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AN ANALYSIS OF VARIOUS FLAXSEED POWDER DOSAGE CONSUMPTION AND LIFESTYLE MODIFICATIONS FOR METABOLIC SYNDROME PATIENTS WITH ABNORMAL BLOOD PRESSURE AND BODY MASS INDEX

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ABSTRACT:

Introduction: Numerous metabolic conditions, such as hypertension, diabetes, and cardiovascular diseases (CVD), result from changes in lifestyle varying from strenuous exercises to indulgences. This study investigated the effects of flaxseed powder on blood pressure and body mass index (BMI) with and without Lifestyle modification (LM). The NCEP ATP III criteria for metabolic syndrome (MetS) include a BMI >22.5 kg/m^3 and systolic and diastolic blood pressures >130 mm and >85 mm of Hg, respectively. Flaxseed powder has been demonstrated to reduce blood pressure and increase BMI, but its dosage, duration of consumption, and effects on health parameters with or without LM are still unclear. This study provides insights into the extent of improvement in blood pressure and BMI upon consumption of flaxseed powder with and without LM.

Method: In this study, 300 individuals were categorized into three groups The first MetS group was recommended 10, 20, or 30 g of flaxseed powder along with LM the second MetS group was recommended only LM and the third group constituted of a healthy individual (control). Baseline parameters were recorded before recommending flaxseed powder and/or LM, the blood pressure and BMI of all individuals were recorded at different time points.

Result: Long-term consumption of flaxseed powder improved BMI and Systolic Blood Pressure (SBP).

Conclusion: We observed a significant reduction in SBP and BMI of MetS patients who consumed 30 g of flaxseed powder with LM. Furthermore, the best results could be obtained when flaxseed powder is consumed for more than 4–5 months.

KEYWORDS: Body mass index, Hypertension, Lifestyle modification, Metabolic syndrome, Systolic Blood Pressure

INTRODUCTION

In recent times, humans have developed a strenuous lifestyle that causes several metabolic disorders such as diabetes and hypertension. Several studies have found that the prevalence of a metabolic syndrome in the human body, which is linked to diabetes, hypertension, and dyslipidemia, has increased significantly. High blood pressure (BP) is significantly associated with the risk of developing chronic diseases [4, 5]. Hypertension is one of the leading causes of death, along with coronary heart disease [1–3]. Hypertension is defined as systolic blood pressure (SBP) greater than 140 mm Hg and diastolic blood pressure (DBP) greater than 90 mm Hg [6].

Hypertension is becoming more prevalent, especially in low- and middle-income countries

(LMICs). Despite the rising prevalence of hypertension, knowledge, treatment, and measures to prevent the disease remain inadequate.
The SBP Intervention Trial (SPRINT), which is a randomized controlled trial (RCT), recently discovered that the SBP treatment target of 120 mmHg was associated with significantly lower risks ofcardiovascular disease (CVD) and mortality when compared to SBP 140 mmHg; however, this was found only among patients with no high CVD risk and no diabetes [7].
Lifestyle modification (LM) may be a feasible therapy option for increased blood pressure. Few studies have found that specific dietary interventions, such as omega-3, soy protein, and plant sterols, could perhaps help control blood pressure abnormalities [8].

Flaxseed is a functional food that contains high amounts of lignans and linolenic acid; these ingredients may reduceCVD risks such as hypertension when flaxseed is consumed [8–10]. Dietary phytoestrogensthat contain lignans can reduce the risk ofdiabetes by regulating inflammatory pathways[11]. A recent study highlighted the importance of including flaxseedsin a diet,to aid in the management of CVD. Flaxseeds contain enterolignan precursors, Secoisolariciresinol diglucoside (SDG)[12], omega-3 fatty acids, fibers, alpha-linolenic acid [13], and various other nutrients.Its medicinal qualities, such as the regulation of inflammatory pathways and the presence of dietary phytoestrogens, can help reduce the risk of diabetes [14].Some studies have shown that flaxseed peptides have an antihypertensive effect due to their high arginine concentration [12].

