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Dextroamphetamine sulfate treatment eradicates long-term chronic severe headaches from temporomandibular joint syndrome - a case that emphasizes the role of the gynecologist in treating headaches in women

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Summary

Purpose: To test sympathomimetic amine therapy on another type of chronic headache syndrome - headaches from temporal mandibular joint (TMJ) syndrome. *Materials and Methods:* A woman with 20 years of severe daily pain from TMJ refractory to all therapies was treated with dextroamphetamine sulfate. *Results:* The woman showed immediate 100% relief from sympathomimetic amine treatment saving her from an expensive jaw breaking operation that was only given a slight chance of helping. *Conclusions:* Unfortunately most treating physicians are unaware of this defect of sympathetic nervous system hypofunction leading to the absorption of toxins, which when it involves brain tissue, leads to severe headaches. Thus, the gynecologist who is aware of this syndrome because sympathetic nervous system hypofunction is the most common cause of pelvic pain, may need to intervene in women with chronic headaches, even TMJ.

Key words: Sympathomimetic amines; Sympathetic neural hyperalgesia syndrome; Temporomandibular joint syndrome; Migraine headaches.

Introduction

Dislocation of the temporomandibular joint (TMJ) occurs when the mandibular condyle is displaced anteriorly beyond the articular surfaces and fixation in that joint, and represents 3% of all dislocated joints reported in the body [1]. Thus with TMJ, the condyle head is displaced out of the glenoid fossa but still remains within the capsule of the joint [2].

Teeth grinding and teeth clenching (bruxism) increases the wear on the cartilage lining of the TMJ and may lead to TMJ disorders. The TMJ syndrome may include any or all of the following symptoms: stiffness, headaches, ear pain, malocclusion (bite problems), clenching sounds or locked jaws. Approximately 80% of patients with TMJ disorder have the complication of headaches. Pain is caused while opening and closing the jaw [1, 2].

There is a disorder related to hypofunction of the sympathetic nervous system that is more common in women and is associated with a wide variety of chronic pain syndromes, including pelvic and bladder pain, gastrointestinal pain, musculoskeletal pain, and headaches [3, 4]. Treatment with the sympathomimetic amine dextroamphetamine sulfate usually leads to quick marked pain relief despite years of suffering and failure to respond to conventional therapy. A case is presented of a woman with long-standing chronic headaches that was believed to be related to TMJ from teeth grinding and clenching, that responded extremely well in a short time period to treatment with dextroamphetamine sulfate.

Case Report

A 41-year-old woman presented to the present reproductive endocrinology/infertility group for secondary infertility of one year duration with her new male partner. In her history it was noted that she suffered from chronic migraine headaches for over 20 years that was present every day and occurred in 60% of her waking hours. These headaches began in her first year of law school. From nervous anxiety she clenched her teeth. TMJ syndrome was confirmed by dental exam and radiological procedures and was thought to be the cause of her migraine headaches.

She advised us that she may need to delay further infertility testing for a couple months since she was scheduled for jaw surgery to try to fix the TMJ problem, to hopefully alleviate her headaches that had failed to respond to conventional medical therapy and to dental devices. She also cautioned us that she may be limited to infertility procedures covered by her insurance since the surgery performed by her doctor of dental surgery was going to be very expensive since she did not have dental insurance.

She was advised of the possibility that her headaches could respond to dextroamphetamine sulfate and that surgery could be avoided. She had such dramatic improvement with just 15 mg of

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dextroamphetamine extended release capsules that she cancelled surgery. Her headaches have for the most part completely resolved with 30 mg per day of the medication.

Discussion

Five interesting cases of chronic refractory migraines responding quickly and effectively to dextroamphetamine sulfate have been reported in Clinical and Experimental Obstetrics and Gynecology. Two cases were published in 2008 and case one involved a 33-year-old woman also presenting for secondary infertility [5]. The pain was unbearable and daily [5]. She had some of the other symptoms of the sympathetic neural hyperalgesia edema syndrome, e.g., nocturia and edema. One dose of ten mg dextroamphetamine release capsules completely removed the pain. On occasion they returned in a mild manner but with increasing the dosage to 30 mg, the headaches never returned [5].

The second case was a 45-year-old whose headaches were premenstrual and thus a pain specialist referred her to us to see if there was a hormonal connection [5]. The headaches, which could be as long as seven days premenstrual, were so intense that she was admitted to the hospital once for an overdose of narcotics. She failed to improve with luteal phase progesterone therapy or norethindrone acetate ten mg daily. After starting dextroamphetamine sulfate 20 mg per day, she reported for the first time in five years no premenstrual headaches. She has had complete relief for five years.

Sometimes to prove efficacy of a given therapy and to provide evidence that the improvement in symptoms following therapy was not merely fortuitous, one has to prove Koch's postulates, i.e., show that symptoms return with cessation of therapy and symptoms disappear again after therapy is reinitiated. Indeed one published case supports this concept and proves Koch's postulates. A 33-year-old woman with severe migraines failed to improve despite beta blockers, topirimate, and ergotamines [6]. She was presently taking 3,600 mg ibuprofen per day but still needed supplementation with oxycodone and acetaminophen but the pain only mildly improved. She came to the present reproductive endocrine practice because she was hoping to find an endocrinological connection since this woman who had been always thin started gaining weight at the same time as the headaches started. She gained 20% extra of her initial body weight over a couple years without changing dietary habits. We explained that the two symptoms were probably connected as she suspected and that she probably has the condition known as the sympathetic neural hyperalgesia edema syndrome related to a defect in cellular permeability that allows toxins and chemicals to absorb into brain tissue, related to hypofunction of the sympathetic nervous system. Also it allows leakage of intravascular fluid to a third space leading to edema and weight gain [7-9]. Once she reached a dosage of 45 mg/day of dextroamphetamine sulfate extended release tablets, her headaches were 100% relieved. The headaches improved before she lost weight, showing that the headaches were most likely from absorption of toxic chemicals into brain tissue rather than edema in a closed space. However, she eventually over one year lost 70 pounds [6].

