

Biofeedback Therapy Improves Continence in Quiescent Inflammatory Bowel Disease Patients with Ano-Rectal Dysfunction

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Abstract

Introduction: Despite optimal disease control and absence of objective markers of mucosal inflammation, fecal incontinence (FI) secondary to anorectal dysfunction is common, difficult to treat and significantly reduces quality of life (QoL) in quiescent Inflammatory Bowel Disease (IBD). Whilst biofeedback therapy (BFT) is an established treatment for FI, its role in IBD patients with anorectal dysfunction has not been explored.

Methods: Retrospectively we reviewed all IBD cases referred for ano-rectal manometry (ARM) and BFT at our institution between 2009-2014. For each patient, data confirming IBD quiescence (endoscopic, histology, radiography and biochemistry), IBD phenotypes, medication, surgical and obstetric histories, baseline FI frequency, QoL scores (rated 0-10) and results of anorectal investigations were recorded. Patients were classified as responders or non-responders to BFT based on symptoms at follow-up.

Results: Nine quiescent IBD patients (6/9 crohn's and 3/9 ulcerative colitis, median age 53, 7/9 females), with baseline median FI frequency 11.5/week and QoL score 6, had BFT following ARM. Manometrically, all had external anal sphincter weakness, 6/9 internal anal sphincter weakness, 2/9 with co-existing dyssynergic defecation and 8/9 had rectal hypersensitivity. Following a median 2 BFT sessions; 8/9 (89%) patients improved with reduced FI frequency ($U=0.5$, $P=0.003$) and 5/9 (56%) became fully continent.

Conclusions: BFT appears to be just as effective for FI in IBD patients as it is in non-IBD populations and may have a role in restoring continence and QoL. This data highlights the importance of anorectal physiology studies in symptomatic patients once active inflammation is excluded.

Keywords: Inflammatory Bowel Disease; Fecal Incontinence; Biofeedback Therapy

Introduction

Recent international consensus guidelines recommend biofeedback therapy (BFT) for fecal incontinence (FI) (1). FI is common in IBD (affecting up to 74%) often causing distressing symptoms such as urgency, tenesmus, and incontinence despite inactive disease (2). These symptoms can be difficult to treat

and significantly impair quality of life (QoL) (2-3). Despite this, there is recognized unmet clinical need for continence care in IBD (2) and failure to recognize anorectal dysfunction leads to underutilization of pelvic floor therapeutic services (4) and may lead to potentially premature treatment 'escalation' and prolonged, futile exposure to corticosteroid therapy (5). Potential mechanisms for anorectal dysfunction in the absence of active inflammation in IBD include; alterations in rectal wall compliance and calibre, widening of the pre-sacral space, altered rectal sensitivity and muscle tone and neuroplastic changes resulting in aberrant dysmotility, sensation, and secretion associated with gastrointestinal inflammation (both during and after) (5-6). Indeed, such alterations in anorectal function, have been demonstrated in physiological studies in both quiescent crohn's disease (CD) (7-8) and in ulcerative colitis (UC) (9). Moreover, manometric parameters have been shown to be associated with severity of symptoms(10). Whilst the role of BFT in FI is well established, its efficacy for FI in an IBD specific population has not previously been reported to our knowledge. Therefore, the aim of this retrospective study was to evaluate outcomes of BFT in quiescent IBD patients with FI at our institution.

Methods

IBD patients

We retrospectively reviewed the clinical data of all consecutive IBD patients referred with FI to the Gastro-intestinal Physiology unit between 2009-14 at the Pennine Acute Hospitals NHS Trust, Greater Manchester, United Kingdom. Data were collected from patient health records.

Protocols

Baseline visit and anorectal manometry: A detailed medical, surgical, dietary, gynae-obstetric history including the parity and medication history was obtained at the baseline visit and entered into a dedicated proforma with recorded details including the baseline FI frequency (number of episodes per week). Data on IBD activity (endoscopy, histology, radiography

and biochemistry), IBD phenotypes and other relevant investigations and QoL scores (on the ten point Visual Analog Scales) were also noted. After informed consent, a conventional anorectal manometry (ARM) study was done on all patients as per the Iowa protocol (11). Following the ARM study, patients received the first session of BFT on the same visit.

