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Behavioral therapy is superior to follow-up without intervention in patients with supragastric belching—a randomized study

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Running title: Behavioral therapy in supragastric belching

Abstract

Background: Behavioral therapy (BT) has been proven effective in the treatment of supragastric belching (SGB) in open studies. The aim was to compare BT to follow-up without intervention in patients with SGB in a randomized study.

Methods: Forty-two patients were randomized to receive 5 sessions of BT, comprising diaphragmatic breathing exercises, or to follow-up without intervention. Patients were evaluated at 6 months, at which point the control group was also offered BT and evaluated after another 6 months. The frequency and intensity of belching and mental well-being were evaluated with a visual analog scale (VAS). Depression, anxiety, and health-related quality of life (HRQoL) were evaluated with four questionnaires: BDI, BAI, 15D, and RAND-36.

Key results: The frequency and intensity of SGB were significantly lower in the therapy group (n = 19) than in the control group (n = 18) at the 6-month control ($P < 0.001$). When all patients (n = 36) were evaluated 6 months after BT, in addition to relief in the frequency and intensity of belching ($P < 0.001$), mental well-being had also improved ($P < 0.05$). Of all 36 patients, 27(75%) responded to BT. Depression scores were lower after therapy ($P < 0.05$). Only minor changes occurred in anxiety and HRQoL.

Conclusions and Inferences: BT is superior to follow-up without intervention in patients with SGB in reducing belching and depression; it also improves mental well-being but has only a modest effect on anxiety and HRQoL.

Key words: anxiety, behavioral therapy, depression, health-related quality of life, supragastric belching

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This study was approved by the Ethics Committee of Helsinki University Hospital (170/13/03/01/2016) and Helsinki University Hospital Abdominal Center (HUS-214-2016-35).

INTRODUCTION

Patients with esophageal symptoms and no gastroscopic findings, non-responsive to anti-acid therapy, are a common problem at the gastroenterologist's office. Some of these patients suffer from belching, which may be related to upper abdominal or esophageal discomfort or a globus sensation in the throat. The prevalence of dyspepsia is roughly 20% in the general population (1). Half of all dyspeptic individuals also report belching, which is severe in 6% of the cases (2).

Combined multichannel intraluminal impedance/esophageal pH monitoring (MII-pH) can be used to differentiate supragastric belching (SGB) from normal gastric belching (3). In patients with excessive belching, the incidence of normal gastric belches is similar to that found in healthy subjects. Excessive belching, however, is caused by a rapid antegrade and retrograde flow of air in the esophagus that does not reach the stomach, i.e. supragastric belching (4). Similarly, supragastric belches have been proven to be the cause of troublesome belching in patients with reflux disease (5). In a retrospective study of 94 patients with atypical esophageal symptoms and not responding to a double-dose proton-pump inhibitor (PPI), SGB was the cause of symptoms in 42% of the cases (6). SGB is seldom the only symptom in dyspeptic patients. In a study on 2,950 patients referred to esophageal impedance monitoring, the prevalence of SGB was 3.4% (7). Ninety-five percent of these patients also had reflux symptoms and 65% dysphagia. Forty-one percent of the patients suffering from belching also had reflux disease and 44% esophageal hypomotility. In a Finnish study, SGB was more often related to globus than to reflux disease (30% vs 4%) (8). Besides being a disturbing symptom, supragastric belching also reduces the health-related quality of life (HRQoL) (9).

SGB is a volitional but subconscious, behavioral disorder which can be caused by either an injection of air into the esophagus through the contraction of the pharyngeal muscles or the suction of air into the esophagus via the creation of a negative intrathoracic pressure by inspiration with a closed

glottis, after which the upper esophageal sphincter relaxes (10, 11). In both mechanisms, the air is expelled by abdominal straining.

No generally accepted therapy is available for SGB. Baclofen alone or combined with pregabalin may reduce SGB, but central nervous side effects usually prevent long-time use (12–14). For this reason, new therapies are needed.

Behavioral therapy (BT) focuses on explaining the belching mechanisms and training the patients to perform breathing exercises at the onset of belching or warning signals (15). This is similar to habit reversal training, which has proven effective in behavioral disorders (16). BT has been successfully used to reduce SGB measured by the patients themselves using a visual analog scale (17, 18), and the positive effect lasts for up to 12 months after treatment (19). BT also reduces SGB as measured objectively by means of MII-pH, in addition to improving social and daily activities and reducing acid exposure in the subgroup of patients with SGB-driven acid reflux (17). In a prospective study of 15 patients affected by PPI-refractory gastroesophageal reflux disease (GERD) with troublesome belching, diaphragmatic breathing reduced belching and PPI-refractory gastroesophageal reflux symptoms significantly and increased the quality of life but there was no change in the symptoms of the 21 patients on the waiting list (20).

