Synergistic effect of Vitamin D Supplement and mindfulness on insulin resistance and different aspects of cognitive function in Vitamin D Deficient Type 2 Diabetic mellitus (T2DM) women: A pilot randomized clinical trial with placebo-controlled

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Research

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Abstract

Purpose

This study aimed to examining Synergistic effect of Vitamin D (VD) Supplement and mindfulness on insulin resistance and different aspects of cognitive function in VD Deficient Type 2 Diabetic women.

Methods

In this randomized-controlled trial, totally 225 women with T2DM and VD deficiency were randomly allocated to five groups: (1) mindfulness, (2) mindfulness and VD, (3) mindfulness and placebo, (4) VD, and (5) placebo. Mindfulness includes 12 sessions and VD patients received a daily 4000 IU oral dosage (two capsules) with 28,000 IU vitamin D weekly for 12 weeks. Sun exposure, anthropometric indices, dietary intake, physical activity, energy levels, laboratory analyses, were measured at the pre-test and after 12-week supplementation. dependent variables include cognitive function (Risky decision making, IQ and Trail Making Test) and insulin resistance.

Results

In baseline, measures were not different among the groups. At the end of treatment, cognitive function results showed improvement for all groups except the “placebo” group. About other groups, there was not any difference between VD and mindfulness groups (or combinations with placebo). but in “VITAMIN + MINDFULNESS” has a greater improvement rather than other groups ($P < 0.05$). This result exactly repeated for insulin resistance. However, there were not any significant difference among groups for IQ($P > 0.05$). There was any difference among groups for sunlight exposure and BMI ($P > 0.05$). For FBS only in combined group (VD + Mindfulness) the FBS significantly reduced that is synergistic effects ($P < 0.05$).

Conclusion

Combining VD Supplement and mindfulness can reduce insulin resistance and improve different aspects of cognitive function in VD Deficient patients.

Introduction

Currently type 2 diabetes mellitus is recognized as a global epidemic and estimated to increase exponentially by more than 500 million patients worldwide in 2035(1). Diabetic patients are at greater risk for long-term difficulties concerning the feet, eyes, heart, kidneys brain, and nervous system(1). In patients with Type 2 Diabetes Mellitus (T2DM), the capacity to generate insulin is not lost, even extreme in some Diabetic patients, but the result of insulin is weak, so insulin is approximately lacking in these patients. Recent studies showed that the onset of T2DM is linked with insulin resistance (IR) caused by reduced insulin sensitivity (2, 3). The effects of IR include (1) feeling hungry even after a meal, (2) frequent infections, (3) increased or frequent urination, (4) feeling more tired than usual and, etc. (3, 4). Therefore, special attention should be paid to improving insulin resistance in patients with type 2 diabetes.

On the other hand, Diabetes heightens the risk of disabilities on cognitive function. Based on recent researches, the frequency of dementia in diabetic patients is two times higher than the general population. Also, cognitive dysfunctions significantly affect the ability to self-management in diabetes patients(5).

In recent researches, results showed that in T2DM patients, by Promoting Inflammation, Vitamin D Deficiency Enhances Insulin Resistance. In other words, vitamin D insufficiency is linked to IR related diseases, especially T2DM(2). So, based on new researches vitamin D supplementation can improve IR (6). moreover, this supplement could improve cognitive

functioning in patients with T2DM (5).but, because of some limitations such as small sample size and unclear inclusion criteria the results are contradictory (5, 7).

Another treatment that demonstrated promising results in T2DM is mindfulness. based on previous researches, mindfulness can improves underlying physiological and behavioral determinants that influence insulin resistance such as stress arousal, physical activity, sleep quality, and eating unhealthy habits(8). Also This treatment with improvement in immediate memory, thinking, and attention, can enhance cognitive function. It has also enhance cognitive function with effects on dlpfc, amygdala, and the limbic system(9).

