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Abstract

Purpose: Nutrition Bio Shield (NBS) supplement is a natural product that is processed from whole wheat grains. We aimed to determine its effects on depression, anxiety, stress, and food craving in women with depression and obesity in a double-blind randomized clinical trial.

Methods: Fifty-six eligible clients with Body Mass Index ≥ 25 and mild or moderate depression signed the informed consent form. They were randomly assigned to receive daily 5 grams of NBS or placebo. The assessments included the Depression Anxiety Stress-21 questionnaire, Food Craving Questionnaire, Visual analogue scale for appetite, precise anthropometric measurements, and body composition analyses. The assessments were conducted at the baseline and repeated after 4 and 8 weeks. One month after the study finished the participants' weight was assessed. We analyzed the data by independent sample t-test, repeated measures Analysis Of Variance (ANOVA), and Multivariate analyses of covariance (MANCOVA).

Results: At the baseline no significant differences were observed between the groups regarding the main and demographic variables. After four weeks stress reduced significantly in the NBS group ($p = 0.04$), and after eight weeks anxiety ($p = 0.02$), stress ($p = 0.008$) and food craving ($p = 0.05$) reduced significantly in the NBS group compared to the placebo. After controlling for the demographic variables and baseline measurements, MANCOVA model revealed a significant effect of NBS in reducing anxiety (Eta-squared = 0.28; $p = 0.001$) and stress (Eta-squared = 0.19; $p = 0.009$). Fisher's exact test showed no significant difference regarding side effects between NBS and placebo ($p = 0.47$).

Conclusion: The NBS product was efficient in reducing stress and anxiety after controlling for demographic variables and baseline measurements compared to the placebo and it was safe.

Trial registration number: IRCT20140203016465N7

Keywords: Nutrition Bio Shield (NBS); depression; anxiety; stress; food craving; obesity; RCT

Introduction:

Major Depressive Disorder (MDD) is a common comorbidity of obesity. The association between depression and obesity is reciprocal. Obesity increases the chance for developing depression by 1.55 times. On the other hand, major depressive disorder increases the chance of obesity by 1.58 times (Luppino et al., 2010). Both disorders are prevalent and are associated with serious outcomes for the patients and impose a great burden of disease on the health care system (Lepine and Briley, 2011, Tremmel et al., 2017). Furthermore, depression and obesity are correlated with anxiety, stress, and food craving especially among women (Hallam et al., 2016). However, some studies reported a negative correlation between anxiety and BMI among students (Gao et al., 2020). Different population, multi-factorial etiology and gender differences could justify this discrepancy. In complicated cases, food craving sometimes occurs following psychiatric symptoms of depression, anxiety, or stress. These complications decrease response to treatment protocols and are the main causes of treatment failure (Ponzo et al., 2020). Furthermore, psychiatric medications often have some side effects such as weight gain, sexual dysfunction, and agitation. For this reason, some patients do not benefit from the first-line treatments (Kutzer et al., 2020). Hence developing a safe supplement with pervasive effects on brain regulation could be helpful in achieving the goals of treatment.

The Nutrition Bio Shield (NBS) supplement is a natural product originated from whole wheat grain enriched by various vitamins, minerals, and bioactive ingredients Due to the broad spectrum of micronutrients, we hypothesized that they may have pervasive effects on different aspects of mental and physical health.

The clinical trials of the effects of whole-grain consumption on brain function and mood is rare but promising. In one of the important trials performed in this field, Sandberg *et al.* investigated the effects of whole-grain rye-based products on the neuronal marker of Brain-Derived Neurotrophic Factor (BDNF) in healthy subjects and observed a 27% increase in BDNF 10.5 hours after the consumption of whole grains compared to the control (Sandberg et al., 2018). They attributed this to the fermentation of dietary fiber and the production of short-chain fatty acids by gut microorganisms (Sandberg et al., 2018). Montonen *et al.*, in an observational study, revealed that higher consumption of whole grains in participants was associated with lower oxidative stress and inflammation biomarkers (Montonen et al., 2013). Gangwisch, and colleagues in a prospective cohort study found that consumption of whole-grain foods could decrease the risk of depression among women (Gangwisch et al., 2015).