This woman proved Koch's postulates in that she remained 100% improved for four years. She moved to another state that did not allow an off-label use of a class 2 drug so therapy ceased. Within a week the headaches resumed to their previous intensity. The pain was so severe and did not respond to analgesics that she even considered suicide. She went to another state for help where off-label use was permitted and she had 100% relief within three days [6]. She remains pain free for another 1.5 years.

One more unreported cause shows dramatic efficacy of sympathomimetic amine therapy for chronic headaches by proving Koch's postulates, but also illustrates why it is important for the gynecologist to play an active role in the diagnostic testing and treating of severe migraines. A 45-year-old woman with menorrhagia came for a consult. In taking her history she revealed 25 years of migraine headaches that had failed every "standard" treatment. Despite seeking the opinion of multiple neurologists, she decided on one who at least, in her opinion, gave her the reason for them, i.e., he suspected that this was the beginning of multiple sclerosis!! However, despite careful testing so far over 25 years, she never developed multiple sclerosis.

Since the headaches occurred many years before the menstrual irregularity began we did not think there was any connection to her menstrual disorders. She responded quickly and with 100% efficacy to treatment with dextroamphetamine sulfate. She kept her appointment with her neurologist after she was completely relieved of pain with dextroamphetamine sulfate. She was advised by the neurologist to stop the dextroamphetamine sulfate immediately because he was unaware of any controlled studies proving its efficacy!! She listened to him and stopped this treatment and the headaches recurred within two days. A month later, at the encouragement of her husband, she re-consulted us. She was re-started on the amphetamine and again her headaches quickly completely disappeared and have remained so for over a year.

The frequent but relatively unknown condition that is more common in women than men by a 10:1 ratio is more known to the gynecologist because it is the most common and most remediable cause of pelvic pain [1, 2, 10, 11]. Most articles dealing with the sympathetic neural hyperalgesia edema syndrome have been published in the gynecological literature, especially in Clinical and Experimental Obstetrics and Gynecology, which in contrast to many other peer reviewed journals, allows a greater amount of space for more in depth description of case reports.

To what extent should the gynecologist became involved with headaches? It certainly seems appropriate for the gynecologist to refer the women to a neurologist to exclude more serious etiologies, e.g., brain tumors or aneurysms, etc. If the neurologist does not find a serious etiology and prescribes therapy that is effective and does not cause side effects, the gynecologist does not need to intervene. If the gynecologist prefers, one could try to make the treating neurologists or internist aware of this disorder of sympathetic nervous system hypofunction and defer to the neurologist, if that specialist is willing to provide treatment with dextroamphetamine sulfate. If not, the gynecologist, who has assumed the role as the primary care physician for women, in our opinion, should then treat the patient themselves.

Other than brain tumors or other vascular space occupying lesions, are there any other types of conditions causing headaches that should not be treated with dextroamphetamine sulfate? A 34-year-old woman presented with severe headaches and papilledema [12]. Fortunately she was not found to have a tumor but instead was diagnosed with intracranial hypertension (pseudotumor cerebri) [12]. She had only mild relief from the combination of topiramate and acetazolamide. She came to our practice having moved from another state to take over her management for hypothyroidism. She complained in addition to the headaches of chronic fatigue, backache, and inability to lose weight. She was advised that hypofunction of the sympathetic nervous system could be the cause of the backache and the chronic fatigue and inability to lose weight despite dieting [9, 13, 14]. Dextroamphetamine sulfate therapy completely alleviated her headaches and chronic fatigue and backache within one month of therapy [12]. Several months later she returned for her appointment with the neuro-opthalmologist and advised her of the tremendous improvement with this new therapy. The specialist did not ask her any questions about this new therapy but merely did a fundoscopic examination, advised her that the papilledema was completely gone, and to return in six months for another fundoscopic examination. Thus, if the specialists are not interested in this new treatment, it behooves the woman's gynecologist, who should be her gatekeeper for medical problems, to institute therapy.

The case of intracranial hypertension illustrates another key point and that is that the gynecologist should be aware of all of the different clinical manifestations that are associated with the sympathetic neural hyperalgesia edema syndrome. The sympathetic nervous system controls the temperature regulation system. Dextroamphetamine sulfate has been found to be effective in treating vasomotor symptoms even in the presence of normal estrogen or in women with estrogen deficiency who are either reluctant to take estrogen or where it is contraindicated [15, 16]. Because of weight issues and fear of estrogen causing weight gain, a 44-year-old woman sought alternative therapy [17]. She also complained of severe headaches that would occur two weeks of the month, but each time she flew on an airplane (which were so severe she could not fly). Both her vasomotor symptoms and headaches completely disappeared following dextroamphetamine sulfate therapy and now she has no problem on airplanes [17].

Thus, to date, there does not seem to be any type of headaches, other than tumors or aneurysms that will not respond to dextroamphetamine sulfate. Even headaches related to TMJ syndrome seem amenable, as evidenced by the present case report. Of course one does not know for sure if the TMJ dislocation was responsible for the headaches or if she has a headache syndrome strictly from hypofunction of the sympathetic nervous system, and the TMJ by itself would not have caused headaches. Nevertheless, institution of dextroamphetamine sulfate saved this woman an expensive surgical procedure that involved breaking her jaw. The surgery that was offered was explained by the surgeon that there was only a small chance it would likely help her headaches.

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