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Case Report

Hypertension and Severe Hypokalemia Associated With Oral Ingestion of Topical Hydrocortisone Cream

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ABSTRACT

Background: Topical use of corticosteroids causes systemic effects, but systemic toxicity by ingesting topical corticosteroid cream has not been reported. We describe a patient admitted with ingestion of over-the-counter (OTC) hydrocortisone cream.
Case Report: A 64-year-old woman presented with 2-weeks of generalized weakness. She had a history of hypertension, anxiety, depression, and chronic fatigue syndrome, but medical records were unavailable and she was not on any medications. She reported taking prednisone 7.5 mg daily for several years, which was discontinued 5 months ago. Due to worsening symptoms, she started ingesting OTC topical hydrocortisone as replacement and admitted to consuming 2 squirts of 1% hydrocortisone cream twice daily over the previous month leading up to hospitalization. Her pulse rate was 77/min, blood pressure was 232/110 mmHg. There was no pedal edema, elevated jugular venous pressure, hirsutism, muscle wasting, or purplish skin striae. Labs revealed potassium 1.5 mg/dL (3.6-5.4), serum cortisol 61.5 μg/dL (2.3-19.4), Creatine Kinase 1864 IU/L (24-173), undetectable adrenocorticotropic hormone. She received potassium, labetalol, and intravenous fluids. Her serum cortisol level decreased to 11 μg/dL and potassium to 4.1 mg/dL within 24 hours. She left the hospital against medical advice on Day 2.
Discussion: Although both prednisone and hydrocortisone have glucocorticoid properties, only hydrocortisone has mineralocorticoid properties. Hydrocortisone 20 mg provides a mineralocorticoid effect equivalent to 0.1 mg fludrocortisone.
Conclusion: Hydrocortisone cream was confirmed as the source of exogenous corticosteroid by an undetectable adrenocorticotropic hormone and rapid decrease in cortisol following discontinuation. Incorrect use of OTC medications can lead to life-threatening side effects.

Introduction

There has been an increase in the use of Food and Drug Administration (FDA)-unregulated over-the-counter (OTC) drugs recently.[1] These drugs can potentially cause clinically significant interactions with prescription medications, and incorrect dosing and usage can lead to toxicity.[2] Topical OTC hydrocortisone preparations are meant for external use only. Cases of systemic toxicity due to topical overuse of these creams have been reported, but there are few if any reports describing the ingestion of OTC hydrocortisone approved only for topical use. This report presents a woman hospitalized with severe hypertension, life-threatening hypokalemia, and rhabdomyolysis following ingestion of topical hydrocortisone cream.

Case Report

A 64-year-old woman presented with a 2-week history of progressive generalized weakness, myalgia, and lack of concentration. She had a history of hypertension, anxiety, depression, and chronic

Abbreviations: ACTH, Adrenocorticotrophic hormone; FDA, Food and Drug Administration; OTC, Over-the-counter.

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fatigue syndrome as reported by her, but no medical records were available and she was not on any prescription medications per preference. She reported taking prednisone 7.5 mg daily for several years in the past for chronic fatigue syndrome attributed to underlying adrenocortical insufficiency, but no outside medical records were available to corroborate the same, and she was unable to provide a coherent history. Prednisone was discontinued 5 months ago when she switched to a new primary care physician. Due to worsening symptoms, she started ingesting OTC topical hydrocortisone cream in view of a lack of access to prednisone a few weeks after it was discontinued. Over the preceding month of her hospitalization, she reported ingestion of 2 squirts of OTC 1% hydrocortisone cream twice daily, allegedly amounting to a total of 3 tubes of 1 oz each. She was not willing to divulge how she decided to obtain topical hydrocortisone as a possible replacement for prednisone. The exact quantity of consumption could not be accurately determined, nor could she confirm the same. Her weakness, lethargy, and myalgia symptoms worsened with the topical cream ingestion, which necessitated a visit to the emergency department. She denied licorice or any herbal supplement ingestion. She had no recent weight changes, leg swelling, acne, or easy bruising.

On examination, her pulse was 77/min, and her blood pressure was 232/110 mmHg. She had no pedal edema, elevated jugular venous pressure, muscle wasting, hirsutism, purplish skin striae, cushingoid habitus or facies, or focal neurological deficits.

The serum potassium was 1.5 mg/dL (3.7-5.2 mg/dL), serum creatinine of 1.07 mg/dL (0.7-1.3 mg/dL), serum cortisol of 61.5 μg/dL (2.3-19.4 μg/dL), serum creatine kinase (CK) of 9864 U/L (24-173 U/L), undetectable serum adrenocorticotropic hormone (ACTH, <1 pg/mL), serum aldosterone (<15 mg/dL), and plasma renin activity of 0.242 ng/mL (0.167-5.380 ng/mL/h) was noted. Electrocardiogram was notable for a prolonged QT interval of 617 milliseconds and T-wave inversions in the precordial leads.