Sadeghi and colleagues in a cross-sectional study investigated that low consumption of whole grains is correlated with increasing anxiety in women, but not in men. They also revealed that consumption of refined grains is significantly correlated with depression and anxiety in women (Sadeghi et al., 2019). In spite of the ease of access and high safety of whole grains consumption, the lack of clinical trial in effects of whole grains on brain function is obvious.

Hence, we hypothesized that by improving the psychiatric symptoms, the food craving may subside. The present study was designed to assess the effects of a whole-grain-based functional food supplement in a vulnerable population with comorbidities of obesity, depression, stress, anxiety, and food craving. Hence we decided to perform this study to determine the effects of the Nutrition Bio Shield (NBS) supplement on depression, anxiety, stress, and food craving in women with depression and obesity in a double-blind randomized controlled trial.

Methods:

Study design and process

This was a double-blind, randomized controlled trial. The period of the clients' recruitment was from June 2020 to August 2021. Ninety patients referring to a nutrition clinic assessed for eligibility criteria and invited to participate in this clinical trial after giving the objectives and study procedure. Fifty-six eligible patients with BMI ≥ 25 and mild or moderate depression signed the informed consent form. They were randomly assigned to receive the Nutrition Bio Shield ® (NBS) supplement or similar placebo both produced by the NBS Company (allocation ratio was 1:1). The NBS product is a supplement naturally processed from the whole wheat grain enriched with multivitamins and minerals at or above Dietary Reference Intake and below the upper limits. It is a proprietary blend and registered patent. Its components include thiamine (vitamin B1), riboflavin (vitamin B2), niacin (vitamin B3), pantothenic acid (vitamin B5), pyridoxine (vitamin B6), folic acid (vitamin B9), vitamin K, β-carotene (vitamin A), alpha-tocopherol (vitamin E), ascorbic acid (vitamin C), vitamin D, phosphorus, potassium, sulfur, magnesium, calcium, boron, iron, manganese, zinc, copper, phenolic compounds and plant based omega-3. The patients were instructed to dissolve 5 grams of the powder per day in a glass of water and consume it before breakfast early in the morning for 8 weeks. The assessments were conducted at the baseline and repeated after 4 and 8 weeks. One month

after the study finished the participants were encouraged to report their body weight. The primary outcome was the change in scores of the depression, anxiety, stress-21 questionnaire and secondary outcomes were change in food craving questionnaire, visual analogue scale for appetite, change in body weight, and body fat percent. No changes made to the study outcomes and the methods after trial beginning.

The placebo and the NBS supplement had similar organoleptic properties and were indistinguishable. Blinding was performed by the manufacturer and the supplement boxes labeled by A or B so that nobody in the research team and patients could recognize which box is the placebo or real NBS supplement. In order to reduce the selection bias, we applied a computer-based simple random allocation method using the RAND function in an Excel sheet. Hence, the researcher who randomized the clients was not aware of the allocation sequence of a prospective participant. Furthermore, the blinding process of the study continued after the final statistical analyses performed and the study groups decoded after the statistical analyses finished. The study protocol was registered in a clinical trial registry approved by the World Health Organization (WHO) under the registration number: **IRCT20140203016465N7**

Participants

The eligible participants included 18 to 50 years old women, with BMI ≥ 25, and diagnosed with major depressive disorder according to the DSM-5 criteria that referred to a private weight reduction clinic. They signed the informed consent form after describing the study's protocol, objectives, possible side effects, and benefits. Then the participants completed the Depression, Anxiety and Stress Scale-21 Items (DASS-21). Exclusion criteria were: severe depression and other severe psychiatric disorders (i.g. bipolar mood disorder, schizophrenia, and those who had suicidal thoughts); taking antidepressants, and other medications which may affect appetite, and body weight, pregnancy, lactation, menopause, and hypothyroidism.

