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Dronabinol-induced diabetic ketoacidosis

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Introduction

The therapeutic potential of cannabinoids has been widely studied and their use has been approved for many purposes especially in the areas of pain management and palliative medicine [1]. Dronabinol (Marinol) is an FDA approved cannabinoid used to treat anorexia among immune-compromised patients [2]. Although its side effect profile has been extensively investigated, dronabinol has not been previously linked to diabetic ketoacidosis (DKA) [2]. Herein, we report the first case to our knowledge of dronabinol-induced DKA in the literature. The case highlights the importance of examining the association between dronabinol and DKA considering increased drug utilization.

Case report

A 62-year-old woman with long-standing history of uncontrolled type 1 diabetes mellitus complicated by peripheral neuropathy and gastroparesis, presented to the hospital with a 3-month history of worsening nausea, vomiting and 30-lb weight loss. Her home insulin regimen consisted of glargine 15 units daily, and lispro 6 units prior meals. Her pre-admission hemoglobin A1c was 8.8% (reference range: 4 - 5.6%). On initial presentation, she was found to be in DKA; her blood glucose (BG) was elevated at 293 mg/dL (reference range: 74 - 99 mg/dL), anion gap (AGAP) was 22 (reference range: 9 - 18 mmol/L) and serum beta-hydroxybutyrate (ketones) was 2.68 mmol/L (reference range < 0.28 mmol/L). She was started on intravenous insulin infusion to manage her DKA and was ultimately transitioned to subcutaneous insulin therapy after resolution of ketoacidosis. Her subcutaneous insulin regimen at the time consisted of 16 units of glargine daily, and 4 units of lispro prior to meals. In the subsequent 24 hours, her BG levels were well controlled in the range of 94 - 200 mg/dL. However, patient continued to experience nausea with intermittent episodes of vomiting related to her long-standing gastroparesis. To aid in the relief of her symptoms and assist with appetite stimulation, patient was started on dronabinol, in an off-label use, at 2.5 mg twice daily. After receiving three doses of dronabinol, patient reported worsening gastrointestinal symptoms, and her BG was found to be elevated at 451 mg/dL from baseline of 165 mg/dL the night prior. Her AGAP was elevated at 30 mmol/L from 16 mmol/L the day prior. Patient's dronabinol was discontinued and she was managed with insulin infusion until the DKA resolved, with no recurrence in the days following.

The endocannabinoid system has fascinated researchers in recent years as potential target for wide variety of illnesses [3,4]. Although no literature describes the association between cannabinoids and development of DKA, recent studies have highlighted a link between the use of dronabinol and gastroparesis. Cannabinoid receptors are found throughout the myenteric and submucosal neurons in the gastrointestinal tract [5]. Recent animal studies have shown that dronabinol acts as an agonist at the level of the gastrointestinal cannabinoid receptors leading to inhibition of peristalsis and increased gastrointestinal transit time [5]. These findings were further evaluated in a recent randomized, placebo-controlled study, where dronabinol was found to be associated with reduction in gastric emptying, particularly in female subjects, suggesting that the effect of cannabinoids on gastric motility may play a role in predisposition to DKA [6]. Since DKA continues to be an important cause of morbidity and mortality in patients with diabetes mellitus, the association between cannabinoids and DKA merits further investigation.

Disclosure statement

The authors declare that there is no conflict of interest regarding the publication of this paper.

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