Previous studies have been open studies with no control group. We designed a randomized study to test the hypothesis that BT is more effective than standardized information about SGB and follow-up with no intervention in patients with SGB. The study results were presented as a poster at the 3rd Meeting of the Federation of Neurogastroenterology and Motility in 2018 and were published as an abstract (21).

METHODS

Patients

The study included 42 consecutive patients referred to our study in the Helsinki University Hospital

between October 2016 and June 2019 from gastroenterology outpatient clinics because of troublesome belching or other esophageal symptoms related to SGB. All patients had responded poorly to PPI-treatment, had undergone gastroscopy and MII-pH, and had been evaluated by routine laboratory tests to rule out other organic diseases.

The inclusion criteria included both belching as a troublesome symptom and SGB diagnosed by means of MII-pH related to the symptom. All MII-pH recordings were evaluated by a clinical physiologist or gastroenterologist with expertise in the method to detect supragastric belches and assess their relation to liquid reflux episodes and symptoms.

The exclusion criteria included a large hiatal hernia or severe esophagitis, which led to exclusion because of possible overlapping symptoms, as well as previous fundoplication surgery, pregnancy, and significant cognitive disorder. All patients received written and oral information about the study, and a written consent was acquired before enrollment. This study was approved by the Ethics Committee of Helsinki University Hospital (170/13/03/01/2016) and by the Helsinki University Hospital Abdominal Center (HUS-214-2016-35).

Study objectives

The primary endpoint was defined as moderate or greater improvement in the individual VAS scores and the VCSS in the therapy group in relation to no or minor improvement in the control group during the randomized phase. Secondary endpoints were improvement in the individual VAS scores and the VCSS in all patients after therapy, including those from the control group after the randomized phase, and improvement in HRQoL and mental health as measured by the 15D, RAND-36, BAI, and BDI at all control visits.

Study Protocol

At the first visit, cases were checked to ascertain whether they fulfilled the inclusion or exclusion criteria. Previous conditions, investigations, use of medications, and symptoms were registered. All patients received standardized oral information about the behavioral nature of SGB, and its mechanisms aiming at an understanding of the fact that the symptom is self-inflicted. The patients also received a two-page leaflet about the mechanisms of SGB, including four images of the air

injection mechanism and four images of the air suction mechanism. The written information described the differences between gastric and supragastric belching, explained the fact that SGB is subconscious but volitional and that SGB is often preceded by anticipatory upper abdominal symptoms, and described how the onset of SGB may be prevented by diaphragmatic breathing.

Next, the patients were randomized to either the therapy group to receive behavioral therapy (BT) or to the control group for follow-up without an intervention (Fig. 1). Randomization was performed by drawing one of the previously sealed envelopes half of which contained a note that read "therapy group" and the other half "control group". All patients were evaluated at 6 months after the initiation of the study. At this point the controls were also offered BT, and these patients were evaluated after a further 6 months.

Behavioral Therapy

The therapy consisted of five one-hour sessions performed by a speech therapist. Our therapist uses a habit reversal and conversion method where the patients are taught a new way of responding to warning signs that have previously preceded belching. The mode of therapy is psycho-educational, and it is similar to the method used in previous studies (15, 18, 20).

The sessions started with a repeated description of the mechanisms of SGB to the patient. The patients were educated in detail to understand the physiology of belching and the pathophysiology of SGB using visual material. We considered it crucial for the success of the study that the patients understood the nature and mechanism of SGB.

The next step was to teach the patients to recognize possible warning signs and symptoms preceding the onset of SGB. The preceding symptom could be an unpleasant sensation in the throat (globus); or discomfort in the chest or in the upper abdomen.

Furthermore, patients were taught awareness of normal breathing to make them understand the different durations of inspiration and expiration during breathing, learn diaphragmatic breathing, and control the frequency of breathing.

The last step was to teach patients to start diaphragmatic breathing upon the appearance of warning signs or at the onset of belching, a process also referred to as habit reversal.

Questionnaires

The frequency and severity of belching as well as mental well-being were evaluated with a visual analog scale (VAS) ranging from 0 to 10 cm at the baseline of the study and at the follow-up visits. If the frequency and intensity of belching had increased, the patient was encouraged to choose a higher score, and if the symptoms had decreased, the patient was advised to choose a lower score. For mental well-being, a deterioration was indicated by choosing a lower and improvement by a higher score.

To calculate the VAS Composite Symptom Score (VCSS), we had to invert the score for mental well-being: inverted score = 10 - original score. The VCSS scale ranged from 0 to 30, with 0 indicating the lowest degree of symptoms and best mental well-being.

For pain, a 9 mm reduction in the VAS score is considered the minimum clinically significant difference (95% CI, 6–13 mm) (22). We chose a 1.5 cm (= 15 mm) cut off value for an individual symptom score, which results in 4.5 cm for the VSCC. For individual symptoms, 1.5–3.0 cm was considered minor, 3.0–6.0 cm moderate, and > 6.0 cm major improvement.

