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Gastric Electrical Stimulation and Sacral Electrical Stimulation: A Long-Term Follow-Up Study of Dual-Device Treatment

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Abstract

Aims—The objective of this study was to investigate sacral electrical stimulation (SES) and gastric electrical stimulation (GES) by comparing upper and lower gastrointestinal (GI) and genitourinary (GU) symptoms and quality of life, before treatment and in the long term after treatment. We hypothesized that dual-device treatment would greatly improve upper and lower gastrointestinal and genitourinary symptoms, as well as quality of life.

Methods—Fifty-four patients who underwent dual-device treatment (GES and SES) were enrolled in this study. Patients who had surpassed 24 months since the second-device insertion were included. Patients were evaluated before and after both devices were implanted and given a symptom questionnaire regarding their upper GI, lower GI, and GU symptoms and their quality of life.

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Conflict of interest Dr. Abell has been a consultant, investigator, and licensor to Medtronic.

Results—With combined treatment, a statistically significant improvement was seen in upper GI, lower GI, and GU symptoms and quality of life. However, fecal incontinence and fecal urgency improvements did not reach statistical significance, likely due to the small sample size.

Conclusion—The implantation of two stimulators appears to be safe and effective to improve patients' quality of life for those with upper GI symptoms, bowel problems, and bladder dysfunction.

Keywords

Neurostimulator; Gastroparesis; Incontinence; Enterra®; Interstim®

Introduction

Gastroparesis (Gp) is a motility disorder that affects the digestive tract in the absence of mechanical obstruction. Frequent complaints associated with Gp include: nausea, vomiting, bloating, pain, malnutrition, dehydration, and an increased risk of thromboembolism [1–3]. Gp has also been associated with diseases of the hindgut. In one study, 19 % of patients suffering from chronic constipation also were found to have delayed gastric emptying [4]. In patients with irritable bowel syndrome (IBS), another investigation demonstrated that 64 % of patients with IBS also demonstrated delayed gastric emptying [5]. These studies demonstrate that patients with upper GI symptoms may have concomitant lower GI symptoms. Patients who suffer from symptoms of gastroparesis, regardless of etiology, often experience decreased quality of life; most severe impairments are in the areas of physical, social, emotional, bodily pain, and vitality [6, 7].

Gastric electrical stimulation (GES) using the Enterra™ system (Medtronic, Minnesota) was granted Humanitarian Use Device status by the Food and Drug Administration (FDA) in 2000 for use in patients with severe gastroparesis [8]. GES involves placing two electrodes on the gastric antrum connected to a pulse generator. GES has demonstrated significant improvement in patients' quality of life, with some instances of complete resolution [9]. Pain symptoms were improved or resolved in a study involving 95 Gp patients who underwent GES [3]. GES provides a substantial reduction in nausea and vomiting symptoms, an improvement in gastric emptying, and a reduction in the need for enteral and parenteral nutritional support [10].

Sacral nerve stimulation (SES) has demonstrated significant symptomatic improvements in the hindgut: 89 % of patients reported an improvement with fecal incontinence and quality of life. SES results in a significant increase in resting and squeeze anal pressures [11]. Long-term use of SES for at least 5 years demonstrated an 89 % improvement, and 36 % of patients reported complete resolution of fecal incontinence; long-term quality of life also significantly improved. SES has also been shown to help with pelvic floor genitourinary disorders: 84 % of patients demonstrated significant improvement in urinary incontinence, and 78 % demonstrated benefits in urinary retention in a worldwide study [12]. The first-line treatment for patients with overactive bladder is anticholinergics [13]. A known side effect of anticholinergics is constipation; since some patients with urinary incontinence also suffer

from constipation, this medication is contraindicated. SES provides a reliable alternative to patients who fail anticholinergic therapy [13].

The objective of this study was to investigate long-term follow-up of dual devices (SES and GES) and compare outcomes of upper and lower GI symptoms, urinary complaints, and quality of life before and after treatment. We hypothesized that combined treatment would greatly improve upper gastrointestinal, genitourinary, and lower gastrointestinal symptoms. This study provides the largest cohort with the longest follow-up of patients with dual devices yet reported.

Materials and Methods

This is a multicentered retrospective cohort study. Institutional review board approval was obtained from all centered sites. From 1995 to 2014, fifty-four patients who underwent dual-device implantation (GES and SES) were enrolled in this study. Patients who had the second device inserted at a minimum of 24 months prior were included in this study. Patients were evaluated prior to and after both devices were implanted and given a symptom questionnaire involving upper GI, lower GI, and GU symptoms and quality of life. Upper gastrointestinal symptoms were rated from 0 to 4 for a maximum total symptom score of 20; lower gastrointestinal symptoms were rated from 0 to 3; genitourinary symptoms were evaluated from 0 to 3; and quality of life was rated from −3 (worst) to +3 (best). All questionnaires were adapted from previously published literature and are included in the supporting information [14]. Since this was a pilot study regarding long-term data of dual devices, and as data in the literature are lacking, this review of patient data was not powered for sample size.

