Dihydrotestosterone may contribute to the development of migraine headaches

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Summary

Purpose: To evaluate the possibility that dihydrotestosterone (DHT) may play a role in the etiology of some people's migraine headaches. *Methods:* Finasteride 5 mg daily was given to a young woman with chronic migraines. *Results:* The chronic migraine headaches almost completely disappeared shortly following therapy. However, symptoms returned shortly after stopping the finasteride due to dry eyes. *Conclusions:* DHT may be an etiologic factor in causing migraines since finasteride suppresses DHT secretion. Alternatively, the benefit could be related to some other property of finasteride possibly by increasing testosterone which may compete with estrogen at the blood vessel level.

Key words: Migraine headaches; Finasteride; Dihydrotestosterone; 5 alpha reductase inhibitor.

Introduction

The obstetrician-gynecologist is frequently also considered the primary care physician for women. Thus the gynecologist is frequently asked for advice about conditions outside of the pelvic cavity. For example it is not unusual for a woman to complain about premenstrual headaches.

Headaches could also be caused by medication prescribed by the gynecologist. It is well known that oral contraceptives may cause headaches. In some instances this symptom may be eliminated or at least alleviated by reducing the dosage of estrogen and if this is ineffective then stopping the oral contraceptive and switching to some other mode of contraception.

Certainly the gynecologist can take the prerogative to refer the woman to a neurologist or internal medicine specialist for evaluation in order to exclude more serious etiologies and even for treatment. Frequently the therapy prescribed will be ergotamine derivatives, beta-blockers or topiramate or other similar drugs sometimes used for seizures. It would not be expected that all gynecologists would treat with these medications, though since primary care physicians do not automatically refer to a specialist unless an appropriate response to treatment fails to occur, it would not be wrong for the gynecologist acting as the primary physician to render this treatment.

However, just as the dermatologist has to be aware of medical conditions that present with certain skin disorders, the gynecologist has a similar responsibility, especially if headaches may be related to a disorder that would be more familiar to the gynecologist. One such entity is the defect related to sympathetic nervous system hypofunction known as the sympathetic neural hyperalgesia edema syndrome leading the infusion of chemicals and toxins into tissues that are normally impervious by the diminished permeability state rendered by inappropriate sympathetic tone.

This sympathetic nervous system disorder is the main etiologic factor for pelvic pain including chronic pelvic pain, mittelschmerz, dyspareunia, dysmenorrhea, vulvar pain, and interstitial cystitis [1]. It is associated with pain in many other areas of the body along with chronic fatigue syndrome, skin disorders, e.g., chronic urticaria, eczema, edema, and weight gain [2]. Frequently headaches, especially migraines, are related to this disorder [2-5].

Similar to pelvic pain disorders, migraine headaches respond very well to treatment with sympathomimetic amines even when they have failed to respond to the "standard" aforementioned therapies. The gynecologist should be aware that other pain syndromes may exist without pelvic pain being present. The gynecologist should also be aware that the predominant number of publications concerning this disorder has been in the gynecologic literature and not in neurology or internal medicine journals. Thus it is very likely that the treating neurologist will be unaware of this condition and prescribe less effective therapies with more side-effects or subject the woman to painful and expensive and sometimes risky diagnostic procedures. Thus it is reasonable for a gynecologist to provide first-line therapy for this sympathetic nervous disorder, and only if the headaches do not resolve, then the patient should be referred to a neurological expert.

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The case described below is another woman with migraines who responded fairly well to treatment with dextroamphetamine sulfate, the sympathomimetic amine of choice for treating these disorders. Her response was less complete than many other women previously treated before her. However in attempting to treat her androgen symptomatology, a new insight into a hormone involved in headaches may have been discovered and a possible new treatment for some individuals.

Case Report

A 21-year-old female presented with a desire to treat various symptoms including secondary amenorrhea, alopecia, hirsutism, and acne. She had previously been prescribed oral contraceptives but despite changing brands, multiple times she could not find any combination that did not cause weight gain and enlarged painful breasts.

Though the oral contraceptive exacerbated weight gain, she continued to gain weight despite dieting. Based on ultrasound showing the classic polycystic ovarian syndrome (PCOS) characteristics, a high luteinizing hormone (LH) to follicle-stimulating hormone (FSH) radio (LH 12 mIU/ml and FSH 5.0 mIU/ml) and a slightly elevated serum testosterone level of 58 ng/dl she was diagnosed with the PCOS syndrome.

Another complaint was chronic headaches that were worsened by oral contraceptives. She was advised that treatment with dextroamphetamine sulfate would likely improve her headaches and also help her to lose weight by inhibiting fluid retention [6]. However for the acne, hirsutism and alopecia spironolactone was advised.

She responded well to both dextroamphetamine amine sulfate (30 mg daily), lost weight, and her breasts were no longer tender. In addition she noted a marked improvement in her constipation and no longer had shortness of breath when climbing a flight of stairs. Her anxiety was also improved, and her energy markedly improved. The headaches improved by 50%. Eventually the headaches were 80-90% improved on the dextroamphetamine sulfate but did not completely disappear. Sometimes they were only 50% better. Hair loss also improved after the use of spironolactone.

The acne had improved on the spironolactone but was not completely gone. We added 5 mg of finasteride daily. The patient stopped the finasteride after one month because of the side-effects of dry eyes. She noted that during the month she took the finasteride her headaches which had been listed as a range of 1-10 as a 10 before dextroamphetamine sulfate became a 5 out of 10 following dextroamphetamine sulfate therapy. Interestingly the headaches diminished to a 1 while she was taking the finasteride. The headache intensity resumed to a 5 within a few days of stopping the finasteride.

Discussion

The patient was questioned as to whether any time during the 1 ¾ years she was treated with the dextroamphetamine sulfate there had been a period of time when the headaches abated to the degree she had following finasteride. Her answer was no.

Though the improvement in headaches could be coincidental, this case report suggests that dihydrotestosterone may have an etiologic role in some headaches in some people. Thus medications that are 5 alpha reductase inhibiters, e.g., finasterade or possibly dutasteride, may be tried in patients who are refractory to standard therapy or have side-effects from standard therapy.

The first time the benefit of sympathomimetic amines was to alleviate migraine headaches refractory to standard therapy the possibility that the improvement was merely fortuitous was considered [3]. However, it has subsequently been found to almost invariably improve migraine symptoms despite years of suffering and failure to respond to standard therapy. Indeed this young woman responded sufficiently well to sympathomimetic amine therapy that she resisted staying on the finasteride in an attempt to alleviate her dry eyes. She also resisted increasing the dosage of dextroamphetamine sulfate being satisfied with the improvement in headaches, energy, weight, and breast tenderness.

Finasteride suppresses the conversion of testosterone to dihydrotestosterone (DHT). Thus the response suggests that DHT may be an etiologic factor in some headaches in at least some patients. Possibly 5 alpha reductase inhibitors may prove to be another drug to use for treatment of refractory migraines.

The possibility exists that too much DHT was not the factor causing headaches. Instead by raising testosterone by blocking its conversion to DHT perhaps the increased testosterone inhibited estrogen from causing vasoconstriction with subsequent vasodilation leading to migraine headaches.

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