

PSYCHOLOGY

Randomized Placebo Controlled Trial of Sildenafil Citrate, Cognitive Behavior Sex Therapy and Integrated Treatment in Men Diagnosed With Non Organic Erectile Dysfunction



Ahmad Bilal, PhD,^{a,b} and Najam ul Hasan Abbasi, PhD^{c,d}

ABSTRACT

Introduction: The integrated treatment combining phosphodiesterase-type 5 inhibitors (PDE5i) and Cognitive Behavior Sex Therapy (CBST) has been shown to yield promising results in the treatment of Non Organic Erectile Dysfunction (NOED) in young men.

Aim: The current study aimed to establish the efficacy of integrated treatment combining Sildenafil Citrate (SC) 50mg and CBST as a treatment of choice in young Pakistani men with NOED.

Methods: One hundred thirty-seven young men were recruited to participate in the study out of 164 men referred from sexual health clinics in Pakistan. They were randomized sequentially into 4 treatment groups namely SC = 35, CBST = 34, integrated treatment = 35, and placebo = 33. 7, 4, 6, and 4 men were dropped out of each treatment group respectively. The data of 116 men were analyzed. The on demand SC 50 mg, twice weekly 50 minutes sessions and home assignments, a combination of SC and 50 minutes sessions, and placebo were administered to first, second, third, and fourth group respectively for a period of 12 weeks. The follow-up assessment was done after 12 weeks of post-treatment for all groups.

Main Outcome Measures: The Urdu standardized versions of International Index of Erectile Functioning-5 (IIEF-5) and Depression Anxiety Stress Scale-21 (DASS-21) were the main outcome measures.

Results: The mixed repeated measures analysis of co-variance yielded significant impact of both CBST and integrated treatment groups in improving IIEF-5 scores at post treatment as compared to placebo. The CBST group experienced reduction in depression scores at post treatment as compared to both SC and integrated treatment. Only the integrated treatment brought reduction in anxiety scores at post treatment as compared to SC. The covariates age and NOED duration did not significantly impact the treatment outcome for all treatment groups.

Clinical Implications: The efficacy of integrated treatment approach for improving symptoms of NOED and associated depression and anxiety is strong clinical implication of the study.

Strengths & Limitations: The effectiveness of integrated treatment approach in the improvement of NOED symptoms and associated depression and anxiety scores is the main strength of the study. The improvement in depression scores is the added strength of CBST component of integrated treatment approach. The study should have included other PDE5i to compare their effects with the CBST or placebo groups.

Conclusion: The study concludes that the CBST and integrated treatments are treatment of choice for NOED and associated depression and anxiety in young men. **Bilal A, Abbasi NH. Randomized Placebo Controlled Trial of Sildenafil Citrate, Cognitive Behavior Sex Therapy and Integrated Treatment in Men Diagnosed With Non Organic Erectile Dysfunction. Sex Med 2022;10:100464.**

Abbreviations: CBST, Cognitive Behavior Sex Therapy; ED, Erectile Dysfunction; NOED, Non Organic Erectile Dysfunction; SC, Sildenafil Citrate
Received September 8, 2021. Accepted October 26, 2021.

^aPhD Research Scholar, Department of Psychology, International Islamic University, Islamabad, Pakistan;

^bAssistant Professor, Department of Applied Psychology, The Islamia University of Bahawalpur, Bahawalpur, Pakistan;

^cAssociate Professor, Department of Educational Sciences, Mianyang Normal University, Sichuan, China;

^dEx Assistant Professor, Department of Psychology, International Islamic University, Islamabad, Pakistan

Copyright © 2021 The Authors. Published by Elsevier Inc. on behalf of the International Society for Sexual Medicine. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).
<https://doi.org/10.1016/j.esxm.2021.100464>

Copyright © 2021 The Authors. Published by Elsevier Inc. on behalf of the International Society for Sexual Medicine. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Key Words: Cognitive Behavior Sex Therapy; Erectile Dysfunction; Integrated Treatment; Men Health; Non Organic Erectile Dysfunction; Pakistan; Placebo; Sex Therapy; Sildenafil Citrate

INTRODUCTION

Erectile Dysfunction (ED) is a leading sexual dysfunction affecting men of all age groups. Recently, there has been found an increase in ED in cohort of young men below 40 years. Twenty five percent of new cases are being reported in young men below 40 years age.^{1,2} Similarly, the studies in Pakistan have also reported increased prevalence of ED in men under the age of 40 years.^{3,4} The prevalence of non organic erectile dysfunction (NOED) was found 51% in Pakistan where the psychogenic or non organic etiology was higher in men under the age of 40 years (70%) compared with organic etiology which was more common in men over the age of 40 years (30%).⁴ Similarly, another study by Nasim (2017) reported the prevalence of NOED 84% in Pakistan where 67% of the men were below 40 years of age.³ Generally, the men under the age of 40 years show more psychogenic or non organic etiology⁵ and experience either mild to moderate NOED severity.⁶ Currently, there is scarcity of research on the effective management plan for this new young population of sufferers with non organic etiology.^{7,8} So, more studies are needed to test the efficacious management plan for this new cohort of sufferers of ED.^{1,5,7,9} This study was conducted to fill this gap.