This work conforms to the requirements of the Declaration of Helsinki in 1995 (as revised in Edinburgh 2000). The subjects gave informed consent, and patient privacy is preserved. The study design was approved by the Ethical Committee of … University of Medical Science under the study number of VCR.REC.1398.703

Sample size

We calculated the sample size using an online platform for estimating the sample size in clinical studies(Sample_Size_Calculator, 2019). We aimed to recognize the difference of 5 score ($\mu 1 - \mu 2 = 5$; SD = 4.59) (Ali Asghari, 2008) in depression subscale of the DASS-21 questionnaire between the NBS and placebo groups with the Type I error $\alpha = 0.05$ and the power of $1-\beta = 0.80$. Accordingly, the required sample size for performing the trial was calculated twenty three clients in each group.

Study procedure

In order to decrease the possible confounding effects from different diets, a clinical dietitian prescribed a uniform weight-loss diet with about -500 kcal fewer calories than their usual diet. The sampling site was a private nutrition clinic. Anthropometric measurements and validated body composition assessments, depression anxiety stress-21 questionnaire, food craving questionnaire, appetite visual analogue scale (VAS) performed at the baseline visit, and repeated 4 weeks, and 8 weeks after the start of the study. At the follow-up period, one month after the study finished, the weight of participants was assessed. In each visit, the patients were asked whether they had experienced any side effects. If any side effects were reported, they would be documented. During the study, we controlled adherence to the study protocol by intermittent phone calls and every two weeks' visits. Non-compliance with the study protocol would cause the withdrawal from the study.

Statistical analysis

We gathered the data in an excel sheet and imported it to SPSS 19 software. After meeting the normality assumptions, we analyzed the data by independent sample t-test, repeated measures ANalysis Of VAriance (ANOVA) and Multivariate analyses of covariance (MANCOVA), and the null hypothesis of similarity of primary and secondary outcomes was tested between the two groups and during the study period.

The assumptions for t-test, repeated-measures ANOVA, and MANCOVA were checked. In particular, no outlier was detected in primary checking, and normality of dependent variables was tested and approved by Kolmogorov-Smirnov and Shapiro-Wilk tests. Also, equality of variances of the differences between all combinations (sphericity) was tested by Mauchly's test of sphericity, and if the assumption was violated in a case, the Greenhouse-Geisser correction would be used alternatively. Additionally, we used the independent sample t-test

and chi-square test for comparison of baseline characteristics between groups. The significance level was maintained at $\alpha = 0.05$.

Results:

Seven participants in the NBS group (only one due to nausea side effect), and 6 participants in the placebo group withdrew their consent, or became unreachable due to personal reasons. Twenty one participants in the NBS group and 22 in the placebo group completed the trial. Figure 1 shows the Consort flow diagram for the study. At the baseline, no significant differences were observed between the groups regarding the main and demographic variables (table-1). After four weeks stress reduced significantly in the NBS group ($p = 0.04$). After eight weeks anxiety, stress, and food craving reduced significantly in the NBS group ($p = 0.02$; $p = 0.008$; $p = 0.05$) (table-2). Trends of the mean depression scores, anxiety scores, stress scores, mean scores for food craving during the study for participants in the NBS group compared with the placebo group are presented in figure 2 respectively. Then we run the multivariate analyses of covariance to confirm the results. After controlling for the baseline variables, age, income, and education level MANCOVA model confirmed the significant effect of NBS in reducing anxiety (Eta-squared = 0.28; $p = 0.001$) and stress (Eta-squared = 0.19; $p = 0.009$) (table-3). Fisher's exact test revealed no significant difference in side effects between NBS and placebo ($p = 0.47$) (table-4). The mean weight decrease in the NBS group was -3.2 ± 3.3 and in the placebo group was -2.6 ± 1.4 ($p = 0.48$). In the follow-up period, the difference between groups regarding the body weight and BMI change from the 8th week was not statistically significant ($p = 0.19$ and $p = 0.17$; respectively).