Treatment for type 2 diabetes involves a complex combination of behavioral-cognitive and biological factors that require multifaceted efforts to manage the disease and reduce the economic and health burden. But, despite the biopsychosocial nature of diabetes, there is not any study that examined this combination of treatments. moreover, when vitamin D and mindfulness used as monotherapy, although they are effective, but they have on average, a small effect size. There has accordingly been interesting in consolidating pharmacological and psychotherapeutic treatments in a trial to improve effectiveness(7–10).Also, behavioral intervention with improve empathy and therapeutic alliance, so enhance drug compliance. Therefore, Regarding with this combination, we can directly and indirectly modify problems (11, 12).

Accordingly, there is the first randomized clinical trial to examining combined Vitamin D Supplement with mindfulness on insulin resistance and cognitive function in Type 2 Diabetic patients.

Methods

Study Design and Participants

This study was a randomized single-blind placebo-controlled clinical trial. In the present study, participants include all T2DM patients with vitamin D insufficiency or deficiency were recruited from rofeyde Hospital in Tehran, Iran. This sampling conduct during 1 September 2019 to 25 October 2019.Type 2 diabetes mellitus was diagnosed by a physician with regard to WHO guidelines(13). From 26 October 2019, to January 18, 2020, interventions have been implemented. The presented research is a piece of a larger cohort project concerning examining various treatment for long-term improvement in metabolic syndromes. Because in Iran, the rate of diabetes in women is much higher than men, all participators are women(14)

Inclusion criteria include (1) vitamin D insufficiency or deficiency [between 10 (ng/mL) to 30 (ng/mL) serum vitamin D], (2) age of 18 to 60 years, and (3) willingness to participations. Exclusion criteria include (1) had psychiatric or neurological disorders, (2) took vitamin D or multivitamin supplements during the last three months, (3) using any illicit substance and alcohol, (4) being in pregnant period, (5) two or more absent in mindfulness groups, (6) using vitamin D supplements over the last 4 months and, (7) Pregnancy or breastfeeding.

Randomization and blinding

Participants were randomly allocated into either intervention or placebo groups (with PC version of random table). All participants blinded to receive vitamin D or placebo. In order to hide the allocation of individuals to groups, closed envelopes containing the code of the assigned group of each person were used along with the number of the person on the envelope.

Sample size

Regarding 0.05 as type 1 error and 0.2 as type 2 error (with 80%power) based on prior research, 35 patients were required in each group. for covering possible dropouts, sample size 25% increased and reach 45 subjects for each group(15).

Grouping

The subjects are randomly allocated into the following groups:

- group 1: receiving mindfulness training only
- group 2: receiving mindfulness training + Vitamin D supplement
- group 3: receiving mindfulness training + Placebo
- group 4: receiving vitamin D supplement only
- group 5: placebo only

interventions

supplement: In vitamin D groups, patients received a daily 4000 IU oral dosage (two capsules) with 28,000 IU vitamin D weekly for 12 weeks (26 October 2019 until 18 January 2020). This supplement includes fourteen oily drops weekly (sobhan darou, Iranian pharmaceutical company). Placebo (Subhan darou) groups receive totally same drops (without any vitamin D content) and time.

mindfulness: mindfulness consisted of 12 sessions (meeting once a week for 90 minutes) with one psychotherapist and his co-therapist. The intervention protocol was an adaptation of mindfulness to medicine context (MBSR) that introduced by L McCracken(16). Sessions consist of activity-based, interactive, motivational content. this treatment focuses on relaxation (and yoga) exercises and techniques. Also some sessions concentrate on cognitive restructuring, self-compassionate and receiving social support. Other elements of Mindfulness based stress reduction include: Implement mindfulness while breathing, exercise meditation while lying, Tarrying to be in the present moment (Here and now), Ticking off balmy thoughts, Recognizing and accepting unpleasant feeling, emotions and thoughts, Moving from the intrapersonal life to the interpersonal world, Recognizing steady life and planning for a more healthful lifestyle, Organizing for individual care, seeking the right refuge for diabetic problems, planning for solving diabetic problems, and how to moderating life-style in diabetes and vitamin D deficiency. For comparing adherence, audios of sessions were recorded with the permission of all the members. Then a mindfulness psychotherapist checked contents secession. Sessions were divided into 30-minute modules that were taken for adherence checks randomly. The treatment position and the occurrence processes were evaluated. Based on the intervention manual, the modules assessed the adherence level as either enough or not sufficient. The majority of content (93%) was judged as implemented adequately.