Few studies have reported that different varieties of brown and golden flaxseeds contain different amounts of metabolites, and provide differential benefits [15]. In their studies, Epaminondas et al. observed that golden flaxseeds contain higher soluble carbohydrates than brown flaxseeds [16]. Golden flaxseeds contain a higher concentration of omega-3 and omega-6 fatty acids than brown flaxseeds, as per researchconducted by Sargi et al. [17].

Considerable evidence suggests that a combination of flaxseeds in the diet and LMcan provide significant benefits in controlling abnormal blood pressure andbody mass index (BMI). The purpose of the present study is to ascertain whether different dosages of flaxseed powder taken in combination with specific LM can affect blood pressure and BMI.

METHODS AND MATERIALS

Participants

A 30-week (approximately 7-month) randomized case-controlled study was conducted at King George's Medical University (KGMU) in Lucknow, Uttar Pradesh, India. From January 2019 to January 2022, 400 subjects aged 20–70 years were shortlisted based on the study's inclusion criteria, and invited to participate in the study. Once they agreed to participate in the study, their voluntary informed consent was obtained. The 400 subjects were split into two groups: Group 1 (200 MetS patients) and Group 2 (200 healthy controls).

Outcome measures

Changes in SBP and DBP (primary outcome) and BMI (secondary outcome) after 30 weeks of flaxseed powder consumption and LM supplementation were assessed.

Ethical considerations

This study was authorizedby King George's Medical University's Institutional EthicsCommittee (Ref. Code: 99th ECM II Ph.D/P2) and registered in the Clinical Trials Registry India (ICMR-NIMS) under CTRI Reg.No. CTRI/2020/07/026318.

Inclusion criteria

Subjectshaving (a) a BMI of 25–34.9 kg/m2, (b) SBP of >130 mmHg and DBP of >90 mmHg, and (c) willingness to participate, were included in the study. During the study period, few patients took medical drugs to control theirBP.

Exclusion criteria

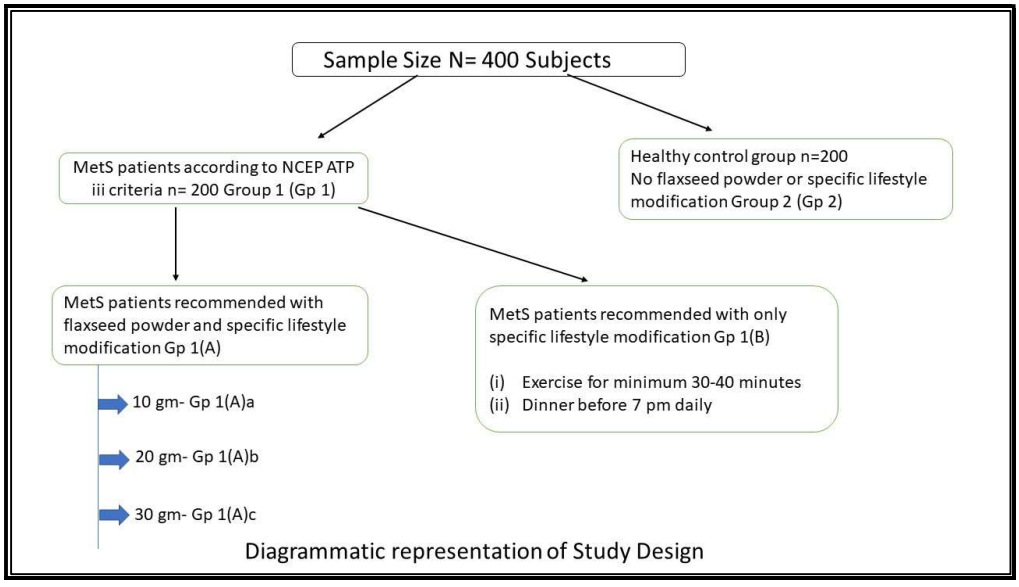
The following categories of people were excluded from the study: (a) patients who were on a specific controlled diet due to any reason during the last two months (b) patients who wereunable or unwilling to participate (c) patients who were using flaxseed, flaxseed oil, omega-3, insulin, or hypoglycemic medications (d) pregnantand breastfeeding mothers.

