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ORIGINAL ARTICLE

COMPARATIVE STUDY BETWEEN BIOFEEDBACK RETRAINING AND BOTULINUM NEUROTOXIN IN TREATMENT OF ANISMUS PATIENTS

By
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Aim: *Anismus is a significant cause of chronic constipation. This study came to revive the results of biofeedback BFB retraining and botulinum toxin A BTX- A injection in treatment of anismus patients.*
Methods: *Forty eight patients with history of constipation underwent anorectal manometry, balloon expulsion, defecography, and electromyography. All patients had a non relaxing puoborectalis muscle. The patients were randomized into 2 groups. Group I patients receive biofeedback, two times per week for one month. Group II patients were injected with BTX- A. Follow up was conducted weekly in the first month then monthly for one year.*
Results: *In BFB training group 3 patients quite before the end of sessions with no improvement, initial improvement was recorded in 12 patients (50%) while long term success was recorded in 6 patients (25%). In BTX-A group, initial improvement recorded in 17 patients (70.83%) with long term improvement in 8 patients (33.3%) There is a significant difference between BTX-A group and BFB group as regarding the initial success, but this significant difference disappeared at the end of follow up.*
Conclusions: *Biofeedback retraining has therapeutic effect on patients suffering from anismus also, BTX-A injection is successful for temporary treatment of anismus and need repeated injection. Initial improvement is better after BTX-A injection*

Keywords: *Obstructed defecation, Constipation, Puborectalis.*

INTRODUCTION

Constipation is a common medical problem which has various etiologies among which are outlet obstruction and slow transit.[1] Anismus is a functional disorder of the anal sphincter and pelvic floor muscle in which the muscles contract, rather than relax, during attempted defecation.[2,3] Since Bleijenberg and Kuijpers first used biofeedback to treat anismus, many others reported improvement of anismus after biofeedback (BFB).[4-7] However, a significant proportion of patients with anismus still failed to respond, and little has been known about the factors that can predict success or failure in biofeedback. The results of biofeedback therapy in anismus were also conflicting, with efficacy rates ranging from 31 and 89 percent. Furthermore, biofeedback is neither universally available nor uniformly successful.[8]

A recently described non surgical alternative is injection of Clostridium botulinum type A (BTx-A) neurotoxin directly into the puborectalis muscle.[9] BTX-A is a potent neurotoxin that causes paralysis of muscles by presynaptic inhibition of acetylcholine release.[10] The results of BTX-A

injection for treating anismus is also conflicting. Some reported that it is extremely successful for short term treatment of anismus. However, because the effect of toxin wears off within three months of administration, longer term results are only 50 percent successful and repeated injection could be necessary to maintain the clinical improvement.[11,12] Other reported that BTX-A injection have a limited therapeutic effect on patients suffering from anismus.[13]

So our study came to compare the results of BFB training and BTX-A injection in treatment of anismus patients.

PATIENTS AND METHODS

This prospective randomized study included 48 patients with outlet obstruction due to anismus. They were referred to our Colorectal Surgery Unit, Mansoura University Hospital during the period from September 2003 to April 2007. All patients fulfilled Rome II criteria for functional constipation in adults:[13]

- two or more of the following for at least 12 weeks (not necessarily consecutive) in the previous 12 month: straining in> 25% of bowel movements,lumpy or hard stools in > 25% of bowel movement,sensation of incomplete evacuation in > 25% of bowel movement , sensation of anorectalobstruction or blockage in> 25% of bowel movement, manual manoeuvres to facilitate > 25% of bowel movement, fewer than three defecation a week
- Loose stool not present, and insuffient criteria for irritable bowel syndrom13. All patients were unresponsive to laxatives or enema use.

Pregnant patients, patients with sphincteric defect, any patient proved to have colonic inertia by colon transit time & any patients with previous history of pelvic surgery e.g. mesh rectopexy, Duhamel operation were excluded

Diagnosis of ansimus was based on determination of intestinal transit time, anorectal manometry, balloon expulsion test, defecography, and electromyography (EMG) activity of the EAS.

Ano-rectal manometry: was performed using a standard low compliance water perfusion system and eight-channel catheters with pressure transducer connected to 5.5 mm manometric probe with spirally located ports at 0.5 cm interval. The protocol of performance is stationary pull through technique with recording the functional length of the anal canal (FL), mean maximum resting pressure, mean squeeze pressure. Rectoanal inhibitory reflex (RAIR) was assessed to exclude Hirshsprung's disease. Pressures were recorded using a computerized recording device (Sandhil Bioview programs, USA) 7. An immediate decrease in the resting pressure to base line rectal pressure was considered as full Manometeric relaxation 12.