Measures

Laboratory analyses: ten milliliters of fasting blood sample from every patient was obtained after nine hours of fasting at the start and at the completion of the study. The blood samples stored at −80°C (with ten minutes centrifuging at 3000 rpm) until further analysis with centrifuged to isolate serums. Fasting blood glucose (FBS), measure was performed by spectrophotometry utilizing Pars Azmun kit (Iran)in auto-analyzer equipment (BT3000, Italy).

Insulin resistance: The formula for measurement of Insulin resistance was HOMA-IR (HOMA IR= (Fasting insulin (μU/ml) ×Fasting glucose ((mmol/l) ÷22.5). patients were demanded be fasting for nine hours prior to coming in for blood measuring. To increase the validity of the insulin and glucose outcomes, ere the blood sample, patients filled out a fasting questionnaire that required particular subjects discussing the last time they had consumed any food or liquids. In fact, for assurance that the patients were obeying the fasting contract we used a questionnaire. questions in this scale include common and less commonly considered foods like breath mints, tea, supplements and etc.

Sun exposure time: before implementing intervention and in the post-test by a validated questionnaire the sun exposure rate was assessed. The span of sun exposure was measured by total hours exposing to the sun in the last two week and divided into two.(17).

Energy levels: for assessing nutrients and energy levels, the fourth version Modified Nutritionist software program was used by a trained nutritionist (three-days food recording include one weekend day and two weekdays.

Anthropometric assessments: BMI (Body mass index) by dividing weight (kg) to square height (m2) was calculated. at the baseline and post-test(18).

Physical activity: The brief version of the International Physical Activity Questionnaire (IPAQ) was applied for determining the level of physical activity participants(19).

Cognitive function tasks

three examinations were utilized for evaluation of different aspects of cognitive function:

- **Risky decision making:** IOWA gambling task analyzing Risky decision-making, impulsivity and attention flexibility. The participators were faced with four cards. The first two cards offer high rewards but sometimes give the participants some huge negative points as well. the last two cards offer fewer amounts of reward but their probability of loss was far fewer than others. The final score is gained by summing up two final cards subtracting from two first cards. we used computer-based version of IOWA (20).
- **Intelligence (IQ)**: for assessing intelligence, we used of Scored General Intelligence Test (SGIT). The purpose of the SGIT is to assess an individual's overall cognitive ability. If the participant receives a score of 25 or below (out of a maximum of 40), it is characteristic of a cognitive problem and further investigation should follow(21).
- **Trail Making Test (TMT):** TMT has been widely used in neuropsychological evaluation. In condition "B" (that we used in current paper) the participant is to draw lines to attach circled digits and words in an alternating numeric and alphabetic sequence in the Persian language as quickly as possible. TMT reflect a broad variety of cognitive functions including sequencing and shifting, visual search and scanning, flexibility, planning, psychomotor speed, abstraction, attention, and the ability to keep two lines of thought simultaneously. Scoring is based on total time spent(22).

Statistical analysis

for assessing data SPSS version 26 was employed and we used paired sample t-test, the one-way ANOVA and, post-hoc test (Scheffe). P-values <0.05 were considered statistically significant.

Results

Two hundred twenty-five (225) TDM2 were included in our research. Finally, 201 participants completed the examination [Figure 1]. In the administration of Vitamin D and placebo for diabetic patients, no side effects were recorded.

Demographic variables were measured in pre-test and end of invention. In pre-test stage participants were not statistically different among groups. ($P > 0.05$). Yet, in post-intervention there are statically differentiation for FBS, physical activity, and energy intake ($P < 0.05$) [Table 1].