The NOED is defined as the persistent inability to attain or maintain sufficient erection or erectile rigidity until the completion of sexual intercourse primarily due to non organic factors.^{10,11} The NOED is often caused by uncertain psychological factors and do not contain a specific biomarker.^{12,13} The uncertain psychological factors may include depression or anxiety,⁵ lack of sexuality education,¹⁴ psychosexual trauma, disrupted childhood attachment and abuse,¹⁵ relationship difficulties,¹⁶ or issues related to previous unsuccessful sexual encounters.^{15,17}

The personal and relationship factors are often overlooked by the medical community when devising management plan for the ED. The traditional management plan of ED included the administration of the phosphodiesterase type 5 inhibitors (PDE5i), the Sildenafil Citrate (SC) to men suffering from ED.^{17–19}

The results of SC administration on NOED cases have mixed results. It has been found that almost a quarter of men do not adequately respond to SC and often end up in despair.⁸ Moreover, there had been individuals who improved their NOED symptoms immediately after diagnosis.¹⁰

A study by Wiggins et al (2018) reported an improvement in erectile function but did not report an improvement in sexual

intercourse satisfaction. This is the area where PDE5i fail to address the issue⁷ especially if the causes related to intrapsychic or marital issues.²⁰ The recent studies report that the ineffective use of PDE5i may be followed by psychosexual therapy to bring about improvement in symptoms of NOED.⁷

On the other hand, there have been reports of efficacy of techniques of traditional sex therapy combined with the now popular cognitive behavior therapy (CBT). The result is cognitive behavior sex therapy (CBST), a non medical psychotherapeutic approach to be used in conjunction with pharmacotherapy in the management of NOED.^{21,22} The CBST consists of several components including psychosexual education, cognitive restructuring of sexuality related attitudes, challenging automatic thoughts through Socratic dialogue and other techniques. Further, the therapy works by instructing the client new sexual communication skills, new meanings of one's sexuality, and other specific techniques for improving male sexual function and overcoming psychological barriers in the way of sexual pleasure and functioning.^{20,23,24} The mindfulness can be integrated with CBST which reduces performance anxiety and helps the man focus on his current sexual process disengaging him from the anxiety producing inhibitory mechanism.^{23,25}

There has been felt a need for a comprehensive management plan for the treatment of NOED.⁹ The comprehensive management plan consists of combination of non medical approaches, often sex therapy in addition to pharmacotherapy in the management of NOED. The previous studies documented the efficacy of integrated treatment approach in cases of ED than the PDE5i or CBST treatment alone.^{20,24} The treatment outcome of ED is generally significant when PDE5is are administered in combination with CBST either in individual format or group format.^{26,27}

In a recent study on Pakistani men, the integrated treatment involving CBT and PDE5i improved score on IIEF in a group of Pakistani men suffering from ED as compared to those who were taking PDE5i alone.²¹ These men reported improved erectile function, intercourse satisfaction, sexual desire, and overall satisfaction as compared to men taking only PDE5is. Such cohort of men reported the lasting effects of integrated treatment at 15 – 18 months follow up later.²² At follow up, the improved effects in domains like erectile function, intercourse satisfaction, and sexual desire remained stable. In another study, the men who received group sex therapy in combination with SC improved erectile function considerably as compared to men who were taking SC only and were less likely to drop out.²⁸ In a pioneer study

on CBST by Banner and Anderson (2007), the CBST was shown to improve the erectile function and overall satisfaction in integrated treatment protocol when CBST was introduced in the integrated treatment with SC.²⁴

Despite the efficacy of an integrated approach for the treatment of ED,^{29–32} the empirical studies documenting the results of an integrated approach are limited.²⁶ The current study aimed at comparing the integrated treatment approach with SC and CBST treatment alone. The study also aimed at comparing the efficacy of all 3 treatment approaches in reducing depression and anxiety scores in men with NOED. The current study hypothesized that integrated treatment group would show more improvement in NOED scores as compared to SC or CBST treatment alone. It was also hypothesized that integrated treatment would show reduction in both depression and anxiety scores as compared to both SC or CBST treatment alone.

MATERIALS AND METHODS

Study Design

The current study employed the sequential, randomized clinical trial research design. The participating men were randomized sequentially to receive SC, CBST, integrated treatment combining both SC and CBST, and placebo. The responses were assessed at three time points namely pre-treatment, post-treatment and follow-up. Both the SC and placebo groups were single blinded whereas the CBST treatment group was not blinded.