Depression, anxiety, and HRQoL were evaluated with questionnaires given to the patients at each control. The patients filled out the questionnaires at home and mailed them to the hospital. Depression was evaluated by the Beck Depression Inventory (BDI), anxiety by the Beck Anxiety Inventory (BAI), and HRQoL by both 15D, a 15-dimensional measure of health-related quality of life, and the RAND-36 Measure of Health-Related Quality of Life (RAND-36) (23-27).

Statistical analysis

For sample size calculation the hypothesis was that at least moderate symptom improvement would be observed in the therapy group (VAS Composite Symptom Score $\geq$ 9.0 cm) and no, or only minor, improvement in the control group (VAS Composite Symptom Score $\leq$ 4.5 cm). A minimum of 16 patients was required for each group to achieve 80% power for a statistical significance of $P < 0.05$.

The VAS, BAI, and BDI scores are presented as medians (interquartile range) and the 15D and RAND-36 scores as means. The VAS, BAI and BDI scores were analyzed using the non-parametric Wilcoxon's signed rank test and Mann-Whitney test. Tests for the analysis of independent samples were used for the comparison of differences in the distributions of variables between the therapy and control groups. Tests for related samples were used for measuring changes in variables within the groups. The 15D and RAND-36 were analyzed using the t-test; the independent samples t-test was applied for the comparison of means between groups and the paired samples t-test for the comparison of means within groups. We considered a P-value of < 0.05 to be statistically significant. The correlation of age as well as the baseline BAI, BDI, 15D, and RAND-36 questionnaire results with VAS scores after therapy were evaluated using the Pearson's Correlation Coefficient.

RESULTS

Patient characteristics

Of the 42 patients enrolled, 37 (29 women, aged 19–79, mean 48 ± 15) finished the randomized phase of the study—19 in the therapy group and 18 in the control group—while 5 patients discontinued the study. At the 6-month control, 17 patients from the control group wished to receive BT and were evaluated after a further 6 months. Thus, a total of 36 patients participated in BT. The main symptoms and additional conditions besides SGB of these patients are presented in Table 1.

At baseline, there was no difference in the belching frequency (6.00 [4.00–7.00] vs 7.25 [5.00–8.50]) or intensity (6.00 [4.00–7.00] vs. 7.00 [5.00–9.00]), mental well-being (7.00 [5.00–8.00] vs 6.50 [3.50–8.00]), or the VCSS (15.00 [11.00–18.00] vs 18.75 [15.00–21.00]) between the therapy and control groups.

The mean HRQoL of the 33 (89%) out of 37 patients who returned the 15D questionnaire at baseline, was lower than that of the general Finnish population on ten dimensions and overall (Fig. 2). The results were compared to the HRQoL of an age-standardized sample of the general population in the same geographical area (urban Southern Finland). The population data came from the Health 2011 Health Examination Survey (26). Among the 34 (92%) out of 37 patients who returned the RAND-36 questionnaire, the mean HRQoL was significantly lower than that of the Finnish general population

as regards the items of Role functioning/physical and Bodily pain. (Fig. 3) (27). For 16 (48%) of the 33 patients who returned the BAI and BDI questionnaires at baseline, the BAI was ≥ 8 indicating anxiety, and in 10 (30%) patients the BDI was ≥ 13 indicating depression. The median BAI was 7.0 (3.0–12.0) and the median BDI 9.0 (3.0–14.0).

MII-pH analysis

All patients approved to participate in the study had SGB-related troublesome belching or other esophageal symptoms, according to an expert analysis of the MII-pH recordings. In addition to this descriptive report, the symptom index (SI) and symptom association probability (SAP) for SGB-related esophageal symptoms were calculated when possible. SI measures the percentage of SGB-associated reflux episodes, with a proportion of ≥ 50% considered to be positive, while SAP calculates the statistical relationship between symptoms and SGB using Fisher's exact test, with ≥ 95% considered positive (28). SI was available for 22 (59%) of the 37 patients who completed the study and additional SAP for 5 of these 22 patients. The mean SI was 69% ± 19% in the 22 evaluated patients, and 20 (91%) of them had an SI of ≥ 50% and/or a SAP of ≥ 95% indicating positive symptom correlation. It was not possible to calculate the exact number of belches because it ranged from dozens to hundreds for each registration period. All patients had at least twice as many supragastric belches as the upper limit of the interquartile range for normal healthy controls, which is 2 (1–6) supragastric belches per 24 hours (29).