Evacuation defecography: With the patient in the left lateral position, the rectum was filled with 120 ml of barium paste then the patient seated upright on a specially designed commode and asked to empty the rectum as rapidly and completely as possible. Plain x-rays were taken under fluoroscopic control with the patient at rest, with voluntary anal contraction and during defecation.[14,15]

Surface electromyography: All patients were investigated with EMG of the external anal sphincter using surface electrodes 1 cm lateral to the anal verge at 3 and 9 o'clock. The patient was carefully instructed and then requested to squeeze and strain while electromyographic activity was recorded. Paradoxical contraction of puobrectals means failure of relaxation of puobrectalis during defecation.[16]

Balloon expulsion test: The balloon expulsion test was done by using a rubber balloon that is inserted into the rectum and inflated with 60 ml saline the patient was asked to expel the balloon in left lateral position or into a toilet.[17]

Ansmius was defined as non relaxing anal sphincter on manometric straining in an attempt to defecate , inability to expel water filled rectal balloon and non relaxing puborectalies on defecography accompanied by prolonged evacuation time or inability to expel the barium past in the presence of normal perineal descent[7,14-17] Only patients fulfilling theses criteria were included in the study.

Patients were then randomized into 2 groups. Randomization was achieved using sealed envelopes. After careful explaining the purpose of the study, an informed consent was taken from every patient.

Group I patients (BFB group) (24 patients), All were subjected to biofeedback therapy, two times per week for about one month (eight sessions). All patients were treated as outpatient procedure. At the first session, the anatomy and physiology of the pelvic floor were explained to the patient, using diagrams and their own tests results.

We used pressure based biofeedback training, using a perfused eight-channel polyvinyl catheter with a compliant

balloon at the tip (SANDHILL Biofeedback programs, USA). The side holes were placed in the distal rectum and the anal canal, and the balloon attached to the tip of the catheter was used for training expulsion. Patients were told that the sphincter should relax during expulsion of the rectal balloon at the urge threshold. They should learn how to relax the pelvic floor muscles and to push down slowly using their abdominal muscles. This was accomplished by trial and error. Straining and relaxing were repeated until a normal pattern of expulsion occurred with or without the help of therapist.

Group II patients (Botulinium toxin "BTX-A" injection) (24 patients) All patients were injected with BTX- A in the left lateral position; anesthesia was not required. The anal canal was cleaned with povidone iodine. A vial of Dysport, 500 u, (Dysport, Ipsen, United Kingdom) is dissolved in 2.5 ml isotonic saline. A volume of 0.5 ml of dissolved toxin, i.e 100 u Dysport, is injected in each patient. The injection is given with an insulin syringe fitted with a needle size of 21 gauze and 3.75 lengths. The needle tip was guided by the contralateral index finger into the anal canal. BTX- A was injected into the left and right sides of the paradoxically contracting muscle i.e on either side of puborectalis and the external anal sphincter at 5 and 7 o'clock in lithotomy position. This procedure was done as outpatient procedure.

Follow up:

Follow up was conducted weekly in the first month then every 2 weeks in the second month then monthly for about one year.

In each visit, patients were assessed regarding the improvement in bowel habits. PR examination was done to assess the relaxation of puborectalis muscle during straining. Patients were asked to fulfill a symptom questionnaire one month following the therapeutic procedure and again at the end of our follow up. By this questionnaire the degree of improvement was assessed as regarding the straining severity, anorectal pain, number of weekly bowel movements, sensation of incomplete evacuation and need for anal digitations or enema .

The term clinical improvement or success was chosen to reflect the patients who returned to normal with regard to their bowel habits with no straining, no digitations, no hard stool, no sense of anorectal obstruction, and defection became more than 3/week

Each patient was assessed one month after the procedure by anorectal manometry, balloon expulsion test, defecography and EMG examination of the anal sphincter to monitor any changes in paradoxical contraction and to show whether the clinical improvement was associated with normalization of objective findings or not.

At the end of follow up, patients were asked allowed to answer a very simple question "Are you satisfied by the result of procedure performed to you? Yes or No".

Statistical analysis of data in this study was performed using SPSS version 10. For continuous variables, descriptive statistics were calculated and were reported as mean+SD. Categorical variables were described using frequency distributions. The Student's t- test for paired samples was used to detect differences in the means of continuous variables and Chi-square test was used in cases with low expected frequencies (P value<0.05 was considered to be significant).

