

Sympathomimetic amine therapy may improve refractory gastroparesis similar to its effect on chronic pelvic pain - case report

P. Boimel¹, B.S.; J.H. Check², M.D., Ph.D.; D. Katsoff², B.S.

¹Albert Einstein College of Medicine of Yeshiva University, Bronx, NY

²The University of Medicine and Dentistry of New Jersey, Robert Wood Johnson Medical School at Camden, Cooper Hospital/University Medical Center, Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology & Infertility, Camden, NJ (USA)

Summary

Purpose: To determine if treatment with sympathomimetic amines can effectively treat gastroparesis that was refractory to other medical therapy. **Methods:** After failing a water load test, a 29-year-old female was treated with 20 mg/day of dextroamphetamine sulfate. **Results:** After several weeks of therapy she noted that most of her symptoms of gastroparesis subsided and she has remained symptom free for eight months. **Conclusions:** Similar to its beneficial effect on chronic pelvic pain of both bladder and non bladder origin, refractory weight gain, esophageal pain, chronic fatigue syndrome, headaches and vasomotor symptoms, sympathomimetic amine therapy can also effectively treat gastroparesis refractory to other medical therapies at least in some cases.

Key words:

Introduction

Gastroparesis, characterized by delayed gastric emptying time, is often accompanied by vomiting, nausea, bloating, malnutrition, electrolyte abnormalities, and abdominal pain in the absence of any obstructions [1]. Patients may be repeatedly hospitalized for malnutrition, and complications which can lead to mortality. Gastroparesis is treated with prokinetic and antiemetic medications that often attempt to treat the symptoms associated with this disorder. Not all patients are responsive to the therapy, and resolution may lie in treating and correcting the underlying etiology. It has previously been the practice for patients failing pharmacologic treatment to undergo various surgical procedures with questionable resolution of symptoms and significant complications [1].

This case study focuses on the treatment of idiopathic gastroparesis, associated with edema which was unresponsive to conventional treatment with prokinetic drugs. Many symptoms may be associated with idiopathic orthostatic edema, such as unexplained pelvic and chest pain, chronic fatigue syndrome, fibromyalgia, joint pain and many others [2, 3]. Symptoms accompanying idiopathic orthostatic edema have been resolved by treating this disorder with sympathomimetic amines. This case indicates that idiopathic orthostatic cyclic edema is an entity that can be associated with gastroparesis, and that treatment for this condition, sympathomimetic amines, was also effective in treating gastroparesis in this patient.

Case Report

A 29-year-old female presented for clinical evaluation with a recent diagnosis of gastroparesis and symptoms of idiopathic orthostatic edema. After being diagnosed by a gastroenterologist, the patient failed to respond to conventional treatment measures for this disorder. She presented for evaluation of a possible endocrine basis of her gastroparesis. Many patients develop gastroparesis associated with diabetes but our patient's fasting glucose and insulin levels were normal.

Some symptoms of gastroparesis can also be similar to those observed in patients with hypoparathyroidism. Hypoparathyroidism was ruled out by normal calcium levels and normal thyroid studies. At that time the patient was unable to lose weight and had an unexplained sudden weight gain, notably of 25 pounds, without any change in diet or activity. She also presented with other symptoms of idiopathic orthostatic edema as well as morning headaches, swelling of the face, and vasomotor flushing. It was at that time hypothesized that her gastroparesis as well as her other symptoms might be a complication due to water retention from idiopathic edema, and that her weight problem and maybe even the gastroparesis could be resolved by treating the idiopathic orthostatic cyclic edema with sympathomimetic amines [4]. Further tests were carried out to rule out any other conditions and a water load test was done to diagnose the idiopathic cyclic edema.