Baseline covariates

The baseline covariates considered in this study were patient socio-demographics, clinical parameters, diseasecharacteristics,andtreatmentmodalities. Socio-demographics included sex, age, and smoking status. Clinical parameters included SBPand DBP. The weight, height, and waist circumference of the participants were also taken into consideration.

Study design

A previous study reports that consuming a maximum dose of 50 gmof flaxseed powderper day is safe and could provide beneficial effects for adults[2]. In the current study, we used a lesser quantity of the aforementioned dose to increase the compliance of participants and ensure ease of consumption.



Diagrammatic representation of Study Design

Onthe first visit of the subjects to the research facility, thestandard procedure waselucidated and

voluntary informed consent was obtained. Interested subjects wereshortlisted and their demographic and anthropometric data were noted atbaseline months (0 months). In this study,400 patients with abnormalBPwere divided haphazardlyintotwo groups—Group1(Gp1) and Group 2(Gp2).Gp1 was further dividedindiscriminately into two subgroups: Gp1(A) and Gp1(B).Gp1(A) was sub-divided into three groupsbased on the flaxseed powder dosage given per day: Gp1(A)a—10 gm,Gp1(A)b—20 gm, and Gp1(A)c—30 gm. These three groups were given the specified doses of flaxseed powder for 30 weeks, along with a specific LM.Gp1(B)received specific LM only. Gp2wasthe healthy control group that did not receive any placebo or any specific LM. Nevertheless,a 10% dropout was considered. Flaxseed powder was bought from an open market-specific vendor and its storage conditions were the same for all participants.

Procedure of study

Flaxseed powder was packed in 50 gm packets and supplied to the participants. They were instructedto takethe daily dosages recommended for them (10 gm /20 gm /30gm)every day with water. All the participants were asked to visit the facility after four weeks (onemonth approx.) for getting replenishments. They were strictly advised to note at least sixBP readings each inthe morning, afternoon, and night respectively for two days before their visit to the facility for collecting new flaxseed powder packets. Before allocating the new packets to the participants,their BP reading (average of three), weight, and waist circumference were recorded.BP measurement was done on the left arm, after 15 minutes of comfortable sitting in an upright position, using the Omron automaticBP monitor. The reading taken two days prior tothe visit and that taken on the day of the visit were averaged to determinethe approximateBP value.

Recommended LM

On the participants'first visitto the facility at the time of their recruitment,information about their dietary and physical activities wascollectedusinga questionnaire; the subjects were asked to answer to the best of their memory. Their routine physical activities in the form of exercise were recorded in minutes.They were instructed to do vigorous exercise of 30–35 minutes (walking or running, depending on their age). They were recommended to take dinner before 7pm to sync with the circadian rhythm concept[11] and suggested to switch to complex carbohydrates instead of simple carbohydrates.

Anthropometric evaluation

The weight of the participants wasmeasured to the nearest 0.1 kg with minimal clothing and without shoes, usinga digital scale. The height of the participants was measured to the nearest 0.5 cm in a standing position without wearing shoes,using a wall-mounted stadiometer. BMI was calculated as the weight in kilograms divided by the height in meters squared. Using non-stretchable tape and light clothing, the waist circumference was accurately measured at 0.1 cm at the narrowest part between the last rib and the top of the iliac crest.

