

A Novel Effective Therapy for Chronic Generalized Pruritus without Presence of Skin Lesions

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ABSTRACT

Rationale: There is evidence that the etiology of many skin disorders with or without obvious lesions may be secondary to excessive infiltration of irritants into the dermis causing inflammation. There is evidence that taking medications that release more dopamine from sympathetic nerve fibers may prove highly effective for treating a larger variety of skin disorders despite resistance to standard therapy. Data support the concept that dopamine acts to diminish cellular permeability thus inhibiting infiltration of excessive irritants.

Objective: to determine if dextroamphetamine, a dopaminergic drug, could relieve generalized pruritus' without skin lesions in a 30-year-old woman with 1 ½ years of pruritus.

Findings: The pruritus had moderately relieved shortly after treatment with 20mg amphetamine salts 11.6 mg dextroamphetamine sulfate (20mg amphetamine salts) and was completely eradicated with 23.2mg (40 mg amphetamine salts). In addition to the drug relieving her pruritus, she had a marked reduction in her fibromyalgia and dysmenorrhea and this probably helped to correct her infertility problems.

Conclusions: A literature search found only one previous case of improvement of generalized idiopathic pruritus but with treatment of dextroamphetamine in a menopausal woman. Her pruritus was ascribed possibly to dry skin related to menopause related to estrogen deficiency. Thus, this is only the second case of successful treatment of idiopathic generalized pruritus without skin lesions with dextroamphetamine sulfate, but the first one in a younger woman.

Keywords

Dextroamphetamine sulfate, Dopaminergic drugs, Generalized idiopathic pruritus, Increased cellular permeability.

Introduction

Pruritus, or itchy skin, is the most common cutaneous symptom [1]. It can be generalized or localized to a specific area of the body. Sometimes pruritus is associated with the presence of skin lesions in which case eczema is the most common cause. Characteristic skin lesions can lead to diagnoses ranging from viral disorders to urticaria. Skin biopsies of lesions causing pruritus may also be performed to indicate the cause and best treatment to alleviate symptoms.

The etiology of generalized chronic pruritus without skin lesions is frequently more difficult to ascertain. Chronic pruritus is considered when the problem lasts longer than 6 weeks. Without the presence of skin lesions, other underlying factors may be the cause, or there may be no known etiology.

One study evaluated 5,127 patients who were referred to their dermatology clinic and found 49 patients with generalized chronic pruritus without skin lesions [2]. Thus, chronic pruritus without skin lesions may represent only 1% of dermatologic complaints [2]. The rate of female to male patients was 58% to 42%. 44% were between the ages of 40-60 years, but women were found to have the age of onset 12 years earlier than males. The average

duration of pruritus was 37 weeks. This study also found that systemic disorders accounted for about 50% of the cases. The most commonly known factor was hypothyroidism (16.7%) associated with dry skin. The second most associated condition was diabetes mellitus (12.5%). The most serious underlying condition was malignancy (8%). Other causes to account for the remaining 12% included uremia and hyperbilirubinemia from chronic liver disease [2].

Thus, 50% of patients with generalized chronic pruritus without skin lesions have no known etiologic factor, and thus no specific therapy. Xerosis (dry skin) is a common manifestation of generalized idiopathic pruritus. Frequent moisturization is of some benefit, but yet sometimes moisturization could worsen pruritus [3]. Moisturization with warmer emollients lowers the threshold of receptors to factors causing itching, and so refrigerated emollients are more effective [4]. In lower concentrations, <5% menthol could help alleviate idiopathic pruritus symptoms by its cooling effects [5].

Gabapentin and pregabalin have been used with some benefit for idiopathic pruritus [6]. Interestingly behavioral therapies have provided benefit to alleviating pruritus in some cases by teaching the patients to consciously suppress the reflex to scratch through distraction and habit reversal [7].

There are case reports of quick marked improvement of long-term skin pruritic conditions, with associated skin lesions e.g., urticaria and eczema, following treatment with dextroamphetamine sulfate [8-12]. There has already been a case report of correction of long-term idiopathic generalized chronic pruritus without skin lesions with dextroamphetamine sulfate [13]. The case presented here is the second case report of marked improvement of chronic idiopathic chronic generalized pruritus without skin lesions following treatment with dextroamphetamine sulfate. The first reported case did have a potential known etiologic factor; i.e. dry skin related to estrogen deficiency in a woman with breast cancer taking an aromatase inhibitor [13]. This is the first reported case of controlling generalized idiopathic pruritus in a younger woman without dry skin.