Reflux-related supragastric belches were observed in 23 (62%) of the 37 patients. In eleven (30%) patients, reflux preceded the supragastric belch, and in 20 (54%) patients the supragastric belch induced reflux. Similar figures have been reported in previous studies (29). The mean acid exposure time of the 37 patients was 1.3% ± 1.2% of the total registration time. Six patients had acid reflux-related heartburn indicating gastroesophageal reflux disease—five of them had a normal acid exposure time of < 4,2 %, and only one had an abnormal acid exposure time of 5.2%. Of the 37 patients who completed the study, 33 underwent MII-pH analysis at Helsinki University Hospital and 4 in other central hospitals in Finland. Therefore, the MII-pH of 33 patients was evaluated at our own unit.

Primary Outcomes—Randomized Phase

Thirty-seven patients completed the randomized phase of the study, 19 in the therapy group and 18 in the control group. After the randomization phase at 6 months, belching frequency (2.00 [1.00–3.00] vs. 4.75 [3.00–7.00], P < 0.001) and intensity (2.00 [1.00–4.00] vs 6.50 [4.00–7.50], P < 0.001) were significantly more reduced in the therapy than in the control group (Fig. 4). Also, the VCSS was significantly lower in the therapy group than in the control group at the 6-month control visit (8.00 [3.50–10.00] vs 14.00 [11.50–18.00], P < 0.001). These were the main primary outcomes of the study. There was no change in the patients' mental well-being (8.00 [7.00–9.00] vs 7.50 [6.00–9.00]).

At the 6-month control, 28 (76%) of the 37 patients returned the BAI and BDI questionnaires (13 from the therapy and 15 from the control group). In the therapy group, the median BAI was 10.0 (4.0–15.0) and the median BDI 12.0 (4.0–15.0), while the median BAI in the control group was 5.0 (3.0–7.0) and the median BDI 6.0 (3.0–9.0), with no significant changes from baseline. Twenty-seven (73%) patients returned the 15D questionnaires (14 from the therapy and 13 from the control group) and 28 (76%) the RAND-36 questionnaires (13 from the therapy and 15 from the control group). In the therapy group, the mean 15Dscore for the dimension of discomfort and symptoms improved from 0.64 to 0.72 (P < 0.05). There were no other significant changes in 15D or RAND-36 scores compared to the baseline at this time point.

Secondary Outcomes—All treated patients

At the 12-month visit 6 months post-therapy, the 17 control patients had experienced a decrease in both the frequency (7.25 [5.00–8.50] vs 2.00 [1.00–3.00], P < 0.001) and intensity (7.00 [5.00–9.00] vs 2.5 [1.00–5.00], P < 0.001) of belching, and mental their well-being had improved (6.50 [3.50–8.00] vs 8.50 [7.00–9.00], P < 0.05).

In total, 36 patients received BT, 19 from the therapy group and 17 from the control group, after the randomized phase. We compared the VAS-scores of these 36 patients at the beginning of the study and 6 months post-therapy (Fig. 5). Belching frequency (6.75 [5.00–8.00] vs 2.00 [1.00–3.00], P < 0.001) and intensity (7.00 [4.75–7.75] vs 2.25 [1.00–4.25], (P < 0.001) were reduced and mental well-being had improved (7.00 [5.00–8.00] vs 8.00 [7.00–9.00], P < 0.05). We also noticed a significant reduction in the VCSS in comparison to the baseline (16.5 [13.00–20.25] vs 7.25 [4.75–11.00], P <

0.001). These were the main secondary outcomes of the study.

Only 23 (64%) of the 36 patients returned the BAI and BDI questionnaires after BT (13 from the therapy and 10 from the control group). Of these 23, 9 (39%) had a BAI score of $\geq$ 8, indicating anxiety and 6 (26%) a BDI score $\geq$ 13, indicating depression. There was a significant reduction in the BDI score between baseline and 6 months after therapy (11.0 [5.0–16.0] vs 7.0 [3.0–13.0], $P < 0.05$), but not in the BAI score (8.0 [3.0–5.0] vs 6.0 [3.0–12.0]) (Fig. 6).

Of the 36 patients who received BT, 26 (72%) returned the 15D questionnaire (14 from the therapy and 12 from the control group). There was no further improvement in 15D, with the exception of the reduction in the score for discomfort and symptoms in the therapy group observed at 6 months after the randomized phase. The RAND-36 questionnaire was returned by 24 (67%) patients (13 from the therapy group and 11 from the control group). Measured by means of RAND-36, HRQoL improved only in the control group at 12 months, i.e. 6 months post-therapy, as regards Role functioning/physical and Social Functioning ($P < 0.05$ for both). There was no significant change in any dimension when all patients (n = 24) where compared at baseline and 6 months after therapy.

Response rate

Using the cut-off value of 4.5 cm for the VCSS, 12/19 (63%) patients from the therapy group and 5/18 (28%) from the control group had improved at the 6-month control visit. For all 36 patients, the number of patients who reported improvements 6 months after therapy was 27 (75%), 12 of whom were from the therapy group and 15 from the control group.