Statistical analysis

The Kolmogorov-Smirnov test of the normality probability plot was used to assess the normality of the data distribution. Logarithmic conversion was used to normalize non-normal values. Pairwise t-tests were used for comparisons within groups, while analysis of covariance (ANCOVA) was used for comparisons between groups. When the p-value was less than 0.05, it was considered significant. GraphPad Prism softwarewas used to statistically analyze all the data and graphs that were gathered from these tests.

RESULTS

This case-controlled study enrolled 400 voluntary informed-consent subjects. Out of these participants, 200 were classifiedascases having MetS, based on their clinical reports, and the remaining 200 were classified as the Healthy Control group,which did not receive any intervention, special supplementation, or any kind of placebo. A total of 388 subjects completed the study successfully. Thus, overall compliance by the participants in the study was 97%.

Characteristics	**Intervention Group**		**Control Group**		
	Male	**Female**	**Male**	**Female**	**P value**
Mean Age	53.00 ± 5.6	47.00 ± 8.1	51.80 ± 2.3	50.44 ± 5.9	0.4759
Sex (%)	61%	39%	51%	49%	---
Weight (kg)	79 ± 4.3	67 ± 6.85	75 ± 2.5	60 ± 3.6	0.0031*
Waist circumference (cm)	90.7 ± 5.8	84 ± 3.7	88.61 ± 4.4	83.49 ± 7.2	0.0205*
Exercise duration	30–40 mins	20–30 mins	20–30 mins	10–20 mins	---
Smoker %	47%	12%	55%	8%	0.5481
Nonsmoker %	53%	89%	45%	92%	---
Residence (Urban)	77%	69%	81%	88%	---
Residence (Rural)	23%	31%	19%	12%	---
BMI (kg/m^2)	30.79 ± 3.12	28.61 ± 9.41	23 ± 7.51	22.44 ± 9.17	0.0321*

Table 1: Data representing parameters of male and female participants in both intervention and control groups. Comparison is made between the intervention group and the control group. Data is presented as mean ± SD (N=388). P value was calculated using one-way ANOVA with Holm–Sidak method; the (*) marks indicate statistical significance (P <0.05).

Table 1 shows different baseline parameters, where no significant change in p-value was observed between male and female participants in both intervention and control groups.

In Table 2, anthropometric parameterswere taken into consideration. Themonth in which the subjects were enrolledinto thestudywas consideredthebaseline month and all improvements were determined by subtracting the ending month data from the starting month data.Patients who were givena 10-gm dose of flaxseed powder and LM did not show any significant improvement(-0.93± 0.5871), as the supplementation dosage was too less to yield any positive outcome. Patients who were given 20 gm of flaxseed powder along with LM showed significant improvement (-2.30± 0.9467) (p=0.0438). Inthe group that was given 30gm flaxseed powder along with LM,very significant improvement (-6.45±.01352) (p=0.0071)was observed, when compared to the baseline months.