Table 1
scores of the participants by groups

Characteristic	placebo	Placebo + mindfulness	mindfulness	Vitamin	Vitamin + Mindfulness	P value
Age (years)[a]	46.4(8.9)	46.3(8.2)	45.9(10.6)	45.1(9.6)	47.6(10.2)	0.8
DURATION OF DIABETES (YEARS	14.3(3.6)	14.02(4.2)	14.8(4.1)	14.3(3.8)	14.3(3.7)	0.9
FBS (pre-test)	152.7(24.8)	156.1(25.8)	161.5(22.1)	163.3(19.5)	157.6(23.02)	0.25
FBS (post-test)	155.5(23.4)	150.6(23.01)	148.2(25.6)	159.87(2.8)	128.09(26.2)	0.00*
FBS duringtime[b]	P > 0.05	P > 0.05	P > 0.05	P > 0.05	P = 0.00*	—-
sun (pre-test)	1.9(1.4)	1.4(1.3)	1.9(1.2)	1.9(1.5)	1.8(1.4)	0.37
sun (post-test)	1.8(1.3)	2.3(1.3)	1.8(1.3)	1.7(1.3)	2(1.4)	0.23
BMI(pre)	29.4(3.36)	30.41(3.5)	30(3.2)	30.8(3.34)	29.7(3.36)	0.36
BMI(post)	29.8(3.01)	30.4(2.09)	30.17(3.6)	30.4(2.9)	29.7(3.30)	0.7
BMI during time	P > 0.05	P > 0.05	P > 0.05	P > 0.05	P > 0.05	—-
Energy (pre)	2206.22(305.09)	2242.27(351.24)	2141.51(346.4)	2174.6(310.2)	2238.02(308.71)	0.5
Energy (post)	2244.7(308.68)	1970.58(281.72)	1954.97(269.6)	1939.9(355.91)	1730.25(277.24)	0.00*
energy DURING-TIMEB	P > 0.05	P < 0.05*	P < 0.05*	P < 0.05*	P < 0.05*	
PHY (pre)	12.5(5.02)	12.57(5)	12.33(5.8)	12.7(5.9)	13.67(5.6)	0.98
PHY (post)	12.12(4.3)	15.38(5.1)	15.05(4.2)	12.8(4.4)	15.2(4.6)	0.002

a = one way anova, b = paired sample t-test, FBS = Fasting blood sugar(mg/dL), Sun: Sunlight exposure, Energy: Energy (pre-test) (kCal/day), PHY: Physical activity (MET/hours*week). VD = Vitamin D intake (mcg/day)

Based these results, in all groups except “placebo”, we faced with reduction in FBS. But only in “Vitamin + Mindfulness” group we had statically reduction in post-treatment rather than pre-test($P < 0.05$). For energy intake, all groups except “placebo” showed statically reduction in post-intervention ($p < 0.5$). in fact, both Vitamin D and mindfulness exercises can improve energy intake. A comparison among other groups which received Vitamin D or mindfulness as a component of their intervention package, done with post-hoc (Scheffe) analysis. Table 2 demonstrated that, “Vitamin + Mindfulness” significantly greater that others can reduction in energy intake. Also there is not any significantly difference between “mindfulness” and “Vitamin D” in energy intake ($P < 0.05$). For physical activity, results showed that only in groups with “mindfulness”, had significantly reduction in physical activity ($P < 0.05$). Yet, among groups with mindfulness component there were no significantly differentiation. Also there was not any difference between placebo and vitamin D groups[Table 2]

Table 2
post hoc for BMI and physical activity in post-test among groups

BMI							
Group I	Group J	Mean difference	P value	Group I	Group J	Mean difference	P value
placebo	Placebo + mindfulness	274.11	0.003*	Placebo + mindfulness	mindfulness	15.61	0.9*
	mindfulness	289.72	0.001*		Vitamin	30.68	0.99
	Vitamin	304.8	0.001*		Vitamin + Mindfulness	240.33	0.01*
	Vitamin + Mindfulness	514.44	0.001*				
mindfulness	Vitamin	15.7	0.9				
	Vitamin + Mindfulness	224.71	0.02*	Vitamin	Vitamin + Mindfulness	209.64	0.04*
				Physical activity			
Group I	Group J	Mean difference	P value	Group I	Group J	Mean difference	P value
placebo	Placebo + mindfulness	-3.16	0.001*	Placebo + mindfulness	mindfulness	0.38	0.69
	mindfulness	-2.77	0.004*		Vitamin	2.61	0.007*
	Vitamin	-0.55	0.56		Vitamin + Mindfulness	0.15	0.8
	Vitamin + Mindfulness	-3	0.002*				
mindfulness	Vitamin	2.22	0.02*				
	Vitamin + Mindfulness	-0.2	0.81	Vitamin	Vitamin + Mindfulness	-2.45	0.01*

