Case Reports

The use of sympathomimetic amines for the treatment of severe constipation refractory to conventional therapy - case report

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Summary

Purpose: Sympathetic nervous system hypofunction has been found to be associated with motility disorders of the bowel, including gastroparesis, pseudointestinal obstruction, and esophageal motility disorders. These disorders respond to sympathomimetic amine therapy. The purpose of this study was to see if this therapy could be effective in treating pathological constipation. *Materials and Methods:* Dextroamphetamine sulfate 15 mg extended release capsules was prescribed to an 18-year-old young woman who had severe constipation with a bowel movement every two to three weeks and sometimes every five to six weeks who did not respond to standard therapy and where no definite etiology was determined. *Results:* Two hours after her first dosage of the sympathomimetic amine, she had a bowel movement and has had regular bowel movements ever since. *Conclusions:* Sympathomimetic amine therapy seems to help severe constipation refractory to standard therapy.

Key words: Constipation; Sympathetic nervous system; Hypofunction; Dextroamphetamine sulfate; Neurotransmitter.

Introduction

There have been several gastrointestinal (GI) pathologic conditions that proved to be refractory to standard therapy and yet responded quickly and quite effectively to treatment with the sympathomimetic amine dextroamphetamine sulfate. Several anecdotal reports have demonstrated that sympathomimetic amine therapy has successfully provided long-term relief from GI motility disorders of the esophagus, gastroparesis, and pseudo-intestinal obstruction that had been refractory to other therapies [1-3]. Similarly marked improvement of some inflammatory bowel disorders, e.g., ulcerative colitis and Crohn's disease, following treatment with dextroamphetamine sulfate have been reported despite failing to respond to other therapies, including drugs that inhibit the cytokine tumor necrosis factor alpha [4, 5]. These GI conditions are all believed to be related to sympathetic nervous system hypofunction to explain the response to sympathomimetic amines. The sympathetic nervous system innervates the enteric nerves and sympathetic hypofunction may then cause diminished function of the enteric nerves leading to depressed motility [6]. Alternatively, the sympathetic nervous system acts to diminish cellular permeability. Sympathetic fibers are known to innervate the mucosal epithelial cells [6]. Thus diminished sympathetic nervous system function could allow absorption of chemicals and toxins from the stool leading to inflammation or muscle paresis [7-9]. The purpose of this report is to describe another GI disorder that failed to respond to standard therapy but responded immediately to dextroamphetamine sulfate therapy.

Case Report

At the age of 16, a young woman developed marked constipation. Bowel movements would occur every two to three weeks and even that would require taking laxatives, e.g., magnesium citrate, metamucil, konsyl, and docusate which did not help very much. A gastroenterologist was consulted. Further evaluation including magnetic resonance imaging (MRI) of the abdomen, gastroscopy, and bowel motility studies all failed to detect any abnormalities.

She was prescribed lubiprostone 24 mcg daily. She did have a bowel movement in three days and then seemed to have one every two days. However after two weeks of therapy, her severe constipation of two to three week intervals (and sometimes five weeks) returned along with moderately severe abdominal pain when a two-week interval was approaching.

Her severe constipation problem persisted for two years. She consulted our group hoping to find a possible endocrine etiology that could be corrected. Her thyroid tests were normal with a free thyroxin level of 1.2 ng/dl (nl 0.7 - 1.8) and her thyroid-stimulating hormone level was 2.76 micro IU/ml (nl 0.35 - 4.50). Considering our very positive experience in treating various GI problems with dextroamphetamine sulfate, she was started on the same with 15 mg extended release capsule once daily [1-5]. The first day she took the sympathomimetic amine, she had a bowel movement two hours after taking it and she has had one everyday for 1.5 years since she has been taking this

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medication. Interestingly, she ran out of medication for a week before she could return to our office for a prescription and her bowel movements ceased the day she stopped only to return the first day she started it again. She has had no side-effects.

Discussion

The hope of publishing these case reports is to generate sufficient interest in some physicians to initiate randomized controlled trials (RCT). If efficacy of this very safe well-tolerated drug which has no dependence or withdrawal effects in the dosages prescribed (usually 30 mg/day is the maximum dosage) and is confirmed by a larger RCT, then hopefully it will be found to be the most effective and safest drug for inflammatory bowel disease and GI motility disorders.

Recently, the importance of the sympathetic nervous system in the pathophysiology of GI motility disorders and inflammatory bowel disease has been established [1-9]. What is not well-known is the potential of quick and effective resolution of symptoms with the sympathomimetic amine dextroamphetamine sulfate, which is usually without immediate side-effects or risk of developing cancer or risk of severe infection.

Catecholamines are the classical neurotransmitters of the sympathetic nervous system and they increase intracellular cyclic adenosine monophosphate, which in turn, inhibit certain proinflammatory cytokines, e.g., tumor necrosis alpha or interferon gamma [10]. It is hoped that this case report will help elicit interest in a randomized controlled or randomized comparison study using dextroamphetamine sulfate for people with GI motility disorders, as in this case, or for cases of inflammatory bowel disease. It should be recalled that this type of therapy may be the treatment of choice for pelvic pain [11]. Thus this condition may be more familial to the gynecologist than most gastroenterologists. Thus it may be prudent for the gynecologist to prescribe this drug first if presented with the symptoms rather than subject the patient to extensive invasive testing and other potential therapies with less efficacy and more side-effects. Obviously if significant improvement does not occur, the gynecologist should then refer the woman to a gastroenterologist to exclude serious pathology, e.g., colon cancer.

References

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