Discussion

Using a natural supplement enriched with wide-spectrum vitamins, minerals, and bioactive compounds instead of a single vitamin or mineral to target a multi-factorial health issue makes this article different from the rest of the studies that are available in the literature. The main finding of this study was that the NBS supplement is effective in reducing the anxiety and stress. Some studies put emphasis on the correlation between nutritional deficiencies and different mental health issues. A systematic review and meta-analyses study has revealed that dietary improvements could be a novel intervention for improving mental health status (Firth et al., 2019). Over the last years, using

nutritional supplements to improve psychiatric signs are extended. Different studies have examined a single micronutrient or combination of micronutrients to treat depression, anxiety, or stress. Long and Benton revealed that vitamin and mineral supplementation decreases the level of perceived stress (standard mean difference [SMD] = 0.35) and anxiety (SMD = 0.32), but not depression (SMD = 0.20). They concluded that supplements with high doses of B vitamins are more efficient in improving psychiatric signs (Long and Benton, 2013). These results were aligned with our findings of the MANCOVA model in effects of the NBS supplement in reducing anxiety and stress. In another similar study of multivitamin combined with calcium magnesium and zinc for healthy male subjects Carroll *et al.* reported a significant improvement in symptoms of anxiety and stress but not depression (Carroll et al., 2000). Armborst *et al.* in a trial of micronutrients combined with amino acids on subjects with chronic psychological stress reported a positive effect of multivitamins on reducing stress (Armborst et al., 2018). Ford *et al.* administered only B vitamins to the subjects being treated for, or had a history of hypertension and reported no improvement in symptoms of depression (Ford et al., 2008). Lewis *et al.* used a B-vitamins supplement on adults with major depression and observed significant difference between treatment and placebo groups regarding depression and anxiety (Lewis et al., 2013). In contrast to our study design, Lewis et al. applied male and females with more severe depressive symptoms and used a narrow range of micronutrients. Mech and Farah used a supplement containing multivitamins, minerals and omega-3 for patients with major depression and reported 42% improvement at week 8 in the treatment group compared with the placebo(Mech and Farah, 2016). In contrast to our results, Pipingas *et al.* reported no significant improvement in mood following the multivitamin administration among participants (Pipingas et al., 2013). Their study was different in terms of participants, study tools and components of supplement used. Furthermore, Harris *et al.* administered multivitamins to sedentary occupation male subjects and reported no significant improvement on symptoms of depression, anxiety, nor stress (Harris et al., 2011). Their cases were 50 to 69 years old men and the component of the supplement was different from our study. They used a vitamin and mineral supplement containing herbal, fruit, and vegetable extracts originated from ginseng, ginger, ginkgo, parsley, papaya, barberry, tomato, fennel, and gotu kola. But the NBS supplement is processed from whole grain wheat enriched with broad spectrum micronutrients. Macpherson *et al.* also administered multivitamins to healthy females for four weeks and reported no significantly improvement in symptoms of depression, anxiety nor stress(Macpherson et al., 2016). They included women with a different age group (50-75 year old). Furthermore, duration of our study was longer (eight weeks) compared with Macpherson *et al.* (four weeks). The trend lines

indicated in figure 2 in our study confirms the relation between duration of supplement consumption and the amount of outcome change. It seems that different results could be attributed to different subjects, severity of disease, duration of supplement consumption, and more importantly components of multivitamins administered.

Minerals also have been identified to play an important role in mental health status. Nakamura, *et al.* revealed that lower dietary intake of zinc, copper, and manganese are associated with increased symptoms of depression and anxiety (Nakamura et al., 2019). Furthermore, other studies have identified that magnesium may play role in mood regulation through the monoamine neurotransmitter system and inhibiting the glutamate receptor. Mlyniec *et al.* revealed that magnesium and zinc deficiency lead to depression through monoaminergic system (dopaminergic, noradrenergic, and serotonergic pathways), Glutamatergic system, and GABAergic system (Mlyniec et al., 2014). Ames *et al.* revealed that high-dose vitamins and mineral supplementation could decrease coenzyme binding affinity and stimulate different enzymes in the brain (Ames et al., 2002). Furthermore, minerals such as zinc, copper, and magnesium may play role as the co-factors of different enzymes in the brain (Osredkar and Sustar, 2011). Zinc is concentrated in the glutamatergic neurons in the brain and play role in biochemical pathways of mood regulation (Paoletti et al., 2009). Russo *et al.* assessed serum zinc concentration of patients with anxiety symptoms and revealed significantly lower zinc levels compared to the control group (Russo, 2011). Similarly, Islam *et al.* showed altered serum elements in patients with generalized anxiety disorder regarding zinc, magnesium, copper, iron, manganese, and calcium (Islam et al., 2013). NBS supplement is enriched with various minerals such as zinc, magnesium, manganese, iron, copper, calcium, and boron as well as B vitamins and antioxidants and via these compounds it could help to decrease signs of anxiety and stress.