For all 36 patients, the number of participants who responded to BT as regards belching frequency was 26 (72%); of these, 4 reported a minor, 14 a moderate, and 8 patients a major response. For belching intensity among all 36 patients, improvement was observed in 32 participants (89%), 12 of whom had a minor, 14 a moderate, and 6 a major response to therapy.

There was no significant difference between male and female patients' responses to therapy. Neither did the BDI, BAI, RAND-36, and 15D questionnaires' baseline results or age correlate with the VAS scores after therapy.

DISCUSSION

To the best of our knowledge, this is the only randomized study to date of BT on patients with SGB. The results suggest that BT is superior to follow-up without intervention in reducing belching in these patients. Symptom improvement was significant in terms of belching frequency and intensity and the Composite Symptom Score, both when comparing the therapy and control groups at 6 months and when evaluating all 36 patients after therapy.

When evaluated by means of the Composite Symptom Score, 75% of the patients responded to BT (minor–major response). The response rate for belching frequency was 72% and for belching intensity 89% (minor–major response). When only patients with a moderate to major response are considered, the response rate is 61% for belching frequency and 56% for intensity. Our results are not as good as those of the Dutch study that reported a sufficient or major response in 83% of the patients (18), but they are more comparable to the British study in which SGB was reduced by > 50% in approximately half of the patients, when measured by means of both MII-pH and VAS (19). These studies are not directly comparable, however, as we used three questions to calculate the VAS scores, whereas the Dutch employed six and the British four questions (17, 18).

As regards mental well-being, measured with the VAS score, there was no difference between the therapy and control groups at 6 months. Mental well-being only improved when all 36 patients were examined 6 months post-therapy ($P < 0.05$). When we look more closely at the development *within* the groups, we observe an improvement in mental well-being only in the control group at 12 months, which is to say 6 months post-therapy ($P < 0.05$). This might be due to the fact that these patients visited the doctor's office three times—at baseline, at 6 months, and at 12 months—and were therefore offered more support than patients in the therapy group, who only visited the doctor twice. Thus, the improvement in mental well-being in the control group accounts for the good result in all 36 patients.

In a Dutch study, hospital scales for anxiety and depression were not elevated in patients with SGB, although the dimension of mental health was lower than in the general population, evaluated by means of the Short Form Health Survey (SF-36) (9). Our BAI and BDI results suggest that depression

and anxiety were far more common among our patients than in the general Finnish population. In population-based studies, the prevalence of depression in Finland has been around 4.6%–7.3% (30). In the Health 2000 health examination, the 12-month prevalence of the four most common anxiety disorders was 1.9% for panic disorder, 1.2% for agoraphobia, 1.0% for social anxiety disorder, and 1.3% for generalized anxiety disorder for adults in Finland (31). In our study, BT reduced the number of patients with elevated BAI and BDI scores. However, the change was significant only for depression ($P < 0.05$). The BAI and BDI results at baseline are more reliable than those after therapy because of the relatively high dropout rate.

The HRQoL of our patients was significantly lower than that of the general Finnish population as regards ten 15D dimensions and two RAND-36 dimensions (26, 27). In the Dutch study, patients with SGB scored low in social functioning, mental health, vitality, bodily pain, and general health in the SF-36 (9). In the British study, as measured by SF-36, HRQoL was lower on all dimensions among patients with SGB, and BT improved their physical functioning, general health, vitality and social functioning ($P < 0.05$), but not mental health (17). In our study, HRQoL improved only in Role functioning/physical and Social functioning for a subset of patients, and the 15D did not show any significant improvement. Our patients had other comorbidities besides SGB which might affect the HRQoL. Based on our study, the 15D and RAND-36 might not be sensitive enough to measure mental health, since BT reduced anxiety and depression and improved the VAS score for mental well-being.

There are certain limitations in the study. It was difficult to find suitable patients for the study, which is also reflected in the relatively small number of patients enrolled. Not all specialists in clinical physiology are aware of SGB, which has to be detected manually from the MII-pH recordings. Neither was it easy to measure the correlation between SGB and symptoms, as most specialists are only used to calculating the symptom index according to the guidelines for symptoms related to reflux, not to SGB (28). Besides belching, the patients expressed a variety of symptoms related to SGB (Table 1). Before inclusion in the study, each patient was evaluated by two experts. Firstly, to analyze the MII-pH recordings and secondly, by a gastroenterologist familiar with SGB to ensure, that the patient fit the study from the clinical point of view. It can be questioned whether the controls on the waiting list comprise an adequate control group as they also received standardized information about the behavioral nature of the condition. However, they did not receive any

behavioral therapy. If we had organized psycoeducation sessions for the controls as a substitute for BT, the study would rather have been a comparison of two therapies. One limitation of the study is that, although the Rome IV criteria for diagnosing SGB are available, there are no generally approved, international criteria for evaluating the response to BT or any other therapy in patients with SGB (32). Thus, there is a need for an international consensus related to this matter. Five (12%) of the 42 patients, two from the therapy and three from the control group, discontinued the study during the randomized phase, which might cause bias in the results. The rate of patients not returning the RAND-36, 15D, BAI, and BDI questionnaires was even greater, but it was similar in both groups.