Physical examination and endocrine studies were normal. A chest X-ray was unremarkable and lymphadenopathy was not found during the initial examination. Her heart rate was 76 beats/min, regular and without murmurs. An abdominal exam was normal with no tenderness, and the patient denied taking any medications which could have an adverse effect on bowel motility. Her CBC was normal with a white blood cell count of $6.1 \times 10^3/\text{ml}$ with a normal differential. Her thyroid tests showed a normal serum T4 at 5.5 $\mu\text{g/dl}$ (nl 4.5-12.0), a normal T3 uptake at 35 (nl 24-39), free thyroxine index was normal at 1.9 (nl 1.2-4.9), and her TSH was normal at 1.396 nIU/ml (nl 0.350-5.5). Her prolactin was 9.5 ng/ml (normal) and free testosterone was 0.8 pg/ml (nl 0-3.8). To determine if her vaso-

motor flushing was due to premature ovarian failure, her third menstrual day serum FSH was tested while the patient was on the placebo portion of oral contraceptives and was only 4mIU/mL. Her serum estradiol was also normal at 45 pg/ml at that time in her cycle. It was thus hypothesized that idiopathic orthostatic edema might be the etiology of her vasomotor flushing which might also resolve with treatment.

To determine if the patient had idiopathic orthostatic cyclic edema a water load test was performed. The patient ingested 1500 cc of water and reclined in the supine position for four hours. During this time she excreted 1650 cc of urine. However, when the test was repeated while the patient was erect she only excreted 800 cc of urine over four hours. These findings led to the diagnosis of idiopathic orthostatic cyclic edema [5].

The patient was treated with sustained release dextroamphetamine sulfate, 10 mg capsules taken in the morning and at noon for a total of 20 mg per day [3, 6]. In two weeks the majority of her symptoms had improved. Her edema was resolved as well as her flushes, sweats, and morning headaches. She lost 18 pounds during this interval and sustained the weight loss. Her vasomotor flushing was 99.9% better with the dextroamphetamine treatment and this was the first documented case of idiopathic orthostatic edema causing vasomotor flushing with normal FSH and estradiol levels [7]. Her gastroparesis did not improve initially but after seeing more gastroenterologists and trying a variety of treatments without help she discontinued these therapies. Eventually her gastroparesis did resolve and her stomach pain disappeared. The patient feels this was a result of the treatment of her edema since she was on no other medications for gastroparesis at that time. She has continued treatment with the dextroamphetamine and has remained symptom free for eight months.

Discussion

Idiopathic orthostatic cyclic edema seems to be a manifestation of a capillary permeability defect in the standing posture. This defect leads to increased leakage through the capillary wall when hydrostatic pressure is elevated in the erect position [3]. Conventional treatment of idiopathic edema has included diuretics, which do not correct the permeability dysfunction occurring mainly at the proximal convoluted tubule (diuretics act at the distal tubule) (thiazide diuretics) or at the ascending loop of Henle (loop diuretics such as furosemide). Diuretics can also be ineffective since the diuretic action is diminished with the fall in renal plasma flow and glomerular filtration rate which occurs when the patient is in the upright position and blood volume falls as leakage occurs [6, 8]. Sympathomimetic amines have proven to be more effective in the treatment of idiopathic edema since their action is more constant and not as transient as that of the diuretic therapies. Sympathomimetic amines are believed to act by stabilizing capillary membranes thereby decreasing permeability, interstitial edema, and orthostatic edema [2, 3, 6].

Water retention in tissues can have many manifestations in different areas of the body which often results in painful symptoms and can lead to a mistaken diagnosis of carpal tunnel syndrome, migraines, esophagitis, and arthritis [3, 9]. An increase of capillary permeability can lead to irritating and toxic substances being absorbed into

surrounding tissues resulting in interstitial cystitis, and chronic urticaria [10-12].

Previously we reported that the vasomotor flushing associated with idiopathic orthostatic edema in this patient responded to dextroamphetamine treatment. We hypothesize that these central nervous system symptoms are related to cerebral fluid retention and increased pressure caused by the edema on the temperature regulation center of the brain, and treatment relieved cerebral pressure [11].