As a result of depression, anxiety and stress biochemical pathways related to oxidative stress may be activated. Hence, antioxidant protection in biological systems is important to reduce oxidative stress. Gautam *et al.* showed that patients with depression and generalized anxiety disorder had lower levels of antioxidant vitamins such as vitamin A, C, and E compared to the control group (Gautam et al., 2012). Furthermore, 6 weeks of administration of vitamin A, C, and E dietary supplements caused a decrease in depression and anxiety scores(Gautam et al., 2012). Mazloom *et al.* showed that vitamin C decreased anxiety scores significantly compared to the control group (Mazloom et al., 2013). Huang *et al.* showed that low serum levels of vitamin D is associated with increased symptoms of depression and anxiety(Huang et al., 2014). Bicikova M. showed a low level of vitamin D in men and

women with depression and anxiety(Bicikova et al., 2015). Fazelian *et al.* in a randomized clinical trial showed that vitamin D supplement could reduce anxiety and depression as well as inflammatory markers in type 2 diabetic women with anxiety(Fazelian et al., 2019). NBS product is full in antioxidant vitamins such as vitamin C, K, A, E, and D

The human brain and neuronal membrane are the main sites of omega-3 polyunsaturated fatty acids deposit in the body. Hence, omega-3 deficit could affect the normal brain and neuronal activity. The reduced omega-3 level is reported in patients with anxiety (Ross, 2009). Su *et al.* demonstrated the correlation between omega-3 consumption and a decrease in the severity of anxiety symptoms (Su et al., 2018). Kiecolt-Glaser *et al.* revealed that omega-3 use can decrease inflammation and anxiety (Kiecolt-Glaser et al., 2011). Emerging literature reveals that omega-3 fatty acids could undergo neuroplasticity and numerous neurobiological processes, interfere with neurotransmitter production, and take a role in reducing inflammation, and by this mechanism they affect anxiety, stress, and depression(Kiecolt-Glaser et al., 2011). These findings are aligned with our results. Furthermore, the combination of alpha-linolenic acid omega-3 fatty acids with bioactive compounds in the NBS product is more promising. However the generalisability of the results remains within the women with depression and overweight subpopulation and more studies are needed to extend to results to other populations.

Limitations

This study was performed during the outbreak of coronavirus. This condition made clients less interested in participating in the study. However, the study was performed with reassurance to patients and full compliance with health protocols, and no cases of coronavirus infection were reported during the study.

Conclusion

The NBS product compared with the placebo was safe and efficient in reducing stress and anxiety after controlling for demographic variables and baseline measurements. Combination of a broad range of vitamins and minerals as well as bioactive compounds in the NBS product is promising in mood regulation especially among women clients with depression and overweight.

Declarations

Funding

Psychiatry and psychology research center and the NBS Company have collaboratively funded this clinical trial. The sponsors do not involved in the study design; data collection, analysis, interpretation of data; and writing of the report.

Competing interest

The research was funded by NBS and the research facilities were provided by the psychiatry and psychology research center, … University of Medical Sciences. We confirm full academic independence to report and publish all the findings and the industry was not involved in the study hypothesis/design, execution, analysis, or interpretation. All raw data will be made available to interested scientists if requested by sending an email to the corresponding author.

Availability of data and material (data transparency)

Additional data are available from the corresponding author on reasonable request.

Ethics approval

The study design was approved by the Ethical Committee of …. University of Medical Science under the study number of VCR.REC.1398.703

Consent to participate

The participants signed the informed consent form after the investigator described the study's protocol, objectives, possible side effects, and benefits.