The upper GI symptoms that were studied were: vomiting, nausea, gastric bloating, and generalized abdominal pain. Lower GI symptoms were evaluated based on frequency: none, occasionally, half of the time, and all of the time. Questionnaires addressed the following symptoms: incontinence of stool, fecal urgency, constipation, and frequency of bowel movements per week; they were modeled on previously published questionnaires [14]. Genitourinary symptoms were also addressed on a similar timing scale. Patients were asked about difficulty voiding, urinary initiation, straining with voiding, urgency, incontinence, and number of pads used per day. The quality-of-life measure addressed patient satisfaction with the procedure; patients were asked to provide feedback before and after GES placement, SES placement, and dual-device placement.

As the data collected were ordinal in nature based on a Likert scale, a nonparametric test was utilized. The medians of each group of pre-dual-device implantation (after the first device before the second device) and post-dual-device implantation along with the median change in score difference were calculated. The interquartile range was calculated to assess distribution of the sample size. A nonparametric Mann–Whitney U test was conducted to assess statistical significance. A p value <0.05 was considered statistically significant.

Results

Fifty female and four male patients with an average age of 44.3 years were included in this study. Thirty-eight patients had idiopathic causes of Gp, ten suffered from diabetes, and six had a prior abdominal surgical history. Of the 54 patients, 49 patients received GES before SES. There was a median six-year follow-up after undergoing GES (maximum 15 years), and a median 4-year follow-up following SES (maximum 10 years) at time of analysis.

With combined treatment, a statistically significant improvement was seen in upper GI, lower GI, and genitourinary symptoms. Most symptoms were improved and reached statistical significance with p values <0.05. Upper GI symptoms significantly improved in all areas including: vomiting (4.0–1.0), nausea (4.0–2.0), satiety (4.0–2.0), bloating (4.0–2.5), and abdominal pain (4.0–2.0), with statistical significance with p values <0.0001. This is seen in Table 1.

Lower GI symptoms improved with constipation (3.0–1.0) and number of bowel movements per week (2.0–7.0). Though there was a trend with improvement with fecal incontinence and urgency episodes, this did not reach significance. This is demonstrated in Table 2. There was an improvement in all of the genitourinary symptoms questioned: difficulty voiding (3.0–0.0), trouble starting a stream (3.0–0.0), straining to urinate (2.0–0.0), urgency (2.0–0.0), and incontinence (1.0–0.0) as seen in Table 3.

Overall quality-of-life scores significantly improved after dual-device placements. Before initial GES implantation, patients rated their quality-of-life score at a median value of −3.0. After implantation, this number rose to +2. With regard to SES placements, quality-of-life scores improved from −2.0 to 2.0. In evaluating the overall treatment with dual-device treatment, scores significantly rose from an initial value of −3.0, after one device was added, to +2.0, after second device was added. All quality-of-life scores reached statistical significance with a p value <0.0001 as seen in Table 4.

Discussion

This long-term follow-up study demonstrates that following dual-device insertion, there appears to be an improvement in upper GI, lower GI, and genitourinary symptoms. All upper GI symptoms demonstrated marked improvement with dual devices. The remarkable improvement of upper GI symptoms following SES insertion further supports the hypothesis that there must be some crossover between these upper GI and lower GI symptoms. Previous studies failed to demonstrate isolated upper GI improvement with SES only [15]. These studies were limited by small sample size, and they focused on motor function, but failed to investigate sensory function which can also affect upper GI symptoms.

SES is currently FDA-approved for genitourinary and lower GI symptoms. SES is hypothesized to work by targeting the afferent pathway from the sacral nerve roots [15, 16]. The afferent activation likely modifies supraspinal control of defecation. The low-level stimulation may inhibit spinobulbar pathways, which reduces inhibition of sphincter function and rectal contractility [15, 16]. Another study of eleven patients demonstrated an increase in retrograde colonic propagating sequences with SES. This suggests that the effect

of SES may be primarily on colonic motility rather than directly affecting external anal sphincter and puborectalis function [16, 17]. Further studies investigating upper GI symptoms following single-device SES may be undertaken to further support this hypothesis. GES is hypothesized to work by fundal gastric relaxation and accommodation, enteric nervous system function, and central neuronal pathways [18].

As expected, there was considerable improvement in genitourinary and lower GI symptoms following the second-device (SES) implantation. Based on our study, patients' fecal incontinence improved, but this did not reach statistical significance. The symptom of constipation improved after implantation of the SES device. Interestingly, in America, the SES is approved for fecal incontinence and not constipation; in Europe, SES has been approved for treatment of constipation, and this use is supported by this study [15]. One of the major reasons to implant SES is to improve urinary incontinence. This has been supported with several studies along with the findings presented here [12].

