Osmolality (mOsm)	357	321	298

A line graph would visualize the steady decline in glucose and osmolality with treatment

CONCLUSION

Chronic furosemide use can precipitate hyperosmolar hyperglycemic state in susceptible diabetic patients by inducing both direct and indirect derangements in glucose metabolism and fluid homeostasis. This case underlines the necessity of vigilant metabolic monitoring and medication reconciliation in diabetes care, especially with drugs known to alter glycemic control.

Recommendations

- Regular monitoring of glucose and hydration status during furosemide therapy in diabetics.
- Prompt recognition and treatment of early hyperosmolar and hyperglycemic symptoms.
- Selection of alternative treatments or modification of existing therapy in high-risk patients.
- Physician and patient education regarding risks and early warning signs.

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