Biofeedback therapy: BFT was undertaken using a dedicated software programme (Polygram Net, Medtronic Inc, Watford, and Hertfordshire, UK) and a 4 channel solid state catheter (Gaeltec, Isle of Skye, Scotland, UK). BFT sessions lasted between 45 and 60 minutes. During BFT, the IBD patients received sphincter exercise training using techniques adapted from the Iowa protocol (12) to condition the external anal sphincter muscles. Finally, patients were given an information leaflet on anal sphincter exercises to take home and advised to practice for at least 20 minutes three times a day at home. Additionally, those that met the criteria for dyssynergic defecation (13) received anorectal co-ordination training to relax the puborectalis/anal sphincter using a commode-based approach as described in the Iowa protocol (12).

Outcome measures

IBD patients were classified into 2 groups following BFT. ‘Responders’ were patients who became fully continent (no FI episodes) or those who reported significant improvement in FI frequency from baseline. ‘Non-responders’ were those in whom there was no improvement in FI frequency from baseline.

Data Analysis

Data were analysed using a Microsoft Excel spreadsheet. FI frequency between response groups was compared statistically

using Mann-Whitney U-test (MWU) using a standard statistical software package (SPSS 20.0, SPSS Inc, Chicago, Illinois, USA). Data are displayed as the median with inter-quartile ranges (IQRs) unless stated otherwise.

Results

Nine IBD patients (median age 53 (IQR 7), 7/9 females), with quiescent IBD (6/9 CD and 3/9 UC), median baseline FI frequency 11.5/week (IQR 22) and QoL score 6 (IQR 2), completed our gastroenterologist-led BFT programme following ARM studies. Two patients also had urinary incontinence and two had previous hysterectomies. Based on all the IBD clinical parameters available to us, all patients appeared to have inactive disease at baseline, including normal baseline serological inflammatory markers (C - reactive protein and/or erythrocyte sedimentation rate) and absence of histological and endoscopic evidence of active inflammation on most recent mucosal assessments. Table 1 summarizes the IBD disease phenotypes and patient outcomes. On ARM, all patients had confirmed external sphincter weakness 9/9, whilst 6/9 had internal anal sphincter weakness and 2/9 met criteria for co-existing dyssynergic defecation. Only two patients (Table 1 - patients 3 and 7) had endoanal ultra-sonography available and in both cases integrity of both sphincters was confirmed. Interestingly, rectal distension studies revealed hypersensitivity in almost all patients, with 6/9 having abnormal first sensation volume, the volume required to precipitate defecation urgency was abnormally low in 8/9 patients and normal in 1/9 and similarly maximum tolerated volume was abnormally low in 7/9 patients (Table 2). The recto-anal Inhibitory Reflex (RAIR) was above the normal range in 6/9 patients (Table 2). Maximum rest pressures were low in 8/9

Table 1: Characteristics of quiescent IBD patients with FI at baseline and their outcomes post BFT.

| Patient No | Gender | IBD Phenotype (Montreal classification) | Past Surgical History | Co-existing Dyssynergic defecation | No. of BFT sessions | Response | Continence Fully restored |
|------------|--------|---|--|------------------------------------|---------------------|----------|---------------------------|
| 1 | Female | Pancolitis (E3) | Ileo-pan-proctocolectomy ileo-anal pouch | Yes | 2 | Yes | Yes |
| 2 | Male | Proctitis (E1) | Nil | No | 2 | Yes | Yes |
| 3 | Female | Procto-sigmoiditis (E2) | Nil | No | 2 | No | No |
| 4 | Female | Crohn's Colitis (L2) | Nil | No | 4 | Yes | No |
| 5 | Male | Ileal Crohn's (L1) | Right Hemicolectomy and TI resection | Yes | 4 | Yes | No |
| 6 | Female | Crohn's Colitis (L2) | Nil | No | 2 | Yes | No |
| 7 | Female | Crohn's Colitis (L2) | Right Hemicolectomy and anterior resection | No | 3 | Yes | Yes |
| 8 | Female | Crohn's Colitis (L2) | Nil | No | 2 | Yes | Yes |
| 9 | Female | Ileal Crohn's (L1-p) | Anal fistula repair | No | 3 | Yes | Yes |