On the whole, the results of our study are encouraging, supporting the current understanding that BT is efficient in patients with SGB. There appears to be a need to train more speech therapists to enable a wider use of BT in patients with SGB.

KEY POINTS

- Behavioral therapy has reduced supragastric belching and improved HRQoL in open studies
- In this randomized study, behavioral therapy reduced supragastric belching more than doctor's advice and follow-up without intervention
- The anxiety and depression scores of patients with suprasgastric belching are higher and their HRQoL is lower than those of the general population
- Behavioral therapy may reduce depression scores and improve mental well-being

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author, Jari Punkkinen (jari.punkkinen@hus.fi). The data are not publicly available due to their containing information that could compromise the privacy of research participants.

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Table 1. Main symptoms, additional conditions besides SGB, and PPI usage in the study patients.

	All patients (n = 37)	Therapy group (n = 19)	Control group (n = 18)
Belching	35 (95 %)	17 (89%)	18 (100%)
Heartburn or discomfort in the chest	22 (59 %)	13 (68%)	9 (50%)
Globus or discomfort in the throat	11 (30 %)	5 (26%)	6 (33%)
Upper abdominal pain or discomfort	7 (19 %)	3 (16%)	4 (22%)
Nausea	4 (11 %)	2 (11%)	2 (11%)
Dysphagia	1 (3 %)	0 (0%)	1 (6%)
GERD	6 (16 %)	3 (18%)	3 (17%)
IBS	6 (16 %)	0 (0 %)	6 (33%)
PPI-usage	15 (41 %)	8 (42%)	7 (39%)

GERD= Gastroesophageal reflux disease, IBS = Irritable bowel syndrome, PPI = Proton pump inhibitor.

LEGENDS

Figure 1. Behavioral therapy in patients with supragastric belching, a randomized study. MII-pH = multichannel intraluminal impedance/esophageal pH monitoring, SGB = supragastric belching, HRQoL = health-related quality of life, VAS = visual-analog scale, BAI = Beck Anxiety Inventory, BDI = Beck Depression Inventory, 15D and RAND-36 = health-related quality of life questionnaires.

Figure 2. The mean 15D profiles and 15D scores of the patients at baseline and those of an age-standardized sample of the general population.

Figure 3. RAND-36 at baseline. The mean HRQoL of the patients was lower than that of the general population in the items of Role functioning/physical and Bodily pain. 1. Physical functioning (PF), 2. Role functioning/physical (RP) 3. Role functioning/emotional (RE), 4. Vitality (V), 5. Mental health (MH), 6. Social functioning (SF), 7. Bodily pain (BP), 8. General health perceptions (GH).

Figure 4. There was no difference in the self-perceived frequency and intensity of belching or mental well-being between groups at baseline. At the 6-month control, the frequency and intensity of belching were significantly lower in the therapy group than in the control group but here was no difference in mental well-being (median, VAS 0–10).

Figure 5. All patients (n = 36), both the therapy (n = 19) and the control (n = 17) group, after the randomization period, at baseline, and at 6 months after behavioral therapy. The self-perceived frequency and severity of belching had decreased and mental well-being had improved significantly (median, VAS 0–10).

Figure 6. BAI and BDI in all patients (n = 23), both from the therapy (n = 13) and the control (n = 10)

group, after the randomization period, at baseline, and at 6 months after behavioral therapy (median, VAS 0–10).

