Marked improvement of pain from long term fibromyalgia with dextroamphetamine sulfate in a woman who failed to improve with conventional pharmacologic treatment

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Summary

Purpose: To determine if treatment with the sympathomimetic amine dextroamphetamine sulfate, which has been so effective in treating a variety of pain syndromes, including severe pelvic pain and interstitial cystitis in women with the sympathetic neural hyperalgesia edema syndrome would also mitigate pain from fibromyalgia which was resistant to multiple therapies. *Materials and Methods:* Dextroamphetamine sulfate extended release capsules once daily was gradually increased to 25mg per day in a woman with treatment resistant fibromyalgia of 20 years duration. *Results:* Within a short time, the woman experienced dramatic relief of pain. Furthermore, her edema improved resulting in a 27 pound weight loss and her chronic fatigue improved. *Conclusions:* Fibromyalgia can be effectively treated with an innocuous dose of dextroamphetamine sulfate.

Key words: Sympathetic nervous system; Fibromyalgia; Sympathomimetic amines; Dextroamphetamine sulfate.

Introduction

There is a common defect of the sympathetic nervous system found more commonly in women that is associated with chronic pelvic pain, dyspareunia, dysmenorrhea, vulvovaginitis, backache, and interstitial cystitis [1-4]. One of the main functions of the sympathetic nervous system is to diminish cellular permeability. It has been hypothesized that various pain syndromes even outside of the pelvis may be attributed to the absorption of chemicals and toxic factors into the tissues (which leads to pain) [5-14]. In fact the elicitation of pain by installation of potassium in the urinary bladder is one of the ways to diagnose interstitial cystitis [15].

The purpose of the present study was to present another unique presentation for this disorder of sympathetic nervous system hypo-function – severe fibromyalgia responding extremely well to treatment with the sympathomimetic amine dextroamphetamine sulfate.

Case Report

A 36-year-old woman sought the authors' medical opinion on why she has not been able to lose weight despite dieting. She was wondering if there could be an endocrinological disorder causing the problem.

She stated that following a traumatic brain injury following a fall 20 years ago, she began gaining considerable weight and over 20 years had gained 100 pounds. Not only was weight gain an issue but she had amnesia for much of her life before the injury and developed severe fibromyalgia which persisted for 20 years. All parts of her body developed hyperalgesia so that even the water from a shower hurt (allodynia).

She was surprised to hear that the authors' opinion was that there was probably a connection between her unexplained weight gain and her fibromyalgia. They explained about the defect in the sympathetic nervous system that leads to increased cellular permeability and that it can lead to weight gain from the inability to compensate to the increase in hydrostatic pressure which would lead to translocation of fluid from intravascular to extravascular space were it not for a signal from the sympathetic nervous system causing a decrease in capillary permeability [16, 17]. She was advised that a controlled study proved the efficacy of treating this orthostatic edema with dextroamphetamine sulfate rather than conventional diuretics [18]. The reason why conventional diuretics fail to improve the edema is that they work predominantly on the ascending limb of Henle and to some degree the distal tubule, whereas the increased capillary permeability causes the fluid to extravasate from the proximal tubule. Dextroamphetamine sulfate, a sympathomimetic amine, replaces the defective neurotransmitter for the sympathetic nervous system and restores sympathetic activity, which allows these afflicted people to maintain body homeostasis by inhibiting capillary permeability when exposed to the increase in hydrostatic pressure [18].

Though the condition was originally termed idiopathic orthostatic cyclic edema [16-18], association with various pain syndromes has resulted in a change of name to the sympathetic neural hyperalgesia edema syndrome [1, 8]. The woman presently was taking five oxycodone-acetaminophen tablets per day. She had failed to respond to a multitude of treatments which in the early days included guaifenesin, non-steroidal anti-inflammatory drugs, and glucocorticoids none of which provided effective relief.

Subsequently she was treated with the tricyclic antidepressant amitriptyline and the dopamine receptor agonist ropinirole which also did not relieve the pain.

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Finally she was treated with the newer balanced dual serotonin and norepinephrine receptive inhibitor duloxetine without relief of pain.

The final therapy that failed and in fact caused her more edema and weight gain was the anticonvulsant pregabalin which is in the family of alpha-2 delta-ligands known to have analgesic, anxiolytic, and anticonvulsant activity.

Within one month of treatment with 15 mg extended release capsules once daily of dextroamphetamine sulfate, she had improvement in her generalized pain which was reduced by 70%. Raising the dosage to 25 mg decreased the pain as she said tremendously to a degree that she could completely discontinue her opioid treatment. She also had lost 27 pounds in six months from 241 pounds to 214 pounds.

Discussion

Fibromyalgia syndrome is theorized to function as an abnormal central processing pain disorder which involves afferent augmentation of peripheral stimuli, especially of the nociceptive types and a variety of neuropathic qualities with symptoms which include pain, fatigue disturbances, and alteration of cognitive/mood [19]. The pain is frequently described as a generalized tenderness without synovitis accompanied by allodynia, hyperpathia, and hyperalgesia [19]. Fibromyalgia has a prevalence of two to four percent of the general population and appears to be a genetic dysregulation with potential alteration in normal neuroendocrine, neuromodulation, neurotransmitter, biochemical, and neuroreceptor function and physiology [19].

The pathophysiology of fibromyalgia involves abnormal levels of serotonin and neuroepinephrine (a sympathomimetic amine) which are key neurotransmitters in endogenous pain inhibiting pathways [20, 21].

