

A novel effective treatment for menière's disease – dextroamphetamine sulfate

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Summary

Purpose: To determine if treatment with dextroamphetamine sulfate could ameliorate the symptoms of long-standing Menière's disease in a menopausal woman with a past history of dysmenorrhea. **Methods:** Dextroamphetamine sulfate was started at 9.4 mg extended release tablets and eventually increased to 18.8 mg (Adzenys®). **Results:** The symptoms of constant ear fullness and severe tinnitus abated and have not returned for 2 years. In addition, the edema of the fingers and ankles have abated along with an 11 pound weight loss. **Conclusions:** Menière's disease can be added to the long list of chronic treatment resistant conditions lumped together under the name of the increased cellular permeability syndrome. This syndrome may or may not be associated with pelvic pain. The common denominator is that these seemingly unrelated conditions affecting many organ systems all respond markedly well to amphetamine therapy. The hypothesis of the efficacy of dextroamphetamine sulfate is that it releases dopamine from sympathetic nerve fibers, which, in turn, diminishes cellular permeability.

Key words: Menière's disease; Increased cellular permeability syndrome; Dextroamphetamine sulfate; Dopamine; Dysmenorrhea.

Introduction

Menière's disease is a chronic condition manifested by episodic attacks of vertigo, tinnitus, fluctuating hearing loss, and pressure sensation in the ears related to endolymphatic hydrops of the inner ear [1]. The frequency is about 200 patients per 100,000 population. The average age is 30-60 years [1].

Menière's disease is at first progressive but fluctuating. The episodes can occur in clusters. They are not always associated with vertigo, but the vertigo may be severe interfering with normal activities. The tinnitus which is frequently described as a sound similar to ocean waves is usually persistent. Diminished hearing does not wane and eventually leads to significant hearing loss [1].

Many of the treatments are aimed at treating the vertigo attacks and they have marginal benefits. Wright performed a literature view concerning treatments of Menière's disease and made the following conclusions [2]. 1 – The combination of beta-histidine plus thiazide diuretic have unknown effectiveness. 2 – Intratympanic gentamicin may improve vertigo but its effect on other functions unclear. In fact, some evidence suggests it worsens hearing loss. 3 – Similarly, it could not be determined that intralymphatic corticosteroids have any benefit [2].

There are non-drug interventions to theoretically prevent attacks and delay disease progression, e.g., psychological support, vestibular rehabilitation, salt restriction and caffeine restriction, but these measures have unknown effec-

tiveness [2].

Increased cellular permeability with infusion of excessive irritants has been hypothesized to be the main cause of pelvic pain of various types including dyspareunia, mittelschmerz, dysmenorrhea, chronic backache associated with or without menses, and pelvic pain of bladder origin irrespective of the presence or absence of endometriotic implants [3]. The increased cellular permeability may be related to insufficient release of dopamine from sympathetic nerve fibers. One function of dopamine is to diminish cellular permeability. Infusion of toxic elements may not be restricted to pelvic tissues but may occur in various tissues in the body leading to various disorders [4]. The most recent term for all of the various chronic pathological conditions that are related to increased cellular permeability is the increased cellular permeability syndrome [5].

Thus women with pelvic pain symptoms may have other associated conditions [6, 7]. Recently Ramin-Wright *et al.* stated that pain from endometriosis is frequently associated with other problems, e.g., chronic fatigue syndrome, and that it behooves the treating physicians to treat all aspects of the woman's health issues not just the pelvic pain [8].

There appears to be one drug that is not only the most effective drug for treating pelvic pain, but also the various other conditions associated with pelvic pain, and that drug is dextroamphetamine sulfate [9-15]. This sympathomimetic amine is believed to work by releasing more dopamine from sympathetic nerve fibers [5, 15].

The case presented, herein, describes a woman with long-term dysmenorrhea, and long-term Menière's disease, who was treated with dextroamphetamine sulfate strictly for her Menière's disease since her amenorrhea from menopause had already corrected her dysmenorrhea.