Quality of life demonstrated improvement with dual devices; however, this may be biased, as any improvement would have been significant. Embarrassment and depression are common signs and symptoms for this group of patients, and a small improvement, even though not completely resolved, could tremendously affect patients' lifestyles.

This first study investigating dual devices with long-term follow-up demonstrates several strengths. Though it is difficult to prospectively power the study, we were able to collect data on 54 patients with dual devices; the practice of implanting two electrical devices is currently unusual, so obtaining such numbers was a substantial challenge to our research. As this is a multicentered study, we were able to reduce the chance of bias by having several different physicians who contribute to the study. This study also had long-term data analysis with a median four-year follow-up after dual-device insertion.

However, this study does have some limitations. Though we had long-term data from many patients, some patients did not complete their surveys. This lack of follow-up may have affected the statistical information gathered. Attempts were made to try to reconnect with patients who had previously enrolled in the study; however, many of these patients relocated and were unable to be contacted to obtain the most recent data. As dual-device insertion is not common practice, it was difficult to power this study. With this preliminary data, future trials would be able to power this study and prospectively investigate symptom improvement.

Conclusion

The implantation of two stimulators appears to be safe and effective to improve the patients' quality of life in patients with upper GI symptoms, bowel problems, and bladder dysfunction. However, the authors recommend using caution when employing two devices. The GES has demonstrated effectiveness for treatment of primarily the foregut, and the SES with the hindgut and GU system. There is an overlap between the two devices as some etiologies of one symptom may be present in another. Future studies of neurostimulation

devices involving the GI and/or GU tracts may want to quantify the presence of both foregut and hindgut dysfunction at baseline and in response to device therapies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Upper gastrointestinal symptoms before and after dual-device insertion (as measured by Mann–Whitney *U*)

***N* = 54**	**Vomiting**	**Nausea**	**Satiety**	**Abdominal pain**	**Bloating**	**Total UGI**
Median pre-op score (IQR)	4.0 (1.0)	4.0 (0.0)	4.0 (0.9)	4.0 (0.4)	4.0 (0.5)	18.0 (4.0)
Median post-op score (IQR)	1.0 (2.0)	2.0 (2.0)	2.0 (2.0)	2.0 (2.0)	2.5 (2.5)	9.75 (7.0)
Median change score (IQR)	−2.0 (2.0)	−2.0 (2.0)	−1.0 (2.9)	−1.0 (2.0)	−1.0 (2)	−8.75 (6.8)
p value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

IQR interquartile range

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Table 2

Lower gastrointestinal symptoms before and after dual-device insertion (as measured by Mann–Whitney *U*)

n **= No. of patients**	**Bowel incontinence** ***n*** **= 39**	**Bowel urgency** ***n*** **= 39**	**Constipation** ***n*** **= 53**	**BM/week** ***n*** **= 34**	**LGITSS**
Median pre-op score (IQR)	0.0 (2.0)	1.0 (2.0)	3.0 (1.0)	2.0 (5.6)	3.0 (1.8)
Median post-op score (IQR)	0.0 (1.0)	0.0 (1.0)	1.0 (3.0)	7.0 (18.2)	2.8 (2.0)
Median change score (IQR)	0.0 (1.0)	0.0 (1.0)	−0.5 (2.0)	+5.9 (11.5)	−1.0 (3.0)
p value	0.264	0.078	0.001	<0.0001	<0.0001

Table 3

Genitourinary symptoms before and after dual-device insertion (as measured by Mann–Whitney *U*)

n **= No. of patients**	**Difficulty voiding *n* = 53**	**Trouble initiating stream *n* = 44**	**Straining to urinate *n* = 44**	**Urinary urgency *n* = 44**	**Urinary incontinence *n* = 44**	**Number of pads *n* = 37**	**Total GU score**
Median pre-op score (IQR)	3.0 (1.0)	3.0 (3.0)	2.0 (2.0)	2.0 (3.0)	1.0 (2.3)	0.0 (3.0)	8.0 (7.0)
Median post-op score (IQR)	0.0 (2.0)	0.0 (1.0)	0.0 (1.0)	0.0 (1.0)	0.0 (1.0)	0.0 (0.0)	2.0 (3.0)
Median change score (IQR)	−1.0 (2.0)	−2.0 (2.0)	−2.0 (1.3)	−1.0 (2.0)	0.0 (2.0)	0.0 (2.0)	−5.0 (8.0)
p value	<0.0001	<0.0001	<0.0001	<0.0001	0.001	0.007	<0.0001

Table 4

Quality of life before and after dual-device insertion of patients (as measured by Mann–Whitney *U*)

n **= 39**	**GES**	**SES**	**Dual devices**
Median pre-op score (IQR)	−3.0 (1.0)	−2.0 (2.0)	−3.0 (0.5)
Median post-op score (IQR)	2.0 (2.0)	2.0 (2.0)	2.0 (2.0)
Median change score (IQR)	+4.8 (3.3)	+2.5 (4.0)	+4.3 (3.3)
p value	<0.0001	<0.0001	<0.0001