Participants

One hundred thirty-seven men with NOED were screened eligible and recruited to participate in the study out of total of 164 men referred to the principal investigator from sexual health clinics in South Punjab, Pakistan. The snowball and purposive sampling technique was employed to collect the sample. Those 137 men with NOED were randomized sequentially into 4 groups to receive SC (n = 35), CBST (n = 34), integrated treatment (n = 35), and placebo (n = 33) based on their order of enrollment in the study and alternating among treatment groups. Seven, 4, 6, and 4 men dropped out of SC, CBST, integrated, and placebo groups respectively. A total of 116 men completed the whole treatment (SC = 28, CBST = 30, integrated treatment = 29, and placebo = 29) and were entered in the statistical analysis. The number of drop out men were negligible so did not include in the analysis. The age of the participating men ranged from 18 – 38 years (M = 27 years for all groups). The duration of NOED ranged from 6 months to beyond 3 years. The men with NOED were categorized into 4 categories namely mild, mild to moderate, moderate, and severe based on assessment of NOED symptom severity done through IIEF-5. The following inclusion and exclusion criteria was referred to while recruiting men for the study:

Inclusion Criteria

The men belonging to age range of 18 – 39 years who were in a heterosexual relationship at least for the last 6 months without history of medical, psychiatric, and hormonal disease and dysfunction, drug use including recreational drugs, obese and those not using hypertension and heart medications were included in the sample.

Exclusion Criteria

The men below 18 years and of or above 40 years age who were not in heterosexual relationship at least for the last 6 months with a history of medical, psychiatric, and hormonal disease or dysfunction, drug use including recreational drugs, obese, and those taking hypertension or heart medications were excluded from the sample. The men of or above 40 years were excluded as most men had organic etiology above 40 years age.⁷ The men having other sexual orientations were excluded from the sample because of cultural sensitivity associated with non-heterosexual orientation in Pakistan.²³

DEMOGRAPHIC AND CLINICAL MEASURES

Demographic Information Measure & Informed Consent Form (DIM&ICF)

All the participating men were required to fill the essential informed consent form prior to enrolling for the study. The DIM contained information about the age, and duration of NOED of each participant of the study.

International Index of Erectile Functioning-5 (IIEF-5)

The International Index of Erectile Functioning-5 (IIEF-5) is a brief version of IIEF-15 developed by Rosen et al in 1999 to assess the erectile functioning in men.³³ The brief version has 5 items formatted in likert type scale with 5 response options. The scale has a minimum score of 5 and max score of 25. The scale has a predefined cutoff points to categorize men in severity categories. The cutoff score ranges from 25 to 22 (no ED), 21 – 17 (mild ED), 16 – 12 (mild to moderate ED), 11 – 8 (moderate ED), 7 – 5 (severe ED). The brief version was standardized in Urdu language in 2012 by a team of Pakistani sexual health professionals. The Cronbach Alpha reliability of the Urdu version is .88.³⁴

Depression, Anxiety, and Stress Scale-21 (DASS-21)

The Depression, Anxiety, and Stress Scale-21 (DASS-21) is a brief version of the original scale DASS-42 developed by Lovibond and Lovibond in 1995.³⁵ The scale contains 3 subscales to assess 3 constructs of depression, anxiety, and stress in general population. Each of those subscale contains 7 items, thus making a total of 21 items designed in a likert type scale having 4 response options. The minimum score on a subscale is zero and maximum score on a subscale is 21. Each subscale has predefined cutoff scores to categorize the constructs of depression, anxiety,

and stress in categories of mild, moderate, severe, and extremely severe. The scale was standardized in Urdu language in 2007 by Aslam. The Cronbach Alpha reliability is 0.84, 0.82, and 0.87 for depression, anxiety, and stress subscales respectively.³⁶

Study Protocols & Procedure

Three different treatments were administered to men in 3 groups while the men in the fourth group received placebo. The men in the first group received on demand SC, 50 mg. The men were instructed to use SC, 50 mg 1 hour prior to desired sexual activity on an empty stomach to maximize its efficacy. The men in the second group received CBST on twice weekly basis for a period of 50 minutes per session. In addition, the men were also assigned the homework assignments as part of CBST treatment. The complete treatment manual of CBST has been referred to in a recently published study by the same authors.²³ The men in the 3rd group received the integrated treatment consisting of both on demand SC, 50 mg and twice weekly CBST. The men in the fourth group received placebo and were instructed to use placebo 1 hour prior to desired sexual activity on an empty stomach. All the treatments and placebo continued for a period of 12 weeks. The decision of administering treatments for 12 weeks period was based on evidence from similar previous study conducted by the same authors.²³ At the end of 12 weeks period, the post-treatment assessment was done which were followed by follow-up assessment after the 12 weeks of post treatment assessment. The IIEF-5 and DASS-21 were the main outcome measures at the post treatment and follow-up assessments for assessing the IIEF-5 scores and associated depression and anxiety scores.

The decision to administer SC, 50mg was made as this PDE5i was easily available in the Pakistani market and the price was affordable. It was hard to get other PDE5i in Pakistani market. The men in the first treatment group reported only mild headaches, and transitory stomach upset as side effects of SC, 50 mg. No other long term side effect of SC, 50 mg was reported. The administration of SC 50 mg was monitored throughout the course of the treatment for both SC alone and integrated treatment groups. The decision

to administer the CBST treatment by the principal investigator was made with a focus to keep thorough monitoring and evaluation of the men receiving CBST treatment. Some men in the second group reported an initial difficulty in practicing present moment, and non judgmental mindfulness at home. Some other men reported it difficult to meet therapist's guideline of refraining from sexual intercourse during the practice of stop & start technique at home. The recipients of CBST treatment showed negligible absence rate and were instructed to keep record of home assignments given by the therapist. No side effects were reported by the men in fourth group who received placebo.