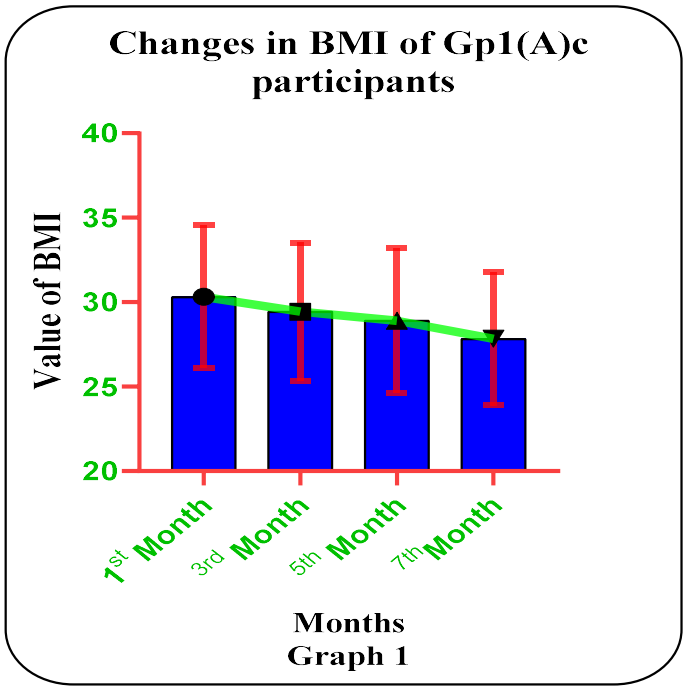
Characteristics	**BMI**	**p-value**	**SBP**	**p-value**	**DBP**	**p-value**
10 gm FX + LM	-0.93 ± 0.5871	0.3820	-0.9400 ± 9.086	0.3021	-0.2145 ± .6130	0.5941
20 gm FX + LM	-2.30 ± 0.9467	0.0438*	-1.130 ± 9.238	0.2227	-0.1134 ± .8932	0.8969
30 gm FX + LM	-6.45 ± .01352	0.0071*	-5.410 ± .7680	0.0047*	-1.345± 0.6740	0.2845
LM	-0.119 ± 0.4511	0.3629	-0.8200 ± 0.8619	0.3425	-1.020 ± 0.6990	0.5832
Control	-0.1090 ± .2356	0.6441	-0.1600 ± 0.8079	0.8432	-0.2580 ± 0.7882	0.3194

Table 2: BMI, SBP, and DBP values recorded for flaxseed powder (FX) dosage of 10 gm, 20 gm, and 30 gm along with LM, only LM, and control group (starting/baseline month data – ending month data).
Values are presented as the mean ± SD (N=388). p-value was calculated using one-way ANOVA with Holm–Sidak method. The (*) marks indicate statistical significance (P <0.05).

This givesthe inference that SDG lignan-enriched flaxseed power gives better results when a minimum of 30 gm/dayis consumed, along with LM,by improving BMI, body weight, andBP.

Changes in BMI of Gp1(A)c participants from 1st Month to 7th Month

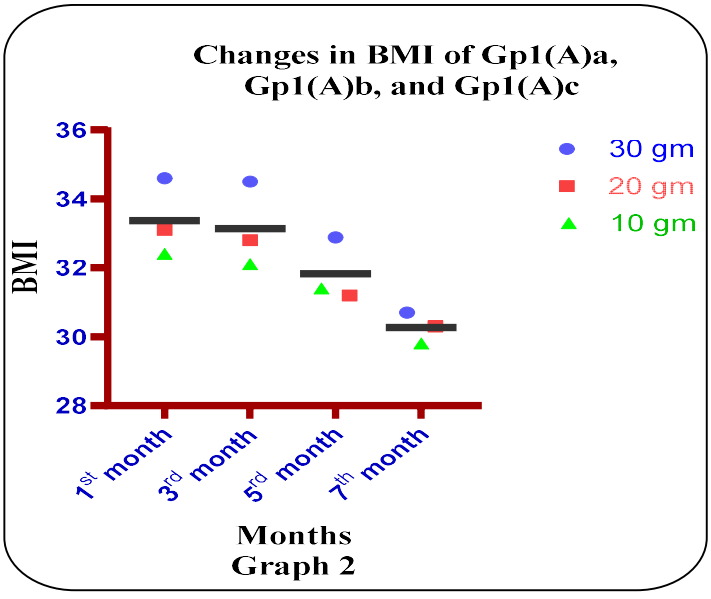
In graph no. 01, flaxseed powder dosage of 30 gm along with LM was recommended for the participants of Gp1(A)c. When the participants' BMI for the first month (baseline) was compared to that of the seventh month, a highly significant improvement, with a mean value of -6.45±.01352 (p=0.0071*) was observed. Based on this difference, we can infer that a substantial improvement in BMI was observed after seven months. The results of the study indicate that when flaxseed powder was given to MetS patients in combination with LM, there was a highly significant difference between the first month mean (30.09±4.222) and the seventh month mean (24.45±4.208).