Author Contributions

Conceptualization of the study (MRM, SAM, AKH), Design (MRM, SAM), implementation (MRM, SAM), analyses (SAM), interpretation and writing the manuscript (SAM), reading approving the final manuscript (MRM, SAM, AKH)

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Table-1 baseline characteristics in the NBS recipients compared to the placebo recipients

	NBS (N=21) Mean ± SD	Placebo (N=22) Mean ± SD	p-value
Age	44.5 ± 8.7	44±12	0.86
Height	161.2 ± 6.9	160.3 ± 4.32	0.58
Weight	83.9 ± 9.0	79.3 ± 10.6	0.13
BMI	32.4 ± 4.5	30.8 ± 4.1	0.24
Depression	13.5 ± 2.8	12.8 ± 2.3	0.34
Anxiety	9.0 ± 4.5	8.0 ± 4.2	0.47
Stress	12.0 ± 3.9	11.8 ± 3.8	0.87
Food craving score	34.3 ± 9.8	40.6 ± 16.1	0.13
VAS for appetite	14.5 ± 4.0	15.9 ± 2.9	0.20
Appetite questionnaire	15.9 ± 2.0	17.0 ± 2.6	0.14
Body fat percent	39.6 ± 4.8	39.7 ± 4.7	0.94

BMI: Body Mass Index; VAS for appetite: Visual Analogue Scale for appetite

Table-2 dependent variables at different time points of the trials in NBS recipients compared to the placebo recipients

		Baseline	p-value	Week 4	P-value	Week 8	p-value	Mean change	p-value
BMI	NBS	32.4 ± 4.5	0.24	31.6 ± 4.6	0.25	31.2 ± 4.7	0.30	-1.2 ± 1.3	0.52
	Placebo	30.8 ± 4.1		30.1 ± 4.0		29.8 ± 3.9		-1.0 ± 0.5	
Depression	NBS	13.5 ± 2.8	0.34	9.0 ± 4.5	0.33	8.3 ± 6.0	0.41	-5.1 ± 5.2	0.16
	Placebo	12.8 ± 2.3		10.1 ± 3.4		9.5 ± 3.3		-3.2 ± 3.6	
Anxiety	NBS	9.0 ± 4.5	0.47	4.9 ± 5.6	0.07	4.6 ± 4.4	**0.02***	**-4.3** ± 3.9	**<0.001** **
	Placebo	8.0 ± 4.2		7.8 ± 4.7		7.9 ± 4.5		-0.1 ± 1.6	
Stress	NBS	12.0 ± 3.9	0.87	7.7 ± 5.1	**0.04***	7.3 ± 4.1	**0.008***	**-4.7** ± 4.7	**0.002***
	Placebo	11.8 ± 3.8		10.9 ± 4.7		11.0 ± 4.5		-0.8 ± 2.7	
Food craving score	NBS	34.3 ± 9.8	0.13	31.8 ± 13.9	0.41	28.1 ± 12.6	**0.05*** Δ	**-6.1** ± 10.1	0.59
	Placebo	40.6 ± 16.1		35.1 ± 12.4		36.1 ± 14.0		-4.4 ± 11.2	
VAS for Appetite	NBS	14.5 ± 4.0	0.20	12.2 ± 2.5	0.25	12.1 ± 3.0	0.25	-2.3 ± 3.7	0.67
	Placebo	15.9 ±		13.1 ±		13.1 ±		-2.8 ± 2.8	

Appetite questionnaire	NBS	2.9 15.9	±	0.14	2.7 13.7	±	0.84	2.1 13.0	±	0.51	-2.9 ± 3.1	0.67
	Placebo	2.0 17.0	±		2.6 13.9	±		2.8 13.6	±		-3.4 ± 3.9	
Body fat percent	NBS	2.6 39.6	±	0.94	3.7 38.8	±	0.95	3.4 38.4	±	0.92	-1.2 ± 2.0	0.64
	Placebo	4.8 39.7	±		4.9 38.7	±		5.0 38.2	±		-1.5 ± 1.6	
		4.7			4.9			5.0				

Δ the difference between groups regarding food craving at 8th week was nearly significant that should be confirmed by multivariate analyses. BMI: Body mass index; VAS: Visual analogue scale; the data are presented as Mean ± SD

Table-3 Multivariate analyses of covariance (MANCOVA) model for the dependent variables at end point after controlling for the baseline variables, age, income, and education level.