Outcome measures

For Cognitive function tasks, results demonstrated that in pre-test there were no difference among groups ($P > 0.05$) [Table3]. But, at the end-of-treatment, for risky decision-making result showed improvement for all groups except “placebo” group. About others groups, although other groups demonstrated significant improvement, but “VITAMIN + MINDFULNESS” has a greater improvement rather than other groups ($P < 0.05$). This result exactly repeated for insulin resistance. ($P < 0.05$). Yet. For SIGT results showed there is not any significantly difference among group before and after of implementation of intervention ($P > 0.05$). however, in Vitamin + Mindfulness group, we faced with somewhat improving, But, this improvement is not statically significant ($P > 0.05$).

Table 3
scores of the participants by groups

Characteristic	placebo	Placebo + mindfulness	mindfulness	Vitamin	Vitamin + Mindfulness	P value
IOWA (pre-test)	0.92(5.9)	-0.38(5.2)	0.51(5.4)	0.72(5.1)	-0.13(5.7)	0.76
IOWA (post-test)	2.30(5.1)	6.28(5.6)	6.3(4.6)	5.97(4.7)	9.89(3.8)	0.001*
IOWA duringtime[b]	P > 0.05	P < 0.05*	P < 0.05*	P < 0.05*	P < 0.05*	
SGIT (pre)	32.5(3.8)	32.9(3.2)	32.4(4.05)	31.8(3.6)	31.6(3.3)	0.45
SGIT (post)	32.2(3.9)	33.1(4.1)	31.6(3.5)	31.6(4.2)	33(3.7)	0.25
SGITduring time	P > 0.05	P > 0.05	P > 0.05	P > 0.05	P = 0.07	---
TMT (pre)	92.8(13.3)	94.3(14.1)	94.1(17.4)	93.6(14.6)	93.7(14.9)	0.9
TMT (post)	97.9(17.4)	86.4(14.1)	84.4(16.7)	81.01(13.5)	68.6(15.9)	0.001*
TMT DURING-TIMEB	P > 0.05	P < 0.05*	P < 0.05*	P < 0.05*	P < 0.05*	
INSULINE (pre)	5.8(1.7)	5.5(1.4)	5.5(1.3)	5.1(1.4)	5.7(1.6)	0.39
INSULINE (post)	5.7(1.2)	4.4(1.5)	4.1(1.08)	4.4(1.2)	3.1(1.2)	0.001*
during time	P > 0.05	P < 0.05*	P < 0.05*	P < 0.05*	P < 0.05*	
a = one way anova, b = paired sample t-test, Ruler: Ruler drop method, TMT: Trial making test;						

