994

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A NOVEL HIGHLY EFFECTIVE AND SAFE MEDICAL THERAPY FOR PAINFUL BLADDER SYNDROME/INTERSTITIAL CYSTITIS

Hypothesis / aims of study

A common condition relatively unknown to the medical community exists where a defect in the sympathetic nervous system leads to a wide variety of symptoms that are generally refractory to standard medical therapies but responds quickly and effectively to treatment with sympathomimetic amines. Prior publications have shown that small dosages of dextroamphetamine sulfate has efficiently controlled urticaria, joint pain, fibromylagia, chronic fatigue syndrome, inability to lose weight despite dieting, severe headaches, mastalgia, gastrointestinal motility disorders, inflammatory bowel disease, chronic pelvic pain, dysmenorrhea, vulvovaginitis and vasomotor symptoms. There has also been a case report publication demonstrating prompt marked improvement of bladder pain following dextroamphetamine sulfate therapy in two women with long-standing suffering who failed to respond to traditional therapy. The present study evaluated sympathomimetic amine therapy for painful bladder syndrome/ interstitial cystitis in a series of six additional cases of chronic painful bladder syndrome refractory to standard therapy.

Study design, materials and methods

The study was an observational case series without placebo controls. Only women were selected for this study since this disorder of the sympathetic nervous system is known to be predominately in women. All subjects had to have painful bladder for over a year and had failed to have adequate improvement from standard therapies. For inclusion in the study the woman had to have bladder pain urgency and frequency despite negative urine cultures for at least 12 months. Furthermore cystoscopy findings had to be consistent with interstitial cystitis. Dextroamphetamine sulfate extended release capsules were started at 15mg daily and increased depending on tolerance and response to a maximum of 30mg per day in one or two divided doses. To evaluate longevity of treatment benefit the study would only include those women responding to sympathomimetic amines who continued the medication for at least six months. If a woman would fail to respond to this treatment it was stopped. She would, however, still be included in the study.

Results

Prior to therapy 4 of the 6 women had such severe symptoms they could not function in every day society. Five of the 6 women in addition to dysuria had nocturia (at least 5x/night), frequency and urgency. Starting at 15mg of dextroamphetamine sulfate extended release capsules all 6 women showed significant relief in dysuria, urgency, frequency and nocturia. All patients increased the dosage to either 25mg or 30mg per day usually after the first month (with 1 exception). Within 2-6 months their urinary symptoms were either completely gone or so mild as to be very tolerable. Four of 6 decreased nocturia to once per night and two women had 2 urinations during the night. All symptoms remained almost completely relieved or gone both at 6 months and 1 year evaluations.

Interpretation of results

This was not a controlled study so one could argue that the sympathomimetic therapy perhaps worked as a placebo. However, all patients did not show any placebo response to pentosan polysulfate sodium, or pelvic floor physical therapy. Thus with the quick and long lasting benefits with dextroamphetamine sulfate it seems highly unlikely that the symptomatic remission was from either placebo effect or spontaneous remission. Further evidence supporting specific benefit from sympathomimetic amine drug therapy was the fact that 3 women who ran out of medication briefly for a few days (the schedule II drug is not allowed refills), the bladder symptoms returned immediately. Resuming dextroamphetamine sulfate again ameliorated symptoms within 24 hours. Though none of the women had postural syncope, evidence of a disorder of the sympathetic nervous system was demonstrated by abnormal water load tests in all 6. The sympathetic nervous system is responsible for maintaining normal intravascular fluid volume in response to the orthostatic position which because of an increase in hydrostatic pressure would tend to cause water to extravasate from intravascular to extravascular space were it not for a signal by the sympathetic nervous system causing precapillary sphincters to constrict. An abnormal water load test is determined when following ingestion of 1500 mL of water over a half hour period of time a woman urinates 75% of the ingested water load over 4 hours supine but the next day fails to excrete at least 75% of the water load over 4 hours while remaining erect.

Concluding message

The autonomic nervous system innervates the mucosal epithelium. It is believed that a diminished sympathetic tone possibly related to antibodies against ganglionic acetylcholine receptors leads to diminished function of this mucosal epithelium especially in its role of preventing absorption of toxins from the lumen to the epithelium. The toxins stimulate inflammatory response. Also the sympathetic nervous system innervates lymphoid tissue possibly facilitating inflammatory response. These pain syndromes are not limited to the bladder and do not always include the bladder depending on which sympathetic nerves are involved. Nevertheless almost all of the various pain syndromes respond quickly and effectively to sympathomimetic amine therapy. The common link is the usual abnormal water load test with $\geq$75% excreted of the water load supine but <75% standing. Dextroamphetamine therapy is without dependence or withdrawal symptoms when used in this small dosage. Patients with other types of pain disorders have been treated with this drug for over 30 years without problems. It is generally well tolerated and if side effects, e.g., insomnia, palpitation or personality change, occur they are usually transient. Thus we have now demonstrated that in 8 consecutive patients (including the 2 from the original case report) severe protracted interstitial

cystitis has dramatically responded to this benign therapy. No other patients with painful bladder syndrome have failed to respond to this therapy. Hopefully this case series will generate more widespread interest in evaluating dextroamphetamine sulfate therapy. Controlled trials are welcome. Perhaps other novel therapies may be generated based on the responses seen to sympathomimetic amines for bladder pain. It would be interesting to determine if sympathomimetic amines can improve bladder pain in male patients also.

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Was this study approved by an ethics committee?	**Yes**
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Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**No**