Statistical Data Analyses

The Statistical Package for the Social Sciences (SPSS), version 25 (SAS Institute, Cary, NC) was used to statistically analyze the data. The data of 116 participating men who completed the treatment were analyzed, and the data of 21 men who dropped out of the treatment were not analyzed as their number was negligible. The mixed repeated measures analysis of co-variance (RM-ANCOVA) was used to compute within subject and between subject effects. The NOED scores on IIEF-5, severity of NOED, depression and anxiety scores across pretreatment, post treatment and follow-up were treated as within subject effects while the treatment groups were treated as between subject effects. The interaction effects were considered significant at the 95% confidence interval. The effect sizes of 0.02, 0.09, and 0.25 were considered as the small, medium, and large effect size respectively and were denoted by partial eta square (η^2).³⁷ The age and duration of NOED were entered as co-variables. The baseline characteristics of the participating men were described by descriptive statistics and frequency reporting of demographic and categorical variables.

RESULTS

Baseline Characteristics

The Table 1 gives the baseline characteristics of the participating men.

Table 1. Frequency of study variables

Demographic Variables	Characteristics	Frequency (Percentage, %)			
		SC	CBST	Combo	Placebo
Age (years)	Minimum	18	21	21	20
	Maximum	38	37	37	38
Age Groups (years)	18 – 29	9(7.8)	13(11.2)	10(8.6)	13(11.2)
	30 – 39	19(16.4)	17(14.7)	19(16.4)	16(13.8)
	Total	28(24.1)	30(25.9)	29(25.0)	29(25.0)
NOED Duration	6mo – 1y	10(8.6)	20(17.2)	18(15.5)	19(16.4)
	1 – 3 y	11(9.5)	3(2.6)	6(5.2)	5(4.3)
	3+ y	7(6.0)	7(6.0)	5(4.3)	5(4.3)
	Total	28(24.1)	30(25.9)	29(25.0)	29(25.0)
Treatment		28(24.1)	30(25.9)	29(25.0)	29(25.0)

CBST = Cognitive behavior sex therapy; SC = Sildenafil citrate.

Descriptive statistics

The Table 2 describes the descriptive statistics of each dependent variable for each treatment group at pretreatment, post treatment and follow-up.

REPEATED MEASURES ANALYSIS OF CO-VARIANCE (RM-ANCOVA)

The Table 3 gives within subject and between subject interaction effects as computed by RM-ANCOVA. There were co-variables of age, and duration of NOED in such analysis.

Within Subjects Effects

The RM-ANCOVA yielded a statistically significant within subjects interaction effects of IIEF-5 scores, depression, and anxiety scores respectively ($F[3.74, 135.89] = 26.06, P < .05, \eta^2 = 0.41$); ($F[5.61, 204.01] = 2.97, P < .05, \eta^2 = 0.07$); ($F[4.43, 161.13] = 5.82, P < 0.05, \eta^2 = 0.13$) where co-variables age, and duration of NOED were controlled. There was statistically significant improvement in IIEF-5 score, depression and anxiety scores across post treatment and follow-up compared with pretreatment. However, the effect size was large for NOED score but effect size was small and medium for depression and anxiety scores interaction respectively.

Table 3. Within subjects effects

Effects	df(error df)	F	Sig.	Partial Eta Square
IIEF-5Score*Treatment	3.74(135.89)	26.06	0.00	0.41
Depression*Treatment	5.61(204.01)	2.97	0.01	0.07
Anxiety*Treatment	4.43(161.13)	5.82	0.00	0.13
Between Subjects Effects				
IIEF-5 Score*Treatment	3(109)	2.90	0.03	0.07
Depression*Treatment	3(109)	3.01	0.03	0.07
Anxiety*Treatment	3(109)	23.02	0.00	0.38

Between Subject Effects

There were found statistically significant between subject interaction effects of treatment with IIEF-5 scores, depression and anxiety scores respectively ($F[3, 109] = 2.90, P < .05, \eta^2 = .07$); ($F[3, 109]=3.01, P < .05, \eta^2 = 0.07$); and ($F[3, 109] = 23.02, P < .05, \eta^2 = 0.38$) where covariates age, and duration of NOED were controlled. The effect size for interaction of treatment with NOED score and depression was small, and large for anxiety and treatment interaction.