RESULTS

Forty eight patients complaining of anismus were managed in colorectal unit, Mansoura university hospital from September 2003 to April 2007. These patients were randomly divided into two groups. Group I (BFB training group) consisted of 24 patients, 16 females and 8 males, with a mean age 39.6+15.94 years (ranging from 20-69 years), underwent 8 sessions of biofeedback retraining and Group II (BTX A group) consisted of 24 patients 17 females and 7 males with a mean age 34.7+12.3 years (range from 20-63 years). All patients in group II underwent botiulinium toxin type A (BTX-A) injection Table 1.

Table 1. Demographic data of our patients.

Variables		BFB group	BTX-A group
Age (years)		39.6+15.9 (20-69)	34.7+12.3 (20-63)
Disease duration (years)		4.8 ± 3.34 (1-10)	5.93 ± 3.28 (2-12)
Sex	Female	16(66.67%)	17(70.83%)
	Male	8 (33.33 %)	7 (29.17 %)

In the biofeedback retraining group 3 patients decided not to continue the study and self-discharged themselves because they found BFB retraining unsatisfactory and psychologically unacceptable. Two patients quit after 2

secessions and other one quit after 4 secessions. All were recorded as non improvement on discharge.

In BFB group, initial improvement was recorded in 12 patients (50%) while long term success was recorded, at the end of follow up, only in 6 patients (25%). In BTX-A group, initial improvement recorded in 17 patients (70.83%) with long term improvement in only 8 patients (33.3 %). There was a significant difference between BTX-A group and BFB group as regards the initial success Table 1, but this significance had disappeared at the end of follow up i.e. after one year Table 2.

Table 2. Clinical outcome after BFB training and BTX-A injection.

Variables	BFB training	BTX-A injection	p
Initial improvement	12 (50%)	17 (70.82%)	.008
Long term improvement	6 (25 %)	8 (33.33 %)	.23
Patient satisfaction	6 (25%)	8(33.33%)	.23

Subjective measures were tested using a visual analog scale of 0 to 10. It was noticed that straining efforts during defection had decreased significantly After BFB training and BTX A injection in 10 patients (41.67%) and 14 patients (58.33%) respectively. With no significant difference between both groups Table 3.

Table 3. Subjective results between BFB group and BTX A group.

VARIBLES	BFB GROUP		p	BTX A GROUP		P	P*
	Pre Training	Post Training		Pre Injection	Post Injection		
Straining pattern(VAS)	8.4+2.3	6.8+3.2	0.04	8.5+1.9	5.9+4.3	0.007	0.23
Pain pattern (VAS)	3.2+3.9	3.0+1.2	0.15	3.7+3.5	3.3+2.9	0.60	0.85
Number of bowel motion /w	5.8+6.7	6.2+2.3	0.069	5.2+6.2	5.8+5.1	0.07	0.76
Overall satisfaction (VAS)	0	2.8+3.4	0.26	0	3.3+4.1	0.34	0.54

P* For comparison of BFB group change to BTX A injection group change.

Table 4. Objective results between BFB group and BTX A group.

VARIBLES	BFB GROUP		P	BTX A GROUP		P	P*
	Pre Training	Post Training		Pre Injection	Post Injection		
Manometeric relaxation	0	13 (54.21%)	0.04	0	17 (70.82%)	0.001	0.54
EMG (paradoxical)	24 (100 %)	14 (58.32%)	0.08	24 (100%)	11 (45.8%)	0.07	0.61
Defecogram (+ve)	21 (87.17 %)	15 (62.51%)	0.085	20 (83.33%)	14 (58.32%)	0.08	0.74
Balloon ET (expulsion)	0	7 (29.22 %)	0.01	0	9 (37.52%)	0.001	0.32
PR (+ve)	24 (100 %)	16 (66.72%)	0.06	24 (100%)	15 (62.51%)	0.02	0.26

P* For comparison of BFB group change to BTX A injection group change.

Anorectal pain and defecation frequency didn't show significant changes after BTX A and BFB retraining

At the end of our follow up, 6 patients (25%) were satisfied by the results of BFB retraining in contrast to 8 patients (33.3%) after BTX-A injection. However this difference did not achieve a significant statistical value Table 3.

Anorectal manometery: Manometeric relaxation was achieved in 17 patients (70.83 %) treated with BTX A injection (p = 0.001) while it was resulted only in 13 patients (54.17%) treated by BFB retraining (p=0.04). The comparison of BFB group change to BTX A injection group change not statistically significant Table 4.

Balloon expulsion: Both groups achieved significant changes in the results of balloon expulsion test as balloon expulsion occurred in 37.5% of patients after BTX injection and 29.17% of patients after BFB retraining. With no significant difference between both groups Table 4

Both groups produced changes in the results of EMG, defecograpy and per rectal examination but did not reach the statistical significance Table 4.