Graph 1

Changes in BMI of Gp1(A)a, Gp1(A)b, and Gp1(A)cparticipantsfrom 1st Month to 7th Month

In graph no. 2, we have cumulatively shown the alteration in BMI value of patients of Gp1(A)a, Gp1(A)b, and Gp1(A)c, who were given 10gm, 20gm, and 30gm dosage of flaxseed powder along with LM, between the first and the seventh month.The graph clearly shows that 30 gm dosage subjects (Gp1(A)c) are indeed the better respondentswho are edging closer to the median line, whilst the 10 gm dosage subjects (Gp1(A)a) have responded the least. We recorded a highly significant (p=0.0071*) difference in the mean value (-6.45±.01352)when we compared the first month and the seventh month BMI values of patients who were recommended to take 30 gm of flaxseed powder along with LM (Gp1(A)c). Similarly, the difference between the first month and the seventhmonth BMI values of patients who took 20 gm of flaxseed powder along with LM (Gp1(A)b) was -2.30±0.9467 (p=0.0438*). When the first month BMI of patients who took 10 gm

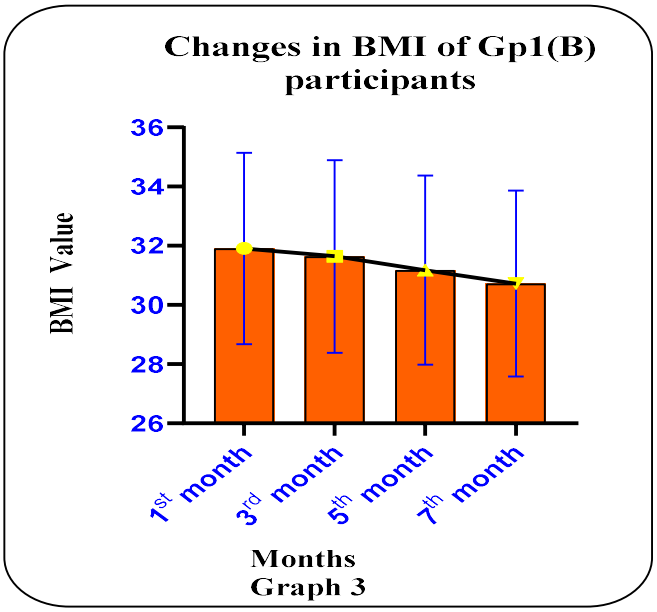


Graph 2

of flaxseed powder along with LM (Gp1(A)a) was compared to their seventh month BMI, the difference was -0.93±0.5871(p=0.3820), which is insubstantial.
In this graph, we can see that the BMI of patients who were given 20 gm and 30 gm dosages of flaxseed powder continued to improve, while that of patients who were given 10 gm dose did not show any significant difference.

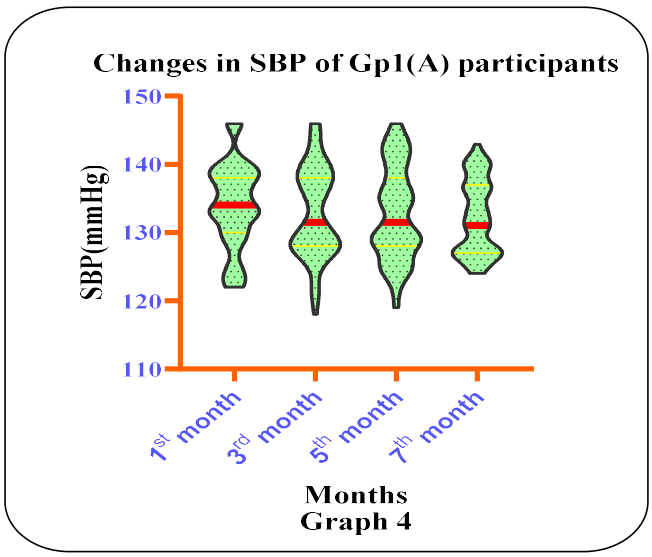
Changes in BMI of Gp1(B) participantsfrom1st Month to 7th Month

This graph no.3 illustrates that the BMI values of Gp1(B) patients, who were exclusively assigned specific LM with no supplementation of flaxseed powder, recorded no noticeable difference (p=0.3629) between the first and the seventh month.
From this, we can infer that LM alone does not alter BMI.

