Cannabis potentially reduces recurrent episodes of hereditary angioedema

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ABSTRACT

Hereditary angioedema (HAE) is a rare disease affecting an estimated 1 in 50,000 individuals in the United States. The clinical presentation involves recurrent episodes of angioedema, without urticaria or pruritus, in mucosal tissues of various organ systems. We present a case of HAE type II with concomitant use of cannabis that possibly decreased the frequency of his episodes of angioedema. Recent studies indicate that cannabis has an important role in regulating innate immunity and inflammatory responses through the inhibition of pro-inflammatory cytokines and upregulation of anti-inflammatory cytokines. These effects might reduce episodes of angioedema, but more research is needed.

Keywords: hereditary angioedema, cannabis, anti-inflammatory cytokines

INTRODUCTION

Hereditary angioedema (HAE) is a rare disease affecting an estimated 1 in 50,000 individuals in the United States (1 in 10,000 to 1 in 150,000 worldwide). Males and females are equally affected without any preference for ethnicity. The clinical presentation includes recurrent episodes of angioedema, without urticaria or pruritus, in mucosal tissues of various organ systems, including the skin, gastrointestinal tract, and respiratory tract. Excessive production of bradykinin causes potent vasodilation leading to significant edema. Symptoms are usually self-limited and resolve within 2-5 days without treatment. Patients may present with prodromal flu-like symptoms before attacks. Cutaneous manifestation includes non-pitting edema, commonly found in the extremities, face, and genitalia. Gastrointestinal attacks may present with nausea, vomiting, gastrointestinal colic, and/or diarrhea secondary to bowel edema. Laryngeal attacks are less common but can lead to life-threatening asphyxiation.

There are three types of HAE. The first two types are associated with autosomal dominant defects in C1 inhibitor (C1 INH). HAE type I is caused by deficiency of C1 INH. In HAE type II, C1 INH levels are normal or elevated; however, the functional C1 INH level is low. A third type of HAE has both normal C1 INH level and function. In this report, we will present a case of HAE type II with concomitant use of cannabis that possibly decreased his recurrent episodes of angioedema.

CASE PRESENTATION

A 23-year-old African-American man was transferred to University Medical Center in Lubbock, TX, for evaluation of angioedema. He has a past medical history of HAE type II diagnosed since the age of 13 at Iberia General Hospital in Louisiana. Episodes usually involved swelling of the extremities and groin that lasted for 2 to 3 days and resolved spontaneously. His face, throat, and abdomen were usually spared.
He had no family history of angioedema. He denied the use of NSAIDs, ACE inhibitors, narcotics, or any acute or prophylactic medications. He had an isolated history of intubation after consuming tomatoes at the age of 17. Epinephrine had no effect on his symptoms. His last severe attack was years ago. In the last few years, he has been smoking marijuana several times daily and noticed a reduction in the frequency of attacks.

In the past four months, he has experienced more frequent attacks. The patient attributed this to anxiety related to completing his college degree and less frequent use of marijuana. One week prior to transfer, he had spontaneous facial, lip, throat, and extremity swelling. He visited a local clinic and was prescribed an antibiotic without clinical response. He presented to Lea Regional Medical Center in Hobbs, NM, later that evening with ongoing facial and posterior oropharynx swelling along with dysarthria. He received intravenous diphenhydramine and methylprednisolone, was intubated for airway protection, and was then transferred to University Medical Center in Lubbock, TX. The Allergy/Immunology service was consulted, and C1 esterase inhibitor (Berinert™, CSL Behring, King of Prussia, PA) was administered. He had an excellent response and was extubated the next morning. He was discharged two days later but refused further management and follow up.

**Discussion**

The information available in this case does not strongly support a temporal relationship between the use of cannabis and a reduction in frequency of angioedema episodes. It did stimulate our interest and led to a review of possible effects of cannabinoids on immune pathways associated with angioedema. A previous case report provides similar evidence that cannabis helps control recurrent episodes of idiopathic angioedema. The use of cannabis by our patient may have been associated with a reduction in the frequency of hereditary angioedema. Cannabis could contain chemicals that minimize or control symptoms of HAE; however, the mechanism of action of this effect is not clearly understood.

Recent studies have demonstrated that cannabis has an important role in regulating innate immunity and inflammatory responses. Cannabinoids have systemic modulatory responses through activation of G protein-coupled cannabinoid receptors CB1 and CB2. CB1 receptors are widely distributed in the brain and produce psychoactive effects; CB2 receptors are expressed in immune and hematopoietic cells and mediate anti-inflammatory and immunomodulatory actions. Cannabinoids produce anti-inflammatory effects by the inhibition of pro-inflammatory cytokines and upregulation of anti-inflammatory cytokines.7

Bradykinin is an inflammatory mediator with potent vasodilatory effects. Excessive production of bradykinin is the main pathogenic mediator of hereditary angioedema. Although a relationship of cannabinoids and bradykinin has not been established, the anti-inflammatory properties of cannabinoids might minimize the recurrence of angioedema by decreasing endothelial vascular permeability in various tissues.8-10 We recommend more observational studies on the relationship between cannabinoid use and hereditary angioedema. In addition, basic science research is needed on the effect of cannabinoids on bradykinin production and endothelial vascular permeability.

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**References**

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