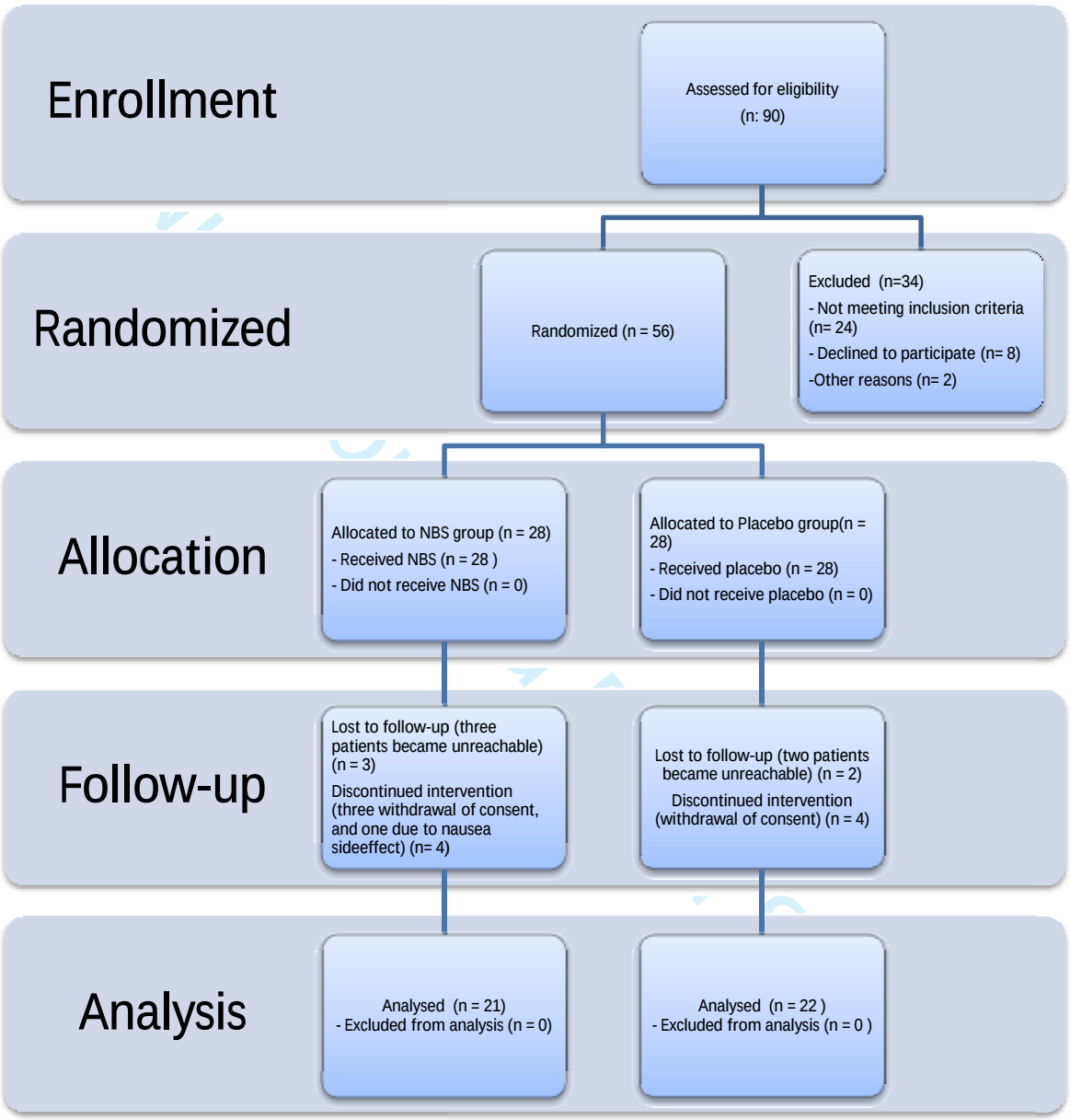
Dependent variable	sig	Eta-Squared	Observed power
Body weight	0.540	0.01	0.09
Depression	0.456	0.01	0.11
Anxiety	**0.001***	0.28	0.92
Stress	**0.009***	0.19	0.76
Food craving	0.466	0.01	0.11
Appetite (VAS)	0.504	0.01	0.10