Table 2. Descriptive statistics

Pre Treatment Treatment	IIEF-5 Score		Depression		Anxiety		N
	M	SD	M	SD	M	SD	
SC	12.25	3.25	4.92	2.07	2.50	1.40	28
CBST	13.40	3.55	6.33	2.10	3.80	1.51	30
Integrated	13.68	3.73	4.89	1.81	5.03	2.11	29
Placebo	13.75	4.42	5.10	1.81	4.55	1.59	29
Total	13.28	3.76	5.32	2.02	3.98	1.91	116
Post Treatment Treatment	IIEF-5 Score		Depression		Anxiety		N
	M	SD	M	SD	M	SD	
SC	16.53	2.45	4.78	1.91	2.57	1.19	28
CBST	16.70	2.65	4.93	1.55	3.0	1.11	30
Integrated	17.03	3.04	4.20	1.23	3.79	1.11	29
Placebo	13.86	4.51	4.96	1.56	5.17	1.46	29
Total	16.03	3.46	4.72	1.59	3.96	1.46	116
Follow up Treatment	IIEF-5 Score		Depression		Anxiety		N
	M	SD	M	SD	M	SD	
SC	16.35	2.24	4.71	1.46	2.78	1.13	28
CBST	16.70	2.66	5.13	1.25	4.40	0.81	30
Integrated	17.20	2.89	4.13	1.05	4.20	1.34	29
Placebo	13.37	4.27	4.82	1.25	5.03	1.14	29
Total	15.91	3.42	4.70	1.29	4.12	1.37	116

M = Mean, SD = Standard deviation

Table 4. Within subjects pairwise comparisons

(I) 3 Time Points	(J) 3 Time Points	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval for Difference	
					Lower Bound	Upper Bound
IIEF-5 Scores						
1	2	-2.75*	0.17	0.000	-3.11	-2.40
	3	-2.63*	0.17	0.000	-2.97	-2.29
2	3	0.12	0.07	0.08	-0.01	0.263
Depression						
1	2	.59*	0.15	0.000	0.29	0.88
	3	.61*	0.13	0.000	0.34	0.87
2	3	0.01	0.12	0.87	-0.21	0.25
Anxiety						
1	2	0.02	0.15	0.89	-0.28	0.33
	3	-0.13	0.14	0.33	-0.41	0.14
2	3	-0.15	0.08	0.07	-0.32	0.01

* $P < .05$

Multiple Comparisons

The multiple comparisons of within subject and between subject interaction effects were described through running least square difference post hoc test.

comparison to pretreatment. However, there was no statistically significant differences in IIEF-5 and depression scores at follow up in comparison to post treatment. The anxiety scores, on the other hand, did not show a statistically significant difference across post treatment and follow up.

Within Subject Multiple Comparisons

The within subject pairwise comparisons have been outlined in Table 4. There was statistically significant difference in IIEF-5 and depression scores at post treatment and follow up in

Between Subject Multiple Comparisons

The between subject pairwise comparison have been outlined in Table 5. The CBST and integrated treatment groups brought

Table 5. Between subjects pairwise comparisons

(I) Treatment	(J) Treatment	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval for Difference	
					Lower Bound	Upper Bound
IIEF-5 Scores						
SC	CBST	-0.33	0.86	0.69	-2.04	1.37
	Integrated	-0.65	0.87	0.45	-2.39	1.08
	Placebo	1.65	0.87	0.06	-0.07	3.38
CBST	Integrated	-0.31	0.85	0.70	-2.01	1.37
	Placebo	1.99*	0.84	0.02	0.31	3.66
Integrated	Placebo	2.31*	0.85	0.00	0.61	4.01
Depression						
SC	CBST	-.77*	0.36	0.03	-1.50	-0.05
	Integrated	0.26	0.37	0.48	-0.47	0.99
	Placebo	-0.30	0.37	0.42	-1.03	0.43
CBST	Integrated	1.03*	0.36	0.00	0.31	1.75
	Placebo	0.47	0.36	0.18	-0.23	1.18
Integrated	Placebo	-0.56	0.36	0.12	-1.28	0.16
Anxiety						
SC	CBST	-1.56*	0.28	0.000	-2.13	-0.99
	Integrated	-1.75*	0.29	0.000	-2.33	-1.17
	Placebo	-2.33*	0.29	0.000	-2.90	-1.75
CBST	Integrated	-0.18	0.28	0.50	-0.75	0.37
	Placebo	-.76*	0.28	0.00	-1.32	-0.20
Integrated	Placebo	-.57*	0.28	0.04	-1.14	-0.00

* $P < .05$

significant improvement in IIEF-5 scores as compared to placebo group. The CBST treatment significantly lowered depression scores as compared to both SC and integrated treatment. The SC group was found significantly different from other treatment groups for anxiety scores. However, the CBST and integrated treatment groups were not significantly different from placebo in reducing anxiety scores. Moreover, the integrated treatment was significantly different from SC in reducing anxiety scores.

DISCUSSION

The new treatment approach, CBST and integrated treatment group were found significantly effective in improving scores on IIEF-5 in comparison to placebo group at post treatment and follow up assessment as compared to pretreatment assessment. However, there was found no significant difference between CBST and integrated treatment groups in improving IIEF-5 scores. Besides, there was found no further improvement in IIEF-5 scores at follow up assessment for both CBST and integrated treatment groups. Previously, the new treatment approach based on sex therapy and CBT principles had been found significantly effective in improving IIEF-5 scores both as a single treatment²³ and in integration with SC in Pakistani men.^{20–22,24}