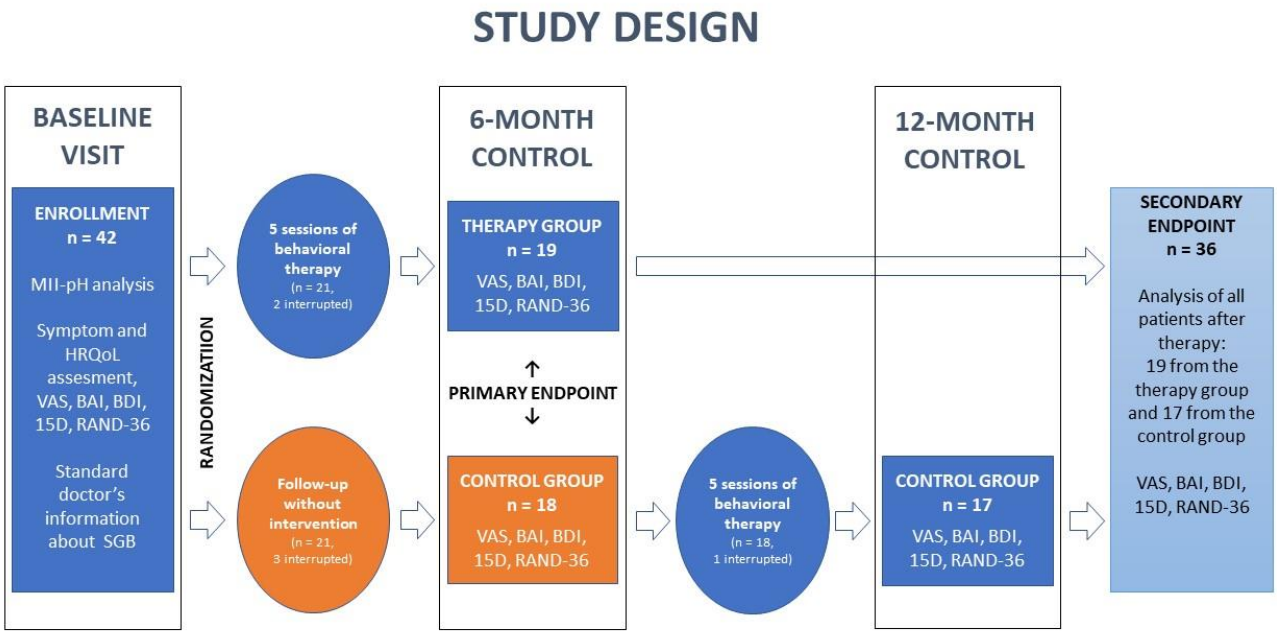

Figure 1

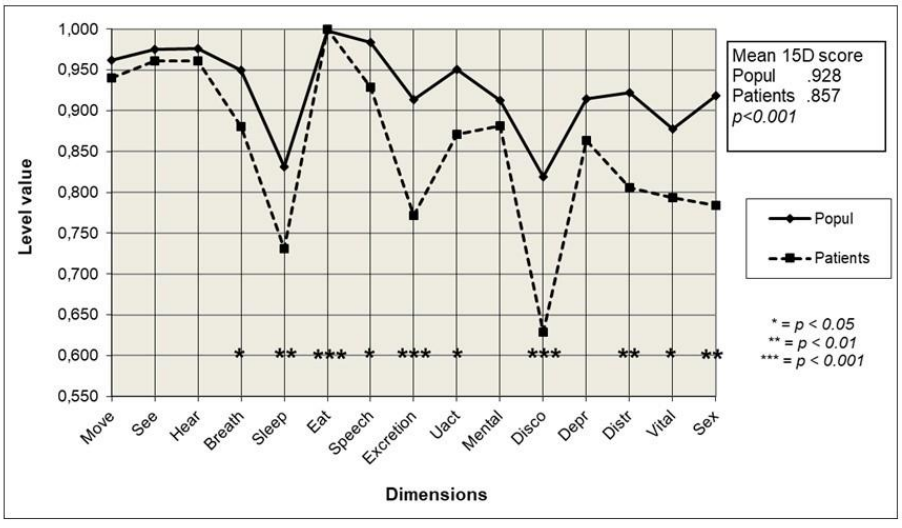

Figure 2

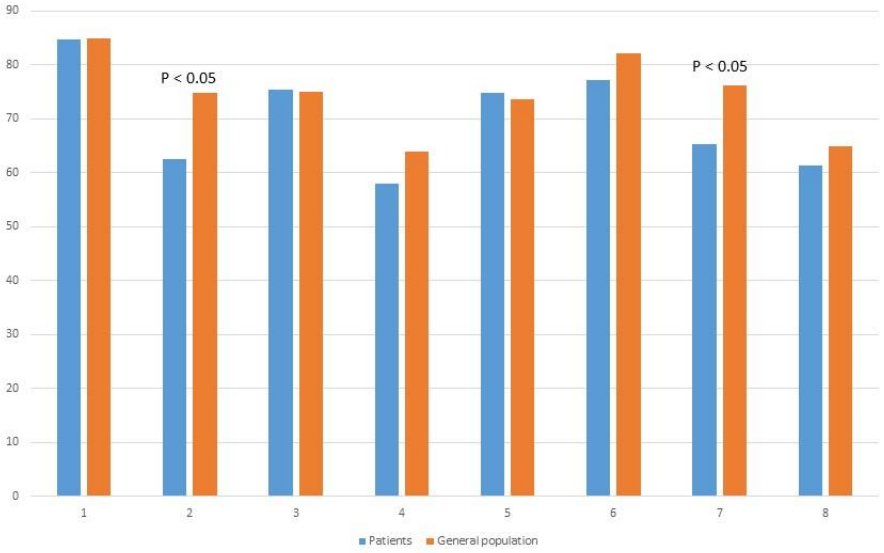

Figure 3

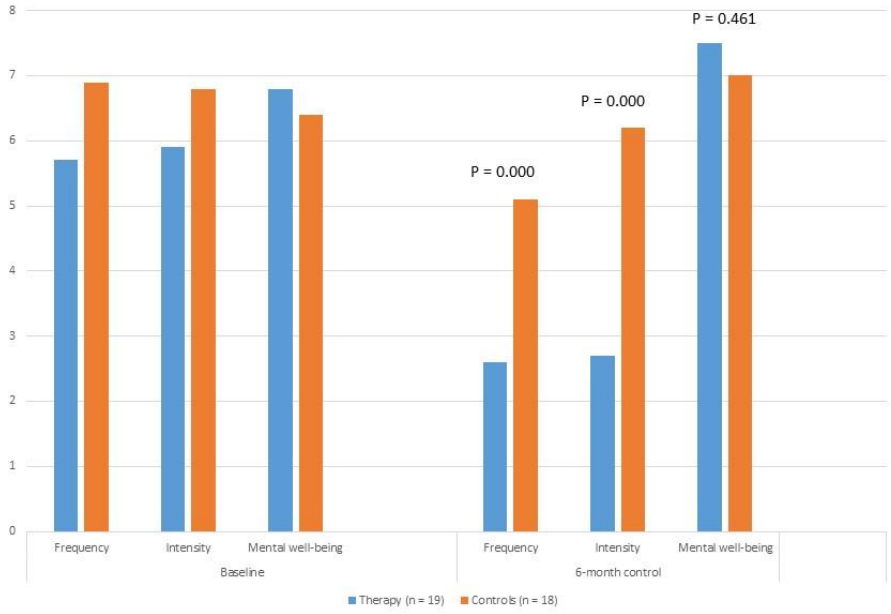

Figure 4

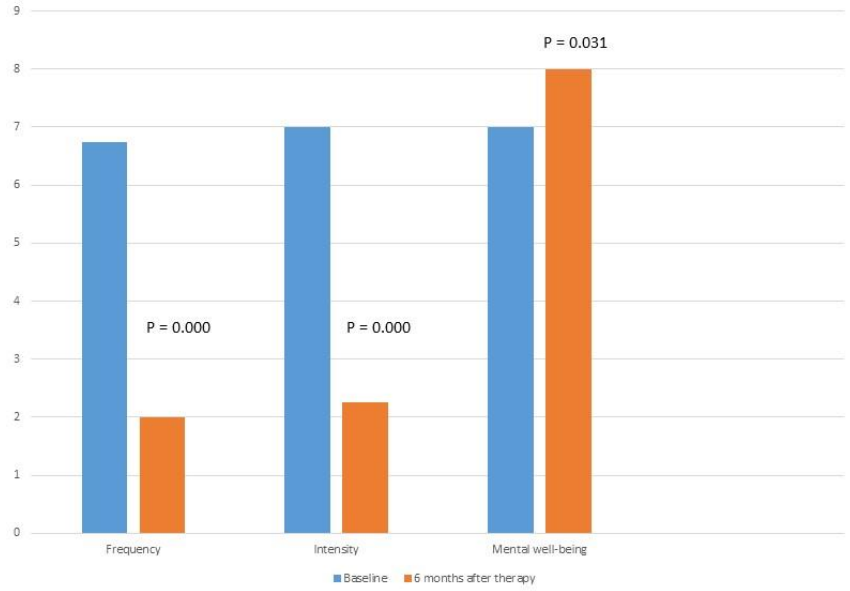

Figure 5

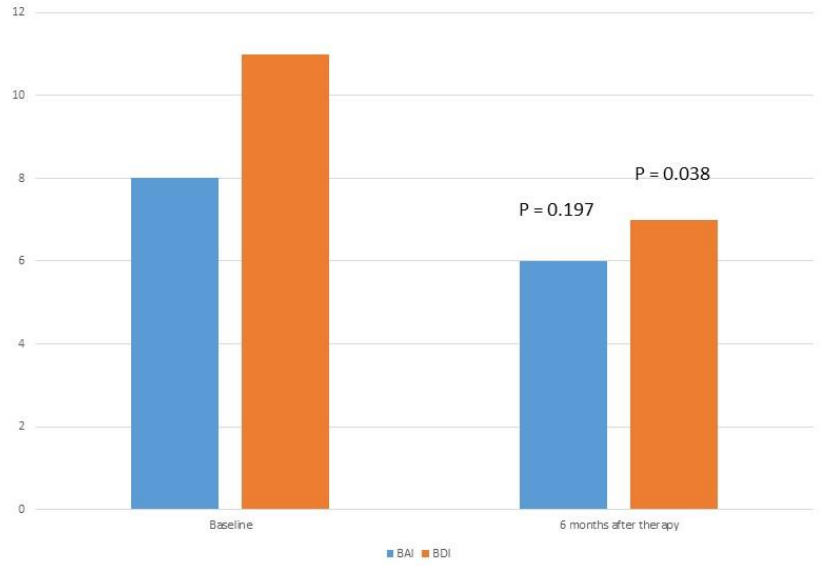

Figure 6