Appetite (questionnaire)	0.456	0.01	0.11

Table-4 descriptive and analyses of the side effects shows no significant difference between the NBS and placebo

	Side-effects descriptive	side-effect counts		p-value *
		Observed N (%)	Not observed N (%)	
NBS	One case reported headache, nausea, dizziness on the first day, One case reported intolerance One case reported nausea	3 (14.3%)	18 (85.7%)	0.47
Placebo	One case reported headache, nausea, fatigue on the first day One case reported constipation	2 (9.1%)	20 (90.9%)	

* Fisher's Exact test


Enrollment
Assessed for eligibility
(n: 90)
Randomized
Randomized (n = 56)
Excluded (n=34)
- Not meeting inclusion criteria (n= 24)
- Declined to participate (n= 8)
-Other reasons (n= 2)
Allocation
Allocated to NBS group (n = 28)
- Received NBS (n = 28)
- Did not receive NBS (n = 0)
Allocated to Placebo group(n = 28)
- Received placebo (n = 28)
- Did not receive placebo (n = 0)
Follow-up
Lost to follow-up (three patients became unreachable) (n = 3)
Discontinued intervention (three withdrawal of consent, and one due to nausea sideeffect) (n= 4)
Lost to follow-up (two patients became unreachable) (n = 2)
Discontinued intervention (withdrawal of consent) (n = 4)
Analysis
Analysed (n = 21)
- Excluded from analysis (n = 0)
Analysed (n = 22)
- Excluded from analysis (n = 0)

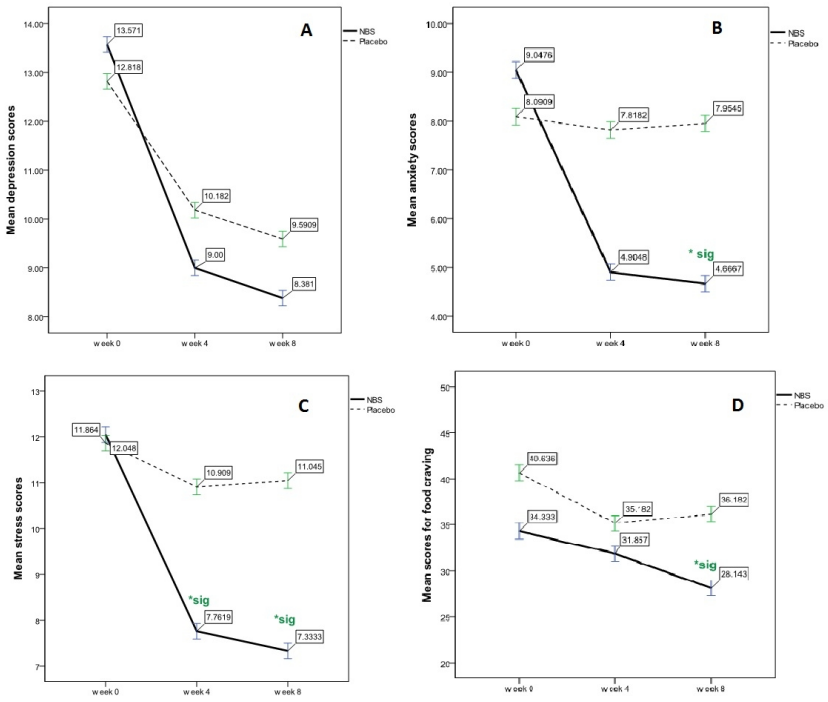


Figure-2 Trends of the mean depression scores (A), mean anxiety scores (B), mean stress scores (C), and mean scores for food craving (D) during the study for participants in the NBS group compared with the placebo group. *sig: significant at ≤0.05 level

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