DISCUSSION

Anismus is a common cause of constipation and outlet obstruction. The affected subjects strain excessively during defection with the higher centers unaware of the in coordination of pelvic floor.[5] Anismus affects more middle aged women.[22]

Attempts to overcome the obstructive effects of the non relaxing puborectalis muscles at defecation in true ansimus have been varied. Non surgical methods includes BFB training or BTX A injection and various surgical methods such as partial division of the puborectalis muscles have been advocated but against this approach is the overriding importance of maintaining continence.[23]

Glia et al. 24 reported that biofeedback therapy is not suitable for all patients with ansimus. Gilliand et al.[25] reported that biofeedback was completely successful in only 35% of his patients, although complete success was achieved in 63% of patients who finished the prescribed training course. Meagher et al.[26] reported that 12 patients underwent placebo treatment followed by biofeedback treatment and concluded that the clinical improvement may be in part due to placebo effect and observer bias. Rhee et al[27] reported that BFB was successful in 68.9% of their anismus patients. In our series, Biofeedback training (BFB) showed an earlier clinical improvement in 12 patients (50%).However, the long term results persisted only in 6 patients (25%).This low success rate may be attributed to self discharging phenomena.

Different results between various studies are probably attributed to different case selection, different regimens, and different methods of biofeedback. Also, the absence of consensus on how to define treatment outcome.[28]

In the BTX-A group clinical improvement was recorded in 17 patients (70.83%). but the improvement persisted only in 8 patients (33.3%). These results goes with the results reported by Joo et al.[10] and Maria et al.[11] who reported that botiulinium toxin could be a promising treatment in patients with anismus and less expensive and easier to perform than BFB training. They also reported that repeated injections could be necessary to maintain clinical improvement. Shafik and El-Sibai[30] injected 15 anismus patients with BTX-A. And noticed that improvement was recorded in 13 patients. However, improvement was maintained for a mean of only 5 months and so re-injection was necessary. Ron et al[12] observed only 37.5% success after the first injection and 28.6% after the second.

Ron et al[12] reported that 37.5% of his patients were satisfied with the overall results of BTX A injection. Straining at defection decreased in 29.2% and defection frequency did not change during follow up as could be expected. Kawimbe et al[5] showed that there was significant improvement in defection frequency after BEB training as it had increased from 5.2+0.8 to 8.8+1 times per week, also straining effort decreased significantly in his patients.

In our study, 41.67% of patients experienced decreased straining efforts after BFB retraining and in 58.33% of patients the straining efforts decreased significantly in BTX A group. With no significance difference between both groups. No of motion per week did not change significantly either after BTX A injection or after BFB retraining. At the end of follow up, 6 patients (25%) were satisfied by the results of BFB retraining in contrast to 8 patients (33.3%) were satisfied after BTX-A injection. However this difference did not achieve a significant statistical value.

Manometeric relaxation was achieved significantly post BFB and post BTX A injection but no significant difference between two groups. Ron et al[12] reported that manometric relaxation after BTX A injection was attained by 75 % of his patients and this effect lasted throughout the entire study and follow up. Glia et al[24] found that there was no difference in the results of anorectal manometry before and after biofeedback therapy also Kawimbe et al[5] reported that no significant difference in the results of manometry before and after BFB training.

In our study, both BFB retraining group and BTX A injection group achieved significant changes in the results of balloon expulsion test but with no significant difference

between both groups. Ron et al[12] found that balloon expulsion ,after BTX A injection, achieved in 37.5% of his patients after the first injection and in 45.8 % after two injection while Kawimbe et al[5] reported that before BFB retraining, only two subjects could expel the rectal balloon, whereas after BFB retraining 13 out of 15 could do so.

Our series showed also difference in EMG, defecographic finding before and after injection of BTX A and BFB training but didn't reach statistical significance. Joo et al.[10] reported that EMG finding accurately correlate with patients' subjective reports. Maria et al.[11] reported that paradoxical pattern at EMG were decreased in all patients and also the anorectal angle measured during straining increased significantly following injection.

The discrepancy between objective and subjective results may be explained by ansimus is a functional disorder and there is always a possibility for placebo effect, also the non-blind fashion of follow up, which could have biased patients responses to therapy

Biofeedback retraining has a therapeutic effect on patients suffering from anismus also, BTX-A injection could be successful for temporary treatment of anismus. However, because the mechanisms of action is short, longer term results are unsatisfactory and further controlled trials are necessary to assess the role of BTX A in treatment of ansimus

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