The CBST is a treatment of choice for NOED when administered either as a single treatment or in combination with PDE5i.^{21–23} The current study found CBST significantly effective in improving IIEF-5 scores, and in reduction of depression scores. The CBST takes into considerations the sexuality related beliefs and sexual activity related behaviors and replaces these with more appropriate beliefs and ways of behaving in sexual situations. The CBST has been found to bring effective changes in symptoms of ED in some previous studies.^{20–22,24} A recent study by the same authors also reported the effectiveness of CBST as a treatment of choice in cases of NOED in Pakistani men.²³ The efficacy of CBST in the improvement of IIEF scores in Pakistani men makes this therapeutic approach both culture fair and effective option for NOED cases.^{21–23}

The integrated treatment program brought significant improvement in IIEF-5 scores, and anxiety scores as compared to placebo and SC group respectively at post treatment. The depression scores decreased further for integrated treatment group only, although, this decrease was not statistically significant. The integrated treatment was the only group which showed reduction in anxiety scores at post treatment as compared to SC. The success of integrated treatment group in improving IIEF-5 scores, and reducing anxiety scores make it equally effective form of treatment as compared to placebo and SC respectively. The earlier studies reported the effectiveness of integrated treatment in cases of NOED as compared to other treatments.^{21,24} The integration of SC and CBST provides the best combination of elements of SC and CBST than the single treatment group in bringing about improvement in IIEF-5 scores, and anxiety

scores. This was validated by previous studies as well that integrated treatment was effective in improving ED symptoms as measured by IIEF and the effects remained stable at follow up 15 months later.^{21,22} This demonstrated that integrated treatment approach was better than monotherapy approach in treating ED.^{20,24}

The CBST treatment group was found to decrease the depression scores at post treatment as compared to SC and integrated treatment groups. The integrated treatment group witnessed decrease in depression scores at follow-up but the CBST group witnessed further increase in depression scores at follow-up, although, both these increase and decrease were not statistically significant. The CBST was found to better reduce the depression scores because of its emphasis on thought challenging and attitude restructuring as compared to SC treatment alone. Similarly, both the integrated and CBST treatment groups were found significantly different from SC but not significantly different from placebo group in lowering the anxiety scores at post treatment. Neither of the treatment groups significantly improved anxiety scores as compared to placebo group. This could be attributed to the limited duration of administration of all treatment approaches. On the other hand, SC and CBST treatments did witness increase in anxiety scores. An earlier study documented that the administration of SC for a temporary period produces anxiety whereas SC reduces anxiety scores if administered for a long term.³⁸

The different treatment groups showed improvement in IIEF-5 scores and reduction in depression and anxiety scores at post treatment as compared to pretreatment. Only the CBST and integrated treatments further decreased the depression scores respectively at follow-up, although, this decrease was not statistically significant. On the other hand, there was further increase in depression and anxiety in SC, CBST and integrated treatment groups respectively, though, this increase was not statistically significant. The results of various treatment groups did not show further improvement at follow up assessment. The improvement at post treatment could not be continued to follow up assessment, this may be attributed to the limited time duration between the two assessments viz post treatment and follow up.²³ On the other hand, the improvement at post treatment did not remain stable or progressed further at follow up like depression scores in CBST group. This may be attributed to the administration of CBST for a short period of time.

This study points towards a feasibility analysis of the integrated treatment approach for the treatment of NOED. The added benefits of CBST make the integrated approach a better option in cases of NOED. Both, CBST and integrated treatment approaches were found significantly effective in improving IIEF-5 scores as compared to placebo. The CBST treatment was found significantly effective in improving depression scores as compared to both SC, and integrated treatment groups. Neither of the treatment was found significantly effective in improving anxiety scores as compared to placebo. However, integrated treatment

was found significant as compared to SC alone in reducing anxiety scores.

Thus, the CBST and integrated treatment approaches have been found to be treatment of choice in improving IIEF scores and associated depression and anxiety scores. Given the significant role of CBST alone and as part of integrated treatment in improving IIEF and associated depression and anxiety scores, the time and cost associated with the CBST administration is justified. This is especially true for Pakistan where finding a CBT trained therapist is easy as compared to buying a PDE5i.²³

The co-variables of age, and duration of NOED did not show any significant interaction effects with either treatment group or IIEF-5 scores, depression and anxiety scores. Generally, the age has been found as a key variable in the epidemiology of ED previously.³⁹ There has been reported a positive correlation between advancing age and symptoms of ED. But there is little data available to show any relationship between age and occurrence of NOED. Similarly, there has not been a study reporting the impact of illness duration on the treatment outcomes for NOED. The feasibility, pilot study on the efficacy of CBST in improving symptoms of NOED in Pakistani men reported similar results.²³

LIMITATIONS

The current study had certain limitations which are outlined below:

1. There was no reporting of detailed medical investigations to rule out the organic etiology of ED and to ascertain the diagnosis of NOED.
2. The use of purposive and snowball sampling techniques to recruit men could result in self-selection of participants and a risk of positive bias toward effectiveness of treatments containing CBST as a component.
3. The randomization and treatment allocation were not blinded truly.
4. The first treatment group only received SC. The other PDE5i could also be administered to assess their effects.
5. The maladaptive cognitions, faulty beliefs and lack of sexual knowledge was not assessed using a measure across three time points in the patients of NOED.
6. The study used IIEF-5 as the main outcome measure. Instead, the IIEF-15 would have provided the measurements of sexual enjoyment and pleasure in addition to erectile function assessment.
7. The frequency of sexual intercourse of men with NOED was not accounted for across three assessments.