Gastroparesis is a serious disorder which can result in many complications without treatment. Nausea and vomiting are treated with antiemetics, and prokinetics are used to try and restore normal gastric motility and function. This patient failed to respond to standard pharmacologic medical treatments for this disorder. Other options for treatment of gastroparesis would have been gastrostomy, jejunostomy, and gastric pacing using electrical stimulation. Surgical success in treating this disorder has proved to be elusive. A recent review on surgical treatments has shown that successful supporting evidence of this approach is lacking [1]. They also reported that surgical treatment is often accompanied by many complications and should be limited. In this patient the gastroparesis took longer to respond to medical treatment than her other symptoms. However, the patient was on no other treatment but dextroamphetamine sulfate when the gastroparesis resolved. We hypothesize that her symptoms may have been due to edema in the gastric wall similar to a case of esophagitis associated with idiopathic edema and possible edema of the esophageal wall, which was resolved with sympathomimetic amine treatment [9]. Correcting her orthostatic edema and increased orthostatic capillary permeability with the dextroamphetamine sulfate resolved her gastroparesis probably by decreasing internal edema affecting gastric emptying.

The purpose of this case report was to describe a unique case where gastroparesis was caused by idiopathic orthostatic cyclic edema and was resolved upon treating the edema with dextroamphetamine sulfate. There are many associated manifestations of idiopathic orthostatic cyclic edema which is a very common condition in women. It is important for physicians to become aware of this disorder and the many symptoms and unexplained suffering which are refractory to treatment with conventional measures. Many of these associated disorders can be resolved by treating the idiopathic edema with sympathomimetic amines.

Whether treatment with sympathomimetic amines will prove effective in most cases of idiopathic gastroparesis, or will be useful only in rare instances remains to be seen in a larger clinical trial. Whether the benefit will be found only in those women with abnormal water load tests also needs to be determined. It is hoped that this case report will generate interest in physicians, especially those who treat many cases of gastroparesis, to try this therapy in refractory cases. Possibly this therapy could even prove beneficial in cases associated with diabetes.

References

- [1] Jones M.P., Maganti K.: "A systemic review of surgical therapy for gastroparesis". *Am. J. Gastroenterol.*, 2003, 98, 2122.
- [2] Streeten D.H.P.: "Understanding and treating idiopathic edema". *Consultant*, 1980, 82.
- [3] Streeten D.H.P.: "Idiopathic edema: pathogenesis, clinical features and treatment". *Metabolism*, 1978, 27, 353.
- [4] Check J.H., Adelson H.G., Shanis B.S.: "Idiopathic orthostatic edema as a cryptic cause of the inability to lose weight despite dieting". *Exp. Clin. Endocrinol.*, 1988, 7, 195.
- [5] Kuchel O., Horky K., Gregovova I., Marck J., Kopecka J., Kobilkova J.: "Inappropriate response to upright postures: a precipitating factor in the pathogenesis of idiopathic edema". *Ann. Intern. Med.*, 1970, 73, 245.
- [6] 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. Prac.*, 1995, 1, 323.
- [7] Check J.H., Katsoff D., Kaplan H.: "Idiopathic orthostatic cyclic edema as a unique etiology for vasomotor flushing in a normal estrogenic woman with normal day 3 follicle stimulating hormone - case report". *Clin. Exp. Obstet. Gynecol.*, 2006, 33, 125.
- [8] De Wardner H.E.: "Idiopathic edema: role of diuretic abuse". *Kidney Int.*, 1981, 19, 881.
- [9] 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.
- [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. Obstet. Gynecol.*, 2005, 32, 247.
- [11] Check J.H., Gentlesk M.J., Falanga V.: "Sympathomimetic amines in the treatment of chronic urticaria: Two case reports". *CUTIS*, 1984, 34, 388.
- [12] 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. Obstet. Gynecol.*, 2005, 32, 241.

Address reprint requests to:
J.H. CHECK, M.D., Ph.D.
7447 Old York Road
Melrose Park, PA 19027 (USA)