Case Report

The patient was referred to our reproductive endocrinology, infertility practice specifically for her Menière's syndrome by another patient, who was aware of the increased cellular permeability syndrome, and the benefits of dextroamphetamine sulfate for various chronic treatment refractory conditions.

Her Menière's disease, diagnosed by an ear, nose, and throat specialist had been present for 12 years. She had only one episode of vertigo which lasted 3 months but it was severe, incapacitating, and required hospitalization. Fortunately it spontaneously remitted and never returned.

However, the audiology issues related to Menière's never abated. She described a constant fullness in her ears. Even more annoying was constant tinnitus, described as not only a ringing sound, but a whooshing sound, and a roaring sound like waves. She was very sensitive to loud noises and in movie theaters had to wear ear plugs.

The only other manifestation of the increased cellular permeability syndrome was edema of her ankles and fingers [5, 16]. She had noted, probably related to the edema that she had trouble losing weight despite dieting and moderate exercise [16].

She was started on dextroamphetamine sulfate and the dosage was increased to the present dosage of 18.8 mg.

Within a few months all of her auditory symptoms disappeared, and this remission has lasted 2 years so far. She has not had any vertigo attacks. Her hearing loss which had been deteriorating is stable by audiology examination.

Her edema also dissipated. Her initial weight for this 60 inch woman was 122 pounds. Associated with the abrogation of the edema was an 11 pound weight loss [16]. She is no longer dieting.

Discussion

Physicians are frequently greatly influenced by marketing techniques of pharmaceutical companies. Indeed, the newest therapy for pelvic pain, with or without endometriosis, is the oral gonadotropin releasing hormone antagonist elagolix [17, 18]. It is unlikely that there will ever be any randomized controlled studies comparing the efficacy in elagolix vs. dextroamphetamine sulfate for controlling pelvic pain because the use of dextroamphetamine sulfate is an off-label use and thus no pharmaceutical company can make a profit if such an expensive study demonstrated the superiority of the amphetamine in both efficacy and lack of side effects. Also, dextroamphetamine sulfate is available as a generic.

This case of Menière's disease, however, serves as a reminder that pelvic pain is frequently associated with other

chronic disorders. Therapies directed specifically for pelvic pain, including surgery, other than amphetamines, will still leave the woman suffering from other pathological conditions, whereas sympathomimetic amine therapy will usually correct all their conditions.

Most of the publications concerning the increased cellular permeability syndrome have been in the gynecologic literature. Thus, many physicians in other specialties are not aware of the benefits of amphetamine treatment for a large variety of chronic treatment refractory conditions. Patients are frequently thus subjected to needless expensive, invasive testing, and non-efficacious therapies that may have significant cost and side effects. Thus, it is important as new manifestations of the increased cellular permeability syndrome become apparent, e.g., Menière's disease, that the gynecologist, who is frequently the family practitioner for women, consider treating with sympathomimetic amines first before referring to other specialists.

It should be noted that not all manifestations of the increased cellular permeability syndrome are associated with pelvic pain in the present or even the past as in the patient described. Thus, if a woman coming for routine check-up mentions suffering from conditions as diverse as headaches, urticaria, chronic fatigue, inflammatory bowel disease, arthritis, fibromyalgia, edema, unexplained weight gain, etc., the gynecologist should consider offering treatment with dextroamphetamine sulfate, even if the area of pathology, e.g., the inner ear of a woman, seems outside their normal scope of therapy [15].

Ethics Approval and Consent to Participate

This patient gave her informed consent for inclusion before she participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Cooper Institute for Reproductive Hormonal Disorders, P.C.

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Conflict of Interest

The authors declare no conflict of interest.

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References

- [1] Gurkov R., Pyyko L., Zou J., Kentala E.: "What is Menière's disease? A contemporary re-evaluation of endolymphatic hydrops". *J. Neurol.*, 2016, 263, S71-S-81.
- [2] Wright T.: "Menière's disease". *BMJ Clin. Evid.*, 2015.
- [3] Check J.H., Wilson C., Cohen R.: "A sympathetic nervous system disorder of women that leads to pelvic pain and symptoms of interstitial cystitis may be the cause of severe backache and be very responsive to medical therapy rather than surgery despite the presence of herniated discs". *Clin. Exp. Obst. Gyn.*, 2011, 38, 175-176.