RECOMMENDATIONS

This study outlines the following recommendations:

1. The integrated and CBST treatment protocols are treatments of choice for men with NOED and should be given priority over other treatment protocols.

2. The mental health professionals trained in CBT should be integrated in team of sexual health professionals so as to offer treatment for psychological concerns of men with NOED.
3. There should be compulsory screening of men with NOED for the presence of mental health conditions such as depression and anxiety.

CONCLUSION

The integrated and CBST treatment protocols are treatments of choice in men with NOED for improving NOED scores and associated depression and anxiety scores. The other treatment protocols such as SC alone may also benefit the symptoms of NOED but integrated treatment provides the best course for the amelioration of NOED symptoms and associated depression and anxiety scores because of integration of SC and CBST.

ETHICS STATEMENT

The study was duly approved by Departmental Research Ethics Committee (DREC) of department of Psychology at the International Islamic University, Islamabad, Pakistan vide No. DREC/IIU-PHDPSY/2017/8203. The Universal Trial Number (UTN) of the study is U1111-1241-5531. The study was duly registered with the clinical trial registry of the USA vide No. NCT04126252. The study period was from August 2018 to September 2019. The written informed consent was signed by all the participating men prior to enrolling for the study.

ACKNOWLEDGMENTS

The original contribution of the participating men is highly acknowledged. We are indebted to the time and involvement of participating men with NOED, they made this research study possible with their active involvement. We also thank and acknowledge the support of sexual health professionals in South Punjab, Pakistan for referring men for the study.

Corresponding Author: Ahmad Bilal, PhD, Faculty of Social Science, Department of Psychology, International Islamic University, Islamabad, Pakistan E-mail: ahmadbilal4@gmail.com; Corresponding Author: Najam ul Hasan Abbasi, PhD, Associate Professor, Department of Educational Sciences, Mianyang Normal University, Sichuan 621000, China E-mail: nhabbasi@gmail.com

Conflict of Interest: The authors declare that there is no conflict of interest regarding the publication of this article.

Funding: The authors received no funding for the current study.

STATEMENT OF AUTHORSHIP

Ahmad Bilal and Najam ul Hasan Abbasi: Conception and design; Ahmad Bilal: Acquisition of data; Ahmad Bilal: Analysis

and interpretation of data; Ahmad Bilal: Drafting the article; Ahmad Bilal and Najam ul Hasan Abbasi: Revising the article for intellectual content; Ahmad Bilal and Najam ul Hasan Abbasi: Final approval.