She received potassium replenishment, intravenous labetalol, and hydralazine for blood pressure control, along with intravenous normal saline. Her serum cortisol improved to 11 μg/dL within 24 hours of admission. Her potassium levels also improved to 4.1 mg/dL, with a sustained response on sequential monitoring. Her blood pressure improved to 118/70 mm Hg without any further antihypertensive requirement. CK levels were found to be uptrending from 9864 U/L to 12,940 U/L 24 hours post-admission.

She left against medical advice on Day 2 of hospitalization and was lost to follow-up.

Discussion

We present a 64-year-old woman who presented with severe hypertension, hypokalemia, rhabdomyolysis, and an elevated serum cortisol level with suppressed ACTH, signifying a hypercortisolism state, attributed to the ingestion of topical hydrocortisone. Although cases of systemic toxicity due to overuse of these creams have been reported, there are few if any reports describing hypercortisolism due to ingestion of the same. She self-reported ingesting tubes of OTC topical hydrocortisone as a replacement for lack of access to her chronic prednisone therapy. However, how she decided to use hydrocortisone as a replacement for prednisone could not be determined. Given the clinical presentation, history of ingestion of topical corticosteroids and suppressed ACTH level, a diagnosis of exogenous corticosteroid toxicity was considered.

Prednisone and hydrocortisone are both synthetic corticosteroids, but they have a significant difference in that hydrocortisone has mineralocorticoid properties and can lead to aldosterone-independent overstimulation of the mineralocorticoid receptors resulting in hypertension and hypokalemia; whereas, prednisone has no significant mineralocorticoid activity.[3,4] This severe hypokalemia can precipitate rhabdomyolysis, which could explain her generalized weakness and myalgia.

We conclude that, given the suppressed serum renin and aldosterone levels, the patient had renin–aldosterone independent mineralocorticoid receptors activation from exogenous hypercortisolism.[3,5] The ingested hydrocortisone cream as the source of exogenous corticosteroids is supported by an undetectable serum ACTH and the rapid decrease in serum cortisol following its discontinuation.[4] The absence of clinical features of hypercortisolism suggested a short duration of ingestion.

The normal dose of hydrocortisone for adrenocortical insufficiency is typically 15 to 25 mg daily, taken in divided doses, with a total daily requirement dependent on body surface area, calculated by 6 mg/m^2/day.[6] However, each tube of 1% hydrocortisone cream (1 oz) contains 284 mg of synthetic cortisol. She would have, thus, ingested 852 mg of cortisol (213 mg prednisone equivalent) over the last 1 month prior to her hospitalization. It remains up to speculation if the number of tubes she reportedly ingested is correct.

Excessive licorice ingestion can lead to similar manifestations, which is a constituent of several OTC herbal supplements used for adrenal fatigue.[7] Licorice causes acquired mineralocorticoid excess from the inhibition of 11β-hydroxysteroid and 5β-reductase, leading to increased cortisol locally in the kidneys to stimulate mineralocorticoid receptors.[5,7] Because there is no systemic hypercortisolism with licorice ingestion, suppression of ACTH does not occur. Our patient had denied ingestion of licorice.

According to guidelines for reporting adverse drug reactions, we classify this case as “dose-related and time-related.” In this class, adverse drug reactions are described as uncommon, related to cumulative dose, and may require the removal of the offending agent.[8] Causality was assessed as “certain” due to the plausible temporal relationship, and unable to be explained by concurrent disease or medications.[8]

All the major classes of OTC medications have the potential to cause adverse effects, such as acetaminophen (liver injury), Nonsteroidal anti-inflammatory drugs (GI ulcers and renal damage), and cough preparations (anticholinergic effects). The risk for medication misuse highlights the importance of reviewing package inserts and labels before taking OTC medications, which acts as a

Highlights

- Glucocorticoids cause hyperaldosteronism by activating mineralocorticoid pathway.
- A history of steroid ingestion with suppressed ACTH points to exogenous toxicity.
- Package inserts of topical medications do not contain adequate information.
- OTC steroid creams are a potent source of hydrocortisone

Clinical Relevance

This case describes the occurrence of severe hypokalemia and hypertension by mineralocorticoid receptor activation through hypercortisolism, attributed to ingestion of over-the-counter topical hydrocortisone cream. It is important for clinicians to be aware of the potential side-effects of these medications, and to increase awareness amongst the patients regarding potential risks of ingestion.

critical source of information, but little data about factors related to label reading are available.[9] Studies have shown that the average grade level of education necessary to understand the material on the labels was above the eighth-grade reading level, and only 75% of the participants read them. The reasons for reading labels included learning how to take the medication, side effects, symptoms affected or treated by the medication, and medication ingredients.[10]

While some labels on OTC corticosteroid creams mention the risk of nausea and gastrointestinal irritation if orally ingested, many do not mention any risks following oral ingestion. This, combined with a lack of scrutiny and poor interpretation of the written information, can often pave the way for adverse events. Enhancing the labels with pictorial representations demonstrating the potential adverse effects of ingestion can be beneficial.

Conclusion

There is an urgent need to enhance patient education and modify existing warning labels on OTC hydrocortisone creams with pictorial representations to highlight potential risks of ingestion in the setting of poor compliance with label reading and interpretation.

Disclosure

The authors have no multiplicity of interest to disclose.

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