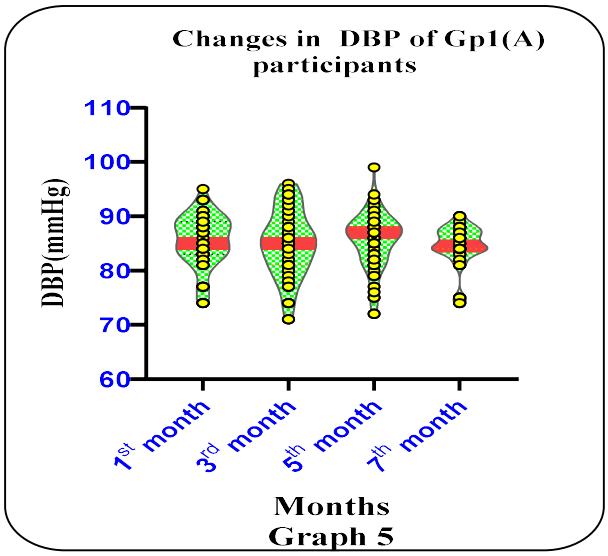


Graph 3

Changes in SBP and DBPofGp1(A) participantsfrom 1st Month to 7th Month



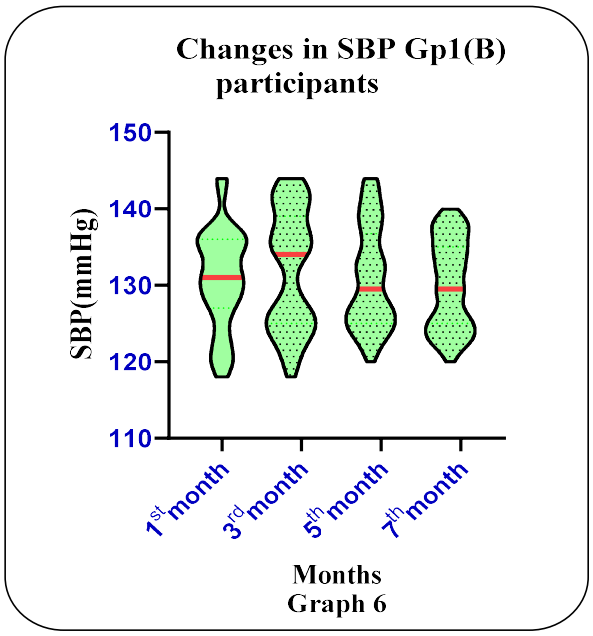
Graph 4



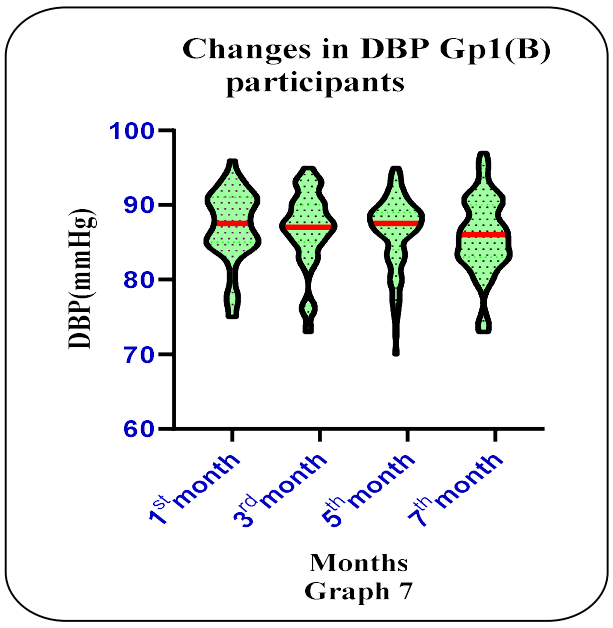
Graph 5

In graph no. 4, there was no significant difference in the SBP of Gp1(A) patients, who took flaxseed powder in different dosages along with LM, between the first month and the third month (p=0.3021),versus the fifth month (p=0.2227).However, there was a massive distinction between the first month andthe seventh month, with a mean difference of-5.410 ± 0.7680 (p=0.0047) *.
In graph no 5, the changes in the DBP of Gp1(A) patients were negligible. The observed results during the first month versus the third month versus the fifth month versus the seventh month were -0.4100 ± .7680 (p=0.5941), -0.0900 ± .6932 (p=0.8969), and -1.1351 ± 0.9239 (p=0.2845) respectively; these were insubstantial as per our study.

Changes in SBP and DBP of Gp1(B) participantsfrom 1st Month to 7th Month



Graph 6



Graph 7

In graph no. 6, the impact of LM on the SBPof Gp1(B) patients, who were exclusively assigned specific LM with no supplementation of flaxseed powder, was insignificant. The following results were obtained: first month versusthe third month (p=0.6852) versusthe fifth month (p=0.3123) versusthe seventh month (p=0.5832), all of which have been insignificant for our study.
In graph no. 7, the effect of LM on the DBPof Gp1(B) patients was insignificant. The differences recorded were: first month versus the third month (p= 0.2433) versus the fifth month (p=0.9309) versus the seventh month (p=0.3425). Thus, it was inferred that LM did not cause any significant improvements in DBP.

Discussion

In this study, flaxseed powder was incorporated into the diets of patients in conjunction with LM, for controllingabnormal blood pressure and high BMI. By the end of the study, patients showed significant improvements in the above parameters. Through this research, we also