Table 4
post. hoc analysis for outcome measures

IOWA							
Group I	Group J	Mean difference	P value	Group I	Group J	Mean difference	P value
placebo	Placebo + mindfulness	-3.98	0.01*	Placebo + mindfulness	mindfulness	-0.02	0.9
	mindfulness	-4.01	0.011*		Vitamin	0.33	0.89
	Vitamin	-3.65	0.024*		Vitamin + Mindfulness	-3.55	0.01*
	Vitamin + Mindfulness	-7.53	0.001*				
mindfulness	Vitamin	0.35	0.89				
	Vitamin + Mindfulness	-3.52	0.03*	Vitamin	Vitamin + Mindfulness	-3.88	0.011*
TMT							
Group I	Group J	Mean difference	P value	Group I	Group J	Mean difference	P value
placebo	Placebo + mindfulness	11.3	0.03*	Placebo + mindfulness	mindfulness	2.1	0.98
	mindfulness	13.4	0.006*		Vitamin	5.5	0.65
	Vitamin	16.8	0.001*		Vitamin + Mindfulness	17.8	0.001*
	Vitamin + Mindfulness	29.2	0.001*				
mindfulness	Vitamin	3.38	0.9				
	Vitamin + Mindfulness	15.7	0.001*	Vitamin	Vitamin + Mindfulness	12.3	0.01*
INSULINE							
Group I	Group J	Mean difference	P value	Group I	Group J	Mean difference	P value
placebo	Placebo + mindfulness	1.30	0.001*	Placebo + mindfulness	mindfulness	0.34	0.8
	mindfulness	1.65	0.001*		Vitamin	0.02	0.9
	Vitamin	1.33	0.001*		Vitamin + Mindfulness	1.2	0.001*
	Vitamin + Mindfulness	2.59	0.001*				
mindfulness	Vitamin	-0.31	0.8				

DSP: Digit Span Backwards, CPT: continuous performance test, INSULINE: Insulin Resistance

				IOWA			
	Vitamin + Mindfulness	0.97	0.014*	Vitamin	Vitamin + Mindfulness	1.26	0.001*
DSP: Digit Span Backwards, CPT: continuous performance test, INSULINE: Insulin Resistance							

Discussion

Our research revealed that twelve weeks' supplementation with 14,000 IU vitamin D per week combined with mindfulness decreased insulin resistance and improved cognitive functions among Vitamin D Deficient Type 2 Diabetic women. This is the first study in combination of vitamin D with 3rd waive behavior therapies and demonstrated high feasibility and efficacy. Regarding the results, Vitamin D and mindfulness training (Mindfulness based stress reduction protocol) in separate groups could improve insulin resistance and cognitive function. Also, when they combined in a package, they can significantly better than separate groups treating these variables. These results are in line of previous studies.

For example, in Shomaker (2019) research, mindfulness training reduced insulin resistance in diabetic adolescents with one-year follow-up(8).Also various meta-analysis showed that vitamin D can reduce insulin resistance in different physical conditions(23, 24). About cognitive function Klainin-Yobas at.el (2019) showed that Mindfulness can improve Cognitive Function and Emotional State in Elderly Individuals With Moderate Cognitive Impairment(25). Moreover, in a randomized control trial, Byrn at.el (2019) showed that vitamin D Supplementation in a variety of dosages can improve Cognition in patients with Type 2 Diabetes(26).

About efficacy of vitamin D and mindfulness on IR above researches showed similarity of our data with previous research literature. mindfulness with develops basic physiological and/or behavioral factors that influence IR such as physical activity, eating habits, sleep behaviors, and stress arousal, reduce insulin resistance. Also, in type 2 diabetes patients, vitamin D deficiency lead to promoting inflammation an enhanced proportion of p-p65/RelB. RelB and p65 protein and in results enhances insulin resistance. generally, animal investigations revealed that vitamin D insufficiency becomes insulin resistance in T2DM rats by increasing inflammation through the NF-kB pathway. Therefore, taking vitamin D will break this pathway and reduce inflammation(2, 8, 27). All in all, as diabetes is a bio-psycho-social problem our combined package with targeting biological and behavioral aspects of IR, so we faced with higher improvement rather than separated pathway to reducing IR. For cognitive function, low levels of 25(OH)D is correlate with increased risk of cognitive impairments. furthermore, vitamin D has a vital role in healthy brain function and deficiency of vitamin D may lead to cognitive impairment(28) and vitamin D supplements improved cognitive function in various medical papulations(29, 30). Also, mindfulness by affecting on dlpfc, amygdala, PFC and limbic system, has revealed improvements in cognitive functions (i.e., executive function, working memory and attention) in younger and older patients(25). So, combination of vitamin D and mindfulness revealed synergistic effects on cognitive functions. But, there is not any difference among groups for IQ. In fact, IQ is somewhat permanent ability and changing IQ is difficult. Also, IQ score of patients were in normal range and there was not any impairment that needs to improvement. So, all improvement happened in other cognitive functions that were impaired.