The treatment of fibromyalgia employs a multidisciplinary team effort using combined treatment approaches, including patient education, aerobic exercise, cognitive behavior therapy and pharmacologic therapies (serotonin norephinephrine receptive inhibitors) (e.g., duloxetine, milnacripram) and alpha 2-delta receptor ligands (e.g., pregabalin) may improve symptoms as well as function of patients with fibromyalgia [19-22].

Though not her main complaint, the patient described having chronic fatigue. She said it was hard to separate pain and fatigue. As mentioned, fatigue is frequently part of the fibromyalgia syndrome. However, fatigue with or without pain may be part of the sympathetic neural hyperalgesia edema syndrome [23].

Dextroamphetamine sulfate is very well tolerated in general and in dosages up to 30 mg per day, is not addicting and can be stopped suddenly without dependence. Especially in women, e.g., the case described, it should be prescribed in women with a history of edema or weight gain over alpha-2 delta ligands, e.g., pregabalin which is notorious for causing edema and weight gain [22].

References

[1] Check J.H., Cohen R.: "Chronic pelvic pain – traditional and novel therapies: part II medical therapy". *Clin. Exp. Obst. Gyn.*, 2011, *38*, 113.

[2] 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.

[3] Check J.H., Wilson C.: "Dramatic relief of chronic pelvic pain with treatment with sympathomimetic amines – case report". *Clin. Exp. Obstet. Gynecol.*, 2007, *34*, 55.

[4] 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.

[5] Leskowitz S.C., Shanis B.S., Check J.H.: "Resolution of atypical chest pain during treatment for idiopathic orthostatic edema". *Am. J. Gastroenterol.*, 1990, *85*, 621.

[6] Boimel P., Check J.H., Katsoff D.: "Sympathomimetic amine therapy may improve refractory gastroparesis similar to its effect on chronic pelvic pain – case report". *Clin. Exp. Obstet. Gynecol.*, 2007, *34*, 185.

[7] Check J.H., Cohen R.: "Successful treatment of a female with chronic pseudo-intestinal obstruction with sympathomimetic amines and thyroid hormone replacement". *Clin. Exp. Obst. Gyn.*, 2010, *37*, 115.

[8] Check J.H, Katsoff B., Cohen R.: "A case report showing that a woman with ulcerative colitis refractory to standard therapy responded well to the sympathomimetic amine dextroamphetamine sulfate". *Inflam. Bowel Dis.*, 2011, *17*, 870.

[9] Check J.H., Katsoff B., Cohen R.: "A novel highly effective medical treatment of severe treatment refractory Crohn's disease using sympathomimetic amines – case report". *Inflam. Bowel Dis.*, 2010, *16*, 1999.

[10] Boimel P., Check J.H.: !Marked improvement of intractable arthritic pain in a woman with rheumatoid arthritis with sympathomimetic amine treatment despite previous failure with standard therapy and possible implications for last trimester unexplained fetal demise – case report". *Clin. Exp. Obst. Gynecol.*, 2007, *34*, 254.

[11] Check J.H., Check D., Cohen R.: "Sympathomimetic amine therapy may markedly improve treatment resistant headaches related to a vascular permeability defect common in women". *Clin. Exp. Obst. Gyn.*, 2009, *36*, 189.

[12] Check J.H., Cohen R., Check D.: "Evidence that migraine headaches in women may be related to a common defect in the sympathetic nervous system as evidenced by marked improvement following treatment with sympathomimetic amines". *Clin. Exp. Obst. Gyn.*, 2011, *38*, 180.

[13] Check J.H., Cohen R.: "Marked improvement of headaches and vasomotor symptoms with sympathomimetic amines in a woman with sympathetic hyperalgesia-edema syndrome". *Clin. Exp. Obst. Gyn.*, 2011, *38*, 88.

[14] Check J.H., Katsoff D., Kaplan H., Liss J., Boimel P.: "A disorder of sympathomimetic amines leading to increased vascular permeability may be the etiologic factor in various treatment refractory health problems in women". *Med. Hypothesis*, 2008, *70*, 671.

[15] Parsons C.L., Breenberger M., Gabal L., Bidair M., Barme G.: "The role of urinary potassium in the pathogenesis and diagnosis of interstitial cystitis". *J. Urol.*, 1998, *159*, 1862.

[16] Thorn G.W.: "Approach to the patient with idiopathic edema or periodic swelling". *JAMA*, 1968, *206*, 333.

[17] Streeten D.H.P.: "Idiopathic edema: pathogenesis, clinical features and treatment". *Metabolism*, 1978, *27*, 353.

[18] Check J.H., Shanis B.S., Shapse D., Adelson H.G.: "A randomized study comparing two diuretics, a converting enzyme inhibitor, and a sympathomimetic amine on weight loss in diet failure patients". *Endoc. Pract.*, 1995, *1*, 323.
[19] Smith H.S., Barkin R.L.: "Fibromyalgia syndrome: A discussion of the syndrome and pharmacotherapy". *Am. J. Ther.*, 2010, *17*, 419.
[20] Bradley L.A.: "Pathophysiology of fibromyalgia". *Am. J. Med.*, 2009, *122*, S22.
[21] Nielsen L.A., Henriksson K.G.: "Pathophysiological mechanisms in chronic musculoskeletal pain (fibromyalgia): the role of central and peripheral sensitization and pain disinhibition". *Best Pract. Res. Clin. Rheumatol.*, 2007, *21*, 465.
[22] Staud R.: "Pharmacological treatment of fibromyalgia syndrome". *Drugs*, 2010, *70*, 1.
[23] Check J.H., Cohen R.: "The sympathetic neural hyperalgesia edema syndrome, a frequent cause of pelvic pain in women, mistaken for lyme disease with chronic fatigue". *Clin. Exp. Obstet. Gynecol.,* 2011, *38,* 412.

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