determined the optimal dose of flaxseed powder to be consumedtocontrolBP, BMI, and other associated abnormalities. Supplementing the diet with flaxseed powder can potentially prevent anomalies in lipid profiles, which could also lead to CVD, if left unchecked.

Although numerous studies have postulated that flaxseed powder can have a favourable effect on BP and diabetes, comparative studies of various dosages of flaxseed powder in combination with a particular LM and their impact on anthropometric parameters are very rare.

In our study, MetS patients whose diets were supplemented with 30 gm of flaxseed powder along with LM showedan improvementin their BMI and SBP. Patients who took 20 gm of flaxseed powder along with LM also recorded a significant difference in BMI.However, patients who took 10 gm of flaxseed powder along with LM did not exhibit much improvement. This indicatesthat adding a very low dosage of flaxseed powder to the diet does not provide much benefits to MetS patients.

Our findings are consistent with those of previous studies. AfroozJavidi et al. studied the effect of flaxseed administration and reported that flaxseed powder significantly decreases SBP while exhibiting no effect on DBP [11]. Roberta Soares et al. report that men with cardiovascular risk can reduce their SBP, weight, BMI, waist circumference, and hip circumference significantly by consuming 60 gm of flaxseed powder daily for 42 days and getting 35% of their energy from carbohydrates [9].

There were few research studies that revealedresults that were contradicting to ours, such as Stuglin et al., who reported that they did not observe any significant reduction in SBP and DBP in healthy adults after giving them 32.7 gm (per day) of flaxseeds for 4 weeks [18]. Paschos et al. discovered a significant decrease in hyperlipidemic men's DBP, but only a slight change in SBP, which contradicts our findings of a greater reduction in SBP than DBP [19]. However, these discrepancies could be attributed to differences in sample sizes [20], flaxseed doses [21], and flaxseed powder administration