Case Report

A 30-year-old female presented with generalized itching on her back and chest that eventually spread to her arms and abdomen gradually over a 3–6-month period. The pruritus had been present for 1 ½ years prior to her initial visit in our office. No dry skin or skin lesions were observed. The patient attempted to use diphenhydramine and cetirizine, but no relief was found. The itching sensation would start in the early evening and grow in intensity throughout the night. To rule out liver or gallbladder issues, the patient was seen by a gastrointestinal specialist, but no abnormal results were seen or recorded. Alongside these cutaneous symptoms, the patient also had flare-ups of fibromyalgia, intense menstrual cramps since her teen years, and edema that began 5 years prior to treatment. The patient had lower back pain, discomfort around the hips, and abnormal bloating

after meals. When treated with 20mg amphetamine salts (11.6mg dextroamphetamine sulfate), the patient reported a decrease in generalized itching from 3-4 times a week to only 1-2 times a week. With an increased dosage to 40mg amphetamine salts (23.2 mg dextroamphetamine sulfate) daily, the patient experienced no itching at all. A decrease in dysmenorrhea, complete resolution of severe bloating, and marked relief of fibromyalgia and back and hip pain was also reported. The patient recently completed the first trimester of her pregnancy and has continued treatment with dextroamphetamine sulfate. She had two years of primary infertility. Her only treatment was dextroamphetamine sulfate and luteal phase progesterone vaginal suppositories during the luteal phase and throughout the first trimester. Her generalized pruritus without skin lesions continued to be perfectly controlled, as is her backache and hip pain. No fibromyalgia or edema has been reported so far either. She had lost 10 pounds prior to becoming pregnant.

Discussion

One hypothesis to explain a lot of inflammatory conditions, including various skin disorders, is that certain tissues become more permeable allowing unwanted irritants to perfuse into the tissue [14]. The type of clinical conditions that result from the failure to block the infusion of unwanted elements may depend on genetic factors, local factors, and extrinsic factors e.g., viral infection and trauma according to the hypothesis [14]. The hypothesis continues that in some instances the condition ultimately results from an exaggeration of a mechanism that is present to promote normal conception. This mechanism allows the development of thin-walled spiral arteries during the luteal phase by autoimmune attack of certain designated thick-walled uterine arteries to develop thin-walled spiral arteries to allow nutrient exchange between mother and fetus. This mechanism of increased cellular permeability also allows infusion of protective cellular immune cells when the body is attacked by pathogens, and that mechanism is to block the biogenic amine dopamine [14,15]. One of the normal functions of dopamine is to diminish cellular permeability, and thus the treatment with dopaminergic drugs e.g., dextroamphetamine sulfate, bromocriptine, and cabergoline can diminish cellular permeability and correct many of these inflammatory and non-inflammatory conditions [16-20].

Increased cellular permeability not only provides a possible explanation for the patient's generalized pruritus, but also for her fibromyalgia and back pain. In an experiment done in 2017, 12 female patients with fibromyalgia performed a series of working memory tasks. Positron emission tomography (PET) with [¹⁸F] fallypride (FAL) was used to measure changes in dopamine during these tasks. The results showed that patients suffering from fibromyalgia had lower binding ability for cortical dopamine D2/ D3 receptors and extra striatal dopamine may have been altered [21]. If patients with fibromyalgia have a diminished dopamine binding ability, treatment with dextroamphetamine sulfate, a dopamine agonist, can be a possible mechanism of recovery. The patient discussed in the case study above may have had a decrease in her fibromyalgia-induced hip and back pain due to

dextroamphetamine sulfate increasing dopamine reception and reducing cell permeability. With fewer stimuli entering the cell, nociceptors will not be triggered as often leading to less pain. The patient's dysmenorrhea also could have been caused by a decrease in dopamine during her luteal phase related to suppression by progesterone.

Though there have been only two cases of generalized pruritus that have been treated with dextroamphetamine sulfate, the fact that both patients responded so well, and considering the long-term safely record of this drug with minimum number of side effects, we think that this amphetamine should be considered as first-line treatment for idiopathic generalized pruritus without skin lesions especially since other treatments have not been very effective. Since excessive chronic inflammation may also contribute to infertility, the combination of dextroamphetamine sulfate and progesterone may have helped this woman solve her infertility problem [22-24]. The benefits of dextroamphetamine treatment ameliorating fibromyalgia and backaches have also been previously reported [25-27].

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