- [4] Check J.H., Cohen R., Katsoff B., Check D.: "Hypofunction of the sympathetic nervous system is an etiologic factor for a wide variety of chronic treatment-refractory pathologic disorders which all respond to therapy with sympathomimetic amines". *Med. Hypoth.*, 2011, 77, 717-725.
- [5] Check J.H.: "Changing the name of a syndrome: sympathetic neural hyperalgesia edema syndrome becomes – the increased cellular permeability syndrome". *Clin. Exp. Obst. Gyn.*, 2017, 44, 819-823.
- [6] Check J.H., Cohen R.: "The triad of luteal phase ocular migraines, interstitial cystitis, and dyspareunia as a result of sympathetic nervous system hypofunction". *Clin. Exp. Obst. Gyn.*, 2014, 41, 575-577.
- [7] Check J.H.: "Increased tissue permeability and sympathetic nervous system hypofunction may be the common link between dysmenorrhea, chronic pelvic pain, Mittelschmerz, and Crohn's disease". *Clin. Exp. Obst. Gynecol.*, 2016, 43, 112-113.
- [8] Ramin-Wright A., Kohl-Schwartz A.S., Geraedts K., Rauchfuss M., Wolfler M.M., Haeberlin F., *et al.*: "Fatigue – a symptom in endometriosis". *Hum. Reprod.*, 2018, 33, 1459-1465.
- [9] Check J.H., Wilson C.: "Dramatic relief of chronic pelvic pain with treatment with sympathomimetic amines – case report". *Clin. Exp. Obstet. Gynecol.*, 2007, 34(1), 55-56.
- [10] Check J.H., Katsoff B., Citerone T., Bonnes E.: "A novel highly effective treatment of interstitial cystitis causing chronic pelvic pain of bladder origin: case reports". *Clin. Exp. Obst. Gyn.*, 2005, 32, 247-249.
- [11] Check J.H., Cohen G., Cohen R., Dipietro J., Steinberg B.: "Sympathomimetic amines effectively control pain for interstitial cystitis that had not responded to other therapies". *Clin. Exp. Obst. Gyn.*, 2013, 40, 227-228.
- [12] Check J.H., Cohen R.: "Marked improvement of vulvovaginitis of unknown origin in a pediatric patient – case report". *Clin. Exp. Obst. Gyn.*, 2014, 41, 723-724.
- [13] Check J.H., Jaffe A.: "Resolution of pelvic pain related to adeno-myosis following treatment with dextroamphetamine sulfate". *Clin. Exp. Obstet. Gynecol.*, 2015, 42, 671-672.
- [14] Check J.H., Cohen R.: "Chronic pelvic pain – traditional and novel therapies: Part II medical therapy". *Clin. Exp. Obst. Gyn.*, 2011, 38, 113-118.
- [15] Check J.H.: "Sympathomimetic amines are a safe, highly effective therapy for several female chronic disorders that do not respond well to conventional therapy". *Clin. Exp. Obst. Gyn.*, 2015, 42, 267-278.
- [16] Check J.H., Shanis B.S., Shapse D., Adelson H.G.: "A randomized comparison of the effect of two diuretics, a converting enzyme inhibitor, and a sympathomimetic amine on weight loss in diet-refractory patients". *Endoc. Pract.*, 1995, 1, 323-326.
- [17] Ezzati M., Carr B.R.: "Elagolix, a novel, orally bioavailable GnRH antagonist under investigation for the treatment of endometriosis-related pain". *Womens Health (Lond)*, 2015, 11, 19-28.
- [18] Taylor H.S., Giudice L.C., Lessey B.A., Abrao M.S., Kotarski J., Archer D.F., *et al.*: "Treatment of endometriosis-associated pain with elagolix, an oral GnRH antagonist". *N. Engl. J. Med.* 2017, 377, 28-40.

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