About demographic variables, there were any difference among groups for sunlight exposure and BMI similar to pervious groups. As, these variable highly associated with life-styles for changing them, patients need to doing variety changes in their life and this action needs more times(7). For FBS only in combined group (VD + Mindfulness) the FBS significantly reduced that is synergistic effects. for other groups we needed more times for examining their results. in fact, in a 16-weeks Vitamin D we faced with reduction in FBS in vitamin D group (7).But, there is not any similar research for mindfulness on FBS, so we need more examinations for mindfulness.

Although various strengths of this study, we have some limitations first, we were unable to explore the seasonal changes that could impact the result. Also, we need monitoring follow-up but as there is the first pilot these limitations must be eliminated

to future studies. Future studies must reduce these limitations.

Conclusion

Combining Vitamin D and mindfulness training could improve cognitive functions and insulin resistance in Vitamin D Deficient Type 2 Diabetic.

Declarations

Ethics approval and consent to participate: Written informed consent (about participation in the study) was received from all patients before the beginning of the study. The scales used in this research were all filled anonymously and a numeric code was used. This project was assessed and certified by the ethics committee of Kermanshah University of medical science (Ir.kums.rce.1399.0403). Moreover, this study is registered in the Thailand Registry of Clinical Trials (TCTR20200629004).

Consent for publication: during sampling individual session was held. We received consent for publication results from each participant.

Availability of data and material: Data of participants who consented to the public sharing of data are accessible from the corresponding author upon reasonable demands.

Competing interests: The authors certify that they have no competing interests.

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Figures

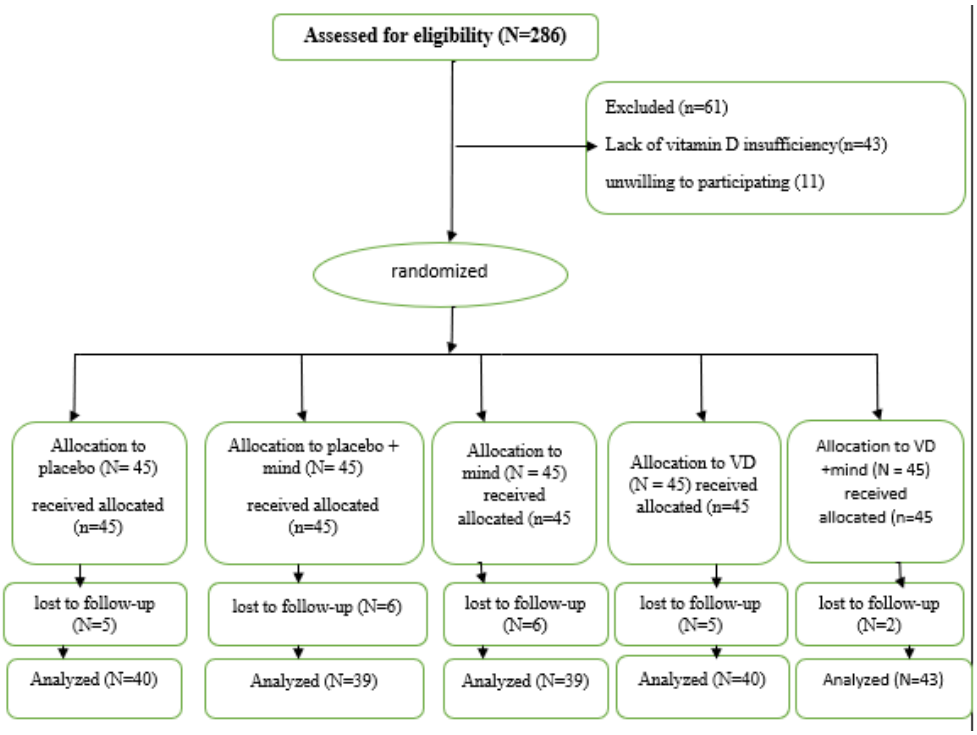

Figure 1

Consort diagram of RCT. VD: Vitamin D, mind: mindfulness