REFERENCES

- Cohen SD. The challenge of erectile dysfunction management in the young man. *Curr Urol Rep* 2015;16:84.
- Capogrosso P, Colicchia M, Ventimiglia E, et al. One patient out of four with newly diagnosed erectile dysfunction is a young man—worrying picture from the everyday clinical practice. *J Sex Med* 2013;10:1833–1841.
- Nasim MAF. Comprehensive treatment of male psychogenic erectile dysfunction by sex therapy and psychotropic drugs (without Pde5 Inh.). *JSM* 2017;14:e338. Supplement 4.
- Khanzada U, Khan SA, Hussain M, et al. Evaluation of the causes of erectile dysfunction in patients undergoing penile doppler ultrasonography in Pakistan. *World J Mens Health* 2017;35:22–27.
- Nguyen HMT, Gabrielson AT, Hellstrom WJG. Erectile dysfunction in young men—A review of the prevalence and risk factors. *Sex Med Rev* 2017;5:508–520.
- Lee JC, Bénard F, Carrier S, et al. Do men with mild erectile dysfunction have the same risk factors as the general erectile dysfunction clinical trial population? *BJU Int* 2011;107:956–960.
- Wiggins A, Tsambarlis PN, Abdelsayed G, et al. A treatment algorithm for healthy young men with erectile dysfunction. *BJUI* 2018;123:173–179.
- Jenkins LC, Hall M, Deveci S, et al. An evaluation of a clinical care pathway for the management of men with nonorganic erectile dysfunction. *J Sex Med* 2019;16:1541–1546.
- Reed-Maldonado AB, Lue TF. A syndrome of erectile dysfunction in young men? *Transl Androl Urol* 2016;5:228–234.
- Cavallini G. Resolution of erectile dysfunction after an andrological visit in a selected population of patients affected by psychogenic erectile dysfunction. *Asian J Androl* 2017;19:219–222.
- Hatzimouratidis K, Amar E, Eardley I, et al. Guidelines on male sexual dysfunction: erectile dysfunction and premature ejaculation. *Eur Urol* 2010;57:804–814.
- Papagiannopoulos D, Nehra A, Khare NAOA. Evaluation of young men with organic erectile dysfunction. *Asian J Androl* 2015;17:11–16.
- Rastrelli G, Maggi M. Erectile dysfunction in fit and healthy young men: psychological or pathological? *Transl Androl Urol* 2017;6:79–90.
- Martins FG, Abdo CHN. Erectile dysfunction and correlated factors in Brazilian men aged 18–40 years. *J Sex Med* 2010;7:2166–2173.
- Rajkumar RP. The impact of disrupted childhood attachment on the presentation of psychogenic erectile dysfunction: an exploratory study. *J Sex Med* 2015;12:798–803.
- Maggi M. Erectile dysfunction. In: *Endocrine Abstracts*. Spain: European Society of Endocrinology; 2018 56 MTE13.
- Wang H, Yuan J, Hu X, et al. The effectiveness and safety of avanafil for erectile dysfunction: A systematic review and meta-analysis. *Curr Med Res Opin* 2014;30:1565–1571.
- Jenkins LC, Mulhall JP. Delayed orgasm and anorgasmia. *Fertil Steril* 2015;104:1082–1088.
- Ferguson 3rd JE, Carson 3rd CC. Phosphodiesterase type 5 inhibitors as a treatment for erectile dysfunction: current information and new horizons. *Arab J Urol* 2013;11:222–229.
- Boddi V, Castellini G, Casale H, et al. An integrated approach with vardenafil orodispersible tablet and cognitive behavioral sex therapy for treatment of erectile dysfunction: a randomized controlled pilot study. *Andrology* 2015;3:909–918.
- Khan S, Amjad A, Rowland D. Cognitive behavioral therapy as an adjunct treatment for Pakistani men with ED. *Int J Impot Res* 2017;29:202–206.
- Khan S, Amjad A, Rowland D. Potential for long-term benefit of cognitive behavioral therapy as an adjunct treatment for men with erectile dysfunction. *J Sex Med* 2019;16:300–306.
- Bilal A, Abbasi NUH. Cognitive behavioral sex therapy: An emerging treatment option for nonorganic erectile dysfunction in young men: A feasibility pilot study [published online ahead of print, 2020 Jun 23] *Sex Med* 2020 S2050-1161(20)30070-2. doi:10.1016/j.esxm.2020.05.005.
- Banner LL, Anderson RU. Integrated sildenafil and cognitive behavior sex therapy for psychogenic erectile dysfunction: a pilot study. *J Sex Med* 2007;4:1117–1125 4 Pt 2.
- Mize SJS. A review of mindfulness-based sex therapy interventions for sexual desire and arousal difficulties: From research to practice. *Curr Sex Heal Rep* 2015;7:89–97.
- Bossio JA, Basson R, Driscoll M. Mindfulness-based group therapy for men with situational erectile dysfunction: A mixed-methods feasibility analysis and pilot study. *J Sex Med* 2018;15:1478–1490.
- Hsu GL, Johnson H, Huang HM, et al. Is the psychogenic factor an exclusive contributor to erectile dysfunction in a man under thirty? *Neuropsychiatry* 2018;8:1815–1827.
- Melnik T, Soares BG, Nasselo AG. Psychosocial interventions for erectile dysfunction. *Cochrane Database Syst Rev* 2007: CD004825.
- Berry MD, Berry PD. Integrative approaches to the treatment of erectile dysfunction. *Curr Sex Heal Rep* 2014;6:114–123.
- Schmidt HM, Munder T, Gerger H, et al. Combination of psychological intervention and phosphodiesterase-5 inhibitors for erectile dysfunction: A narrative review and meta-analysis. *J Sex Med* 2014;11:1376–1391.
- Li H, Gao T, Wang R. The role of the sexual partner in managing erectile dysfunction. *Nat Rev Urol* 2016;13:168–177.
- Simopoulos EF, Trinidad AC. Male erectile dysfunction: integrating psychopharmacology and psychotherapy. *Gen Hosp Psychiatry* 2013;35:33–38.

33. Rosen RC, Cappelleri JC, Smith MD, et al. Development and evaluation of an abridged, 5-item version of the International Index of Erectile Function (IIEF-5) as a diagnostic tool for erectile dysfunction. *Int J Impot Res* 1999;11:319–326.
34. Mahmood MA, Rehman KU, Khan MA, et al. Translation, Cross-cultural Adaptation, and Psychometric Validation of the 5-item International Index of erectile function (IIEF-5) into Urdu. *J Sex Med* 2012;9:1883–1886.
35. Lovibond SH, Lovibond PF. Manual for the depression anxiety stress scales. 2nd Ed Sydney: Psychology Foundation; 1995.
36. Aslam N. Psychological disorders and resilience among earthquake affected individuals (Unpublished MPhil Dissertation). Islamabad: Pakistan: National Institute of Psychology, QAU; 2007.
37. Cohen J. Statistical power analysis for the behavioral sciences. New York: Academic Press; 1977 revised edition.
38. Liebenberg N, Harvey BH, Brand L, et al. Chronic treatment with the phosphodiesterase type 5 inhibitors sildenafil and tadalafil display anxiolytic effects in Flinders Sensitive Line rats. *Metab Brain Dis* 2012;27(3):337–340.
39. Feldman HA, Goldstein I, Hatzichristou DG, et al. Impotence and its medical and psychosocial correlates: Results of the Massachusetts Male Aging Study. *J Urol* 1994;151(1):54–61.