Marked improvement of headaches and vasomotor symptoms with sympathomimetic amines in a woman with sympathetic hyperalgesia-edema syndrome

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Summary

Purpose: To determine if relief from various pain conditions with sympathomimetic amines may be a direct effect on pain fibers or related to improvement of edema. *Methods:* A woman with severe migraine headaches resistant to standard therapy was treated with dextroamphetamine sulfate. *Results:* The headaches markedly improved shortly after treatment as did her vasomotor symptoms. However, in this case the inability to lose weight despite dieting related to edema did not improve. *Conclusions:* The improvement of pain and vasomotor symptoms in this disorder of the sympathetic nervous system does not seem to necessarily be related to edema causing pain. Sympathomimetic amines may have a direct effect on sympathetic nervous system fibers. Thus, a more appropriate term for this condition instead of idiopathic orthostatic cyclic edema would be sympathetic hyperalgesia-edema syndrome.

Key words: Headache, sympathomimetic amines; Edema; Permeability defect.

Introduction

A disorder of sympathomimetic amines has been described that is associated with a large variety of pain syndromes especially in women [1]. Medical syndromes associated with severe pain refractory to conventional therapy, that have responded quickly and very effectively to treatment with sympathomimetic amines, include interstitial cystitis, pelvic pain, esophageal pain, gastroparesis, arthritis and pain from pseudointestinal obstruction [2-7].

Treatment with dextroamphetamine sulfate has not only been used to treat pain syndromes but has been used to treat idiopathic edema and its associated weight gain not explained by dietary habits [8-11]. Many of the women whose pain improves with dextroamphetamine sulfate also exhibit weight loss and control of edema with the treatment. Thus the possibility exists that in some or all cases the cause of the pain is the edema.

However, one of the conditions that has shown dramatic relief in a short time after initiating dextroamphetamine sulfate despite long-standing pain resistant to standard therapy is interstitial cystitis [2]. One of the theories of the etiology of interstitial cystitis that is favored by most clinicians involves changes in epithelial permeability that allows transepithelial absorption of urea and potassium leading to tissue damage and pain [12].

The edema, referred to as idiopathic orthostatic cyclic edema where no other abnormality in free water clearance is found (e.g., hypothyroidism, nephrosis, cirrhosis and congestive heart failure), and where the fluid retention is predominately in the erect position, has been attributed to a capillary permeability defect [10]. The beneficial effect of sympathomimetic amines on water retention seems to be related to allowing the closure of a precapillary sphincter when one stands to inhibit the effect of an increase in hydrostatic pressure which would tend to force fluid from the intravascular to extravascular spaces [10].

The pain from interstitial cystitis could be related to edema of the bladder wall. Thus by releasing the edema the mechanism of improvement of pain with this disorder could be by correcting the leakage of fluid into the bladder wall and other tissues. However, it is also possible that sympathomimetic amines may also control permeability of epithelial cells. Thus its beneficial effect could be by correcting an epithelial cell permeability defect and thus inhibiting absorption of potassium and urea into the bladder wall.

The possibility exists in some of the pain syndromes that respond to treatment with dextroamphetamine sulfate that the mechanism may not always be related to inhibition of edema but to some direct effect as hypothesized for interstitial cystitis. The case described below illustrates the use of sympathomimetic therapy for relief of severe headaches in a woman unresponsive to conventional therapy. Furthermore this case supports the contention that the relief from pain may not always be related to diminishing edema.

Case Report

A 44-year-old woman presented with a history of severe migraine headaches, vasomotor symptoms and edema with inability to lose weight despite dieting. The headaches were excruciating when they occurred and although one-sided, did not present with an aura and would not respond to ergotamine

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therapy. They occurred usually twice a month but were not related to her menses and would last for a few days when they occurred. Furthermore, they interfered with her lifestyle. They occurred every time she flew on an airplane.

The woman's initial weight was 171 pounds, height 5'9" tall with a blood pressure of 122/70; her heart rate was 80 and regular, no murmurs or gallops heard. She was started on 15 mg dextroamphetamine sulfate extended release capsules (Adderall) daily and immediately got relief from the headaches but the edema did not improve much. Despite increasing the dosage to 30 mg the most weight she dropped was nine pounds but after six months her weight increased to 167 pounds. However, the headaches have not returned. Also the vasomotor symptoms have disappeared.

Thus though the edema for some reason proved to be somewhat resistant to treatment, the headaches and vasomotor symptoms markedly improved to 100% relief. The patient is now able to fly on airplanes.

Conclusions

The marked improvement in migraine headaches and vasomotor symptoms without much improvement in edema and weight lends support to the hypothesis that sometimes pain syndromes and possibly vasomotor symptoms may be independent of edema of the tissues. This case suggests that the beneficial effect on sympathomimetic amine therapy in some pain syndromes could be related to a direct effect on sympathetic nerve fibers. At the time of writing this manuscript we could find no other publications showing the benefit of dextroamphetamine sulfate for headaches. However, in view of the plethora of other pain syndromes helped by sympathomimetic amines its beneficial effect on headaches is not surprising. The beneficial effect of dextroamphetamine sulfate on vasomotor symptoms has been previously published [13].

Up to this point because of the possibility that the edema was the sole cause of pain the condition has been referred to as idiopathic edema or idiopathic orthostatic cyclic edema [8, 10]. Based on this case a more appropriate descriptive term would be the sympathetic hyperalgesia-edema syndrome. Possibly the sympathetic nervous system is normally involved in diminishing pain response or interpretation. A defect leads to increased pain and sympathomimetic amines can correct the defect.

Dextroamphetamine sulfate is usually very well tolerated in dosages up to 30 mg per day. There is no dependence or withdrawal after stopping.

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