Table 2: Median (IQR) baseline ano-rectal physiology data (n=9) IBD patients with FI.

| Physiological Test | Median (IQR) | Normal range values |
|-----------------------------------|--------------|---------------------|
| First Sensation volume (ml) | 10 (20) | 15-25 |
| Urge to defecate volume (ml) | 70 (70) | 152-218 |
| Maximum tolerated volume (ml) | 155 (63) | 223-275 |
| Recto-Anal Inhibitory Reflex (ml) | 20 (9) | 9-16 |
| Maximum resting pressure (mmHg) | 46 (42) | 56-80 |
| Maximum squeeze pressure (mmHg) | 103 (79) | 124-211 |

patients and similarly low maximum squeeze pressures were observed in 6/9 patients (Table 2).

Following a median of 2 (IQR 1) BFT sessions with a median 71 (IQR 42) days between sessions; 8/9 (89%) patients were responders with statistically significant improvement in FI frequency (median FI frequencies: Baseline 11.5/week vs. post BFT 0/week, Mann-Whitney $U=0.5$, $P=0.003$) and 5/9 (56%) reporting no FI episodes. Incidentally, 6/9 patients had documented evidence of self-practices with sphincter exercises at home as prescribed. The one non-responder self-discharged from the BFT service after two sessions.

Discussions

Data from our heterogeneous IBD series suggest that BFT is just as effective in this population as it is in non-IBD cohorts. Previously, we have reported on a large series of non-IBD FI patients using the same outcome measures, protocols, follow-up intervals and the outcome data are similarly positive in the present study (14). Our present IBD cohort had demonstrable anorectal dysfunction with sphincter weakness, low resting and squeeze pressures and several other physiological abnormalities which merit further discussion.

Whilst detection of abnormalities in anorectal physiology findings was not the primary aim of this retrospective study, our data support previous findings in both UC (9) and CD (7) demonstrating abnormalities in RAIR, which may be suggestive of dysfunction of the enteric nervous system in these patients (7). Our findings of severe rectal hypersensitivity in our quiescent cohort have been reported by some authors previously (8, 15) and are of interest as they may have implications for topical therapies in such patients (5) and may account for urgency symptoms secondary to heightened perception of rectal filling (15).

One of the most striking features in our dataset are the four patients with recognized pre-disposing factors to anorectal dysfunction and FI including; anal fistula surgery and colo-rectal surgeries (2). Surprisingly, all 4 of these patients improved with three regaining full continence post-BFT. Given the

observed multitude of sensory and motor abnormalities and likely enteric neuropathic dysfunction one must ask how does BFT restore anorectal function in such patients? Recent studies using cortically evoked potentials before and after therapies, suggest that BFT improves bowel function via neuroplasticity by modulating the brain-gut axis and strengthening transmission in cortico-anal and cortico-rectal neural pathways (16). Trans sacral and Trans lumbar magnetic stimulation are other exciting tools with potential to evaluate damaged neural pathways in patients with FI (17) and may be the subject of future research to unlock the pathophysiology of ano-rectal dysfunction in IBD.

Limitations of this retrospective study include the small sample size which precluded comparisons of physiological parameters between disease sub-types, the limited availability of endoanal ultrasound and the study also pre-dated the availability of fecal calprotectin as a surrogate marker of disease activity and high-resolution manometry at our hospital. Also, due to the retrospective nature of the study and given that all patients were in stable clinical remission, 7/9 patients had mucosal assessments that were between 6-12 months old prior to the baseline visit. Whilst the infrequency of BFT sessions could also be seen as a limitation, we have previously shown that less-intensive BFT regimes have comparable outcomes to more intensive regimes(14) and the data shown here would also support that.

In summary, BFT appears to be effective in quiescent IBD patients with anorectal dysfunction regardless of the disease phenotype, previous surgeries and complications. Symptomatic IBD patients with FI should be referred for ARM once active inflammation is excluded. Further prospective research is now required using modern brain-gut imaging technologies and trans-lumbar/sacral magnetic stimulation to probe the mechanisms of anorectal dysfunction in IBD further to guide novel therapies which may include neuromodulatory techniques. Future prospective studies of BFT in IBD patients with FI may also explore the effects of BFT on correction of physiological parameters such as rectal sensitivity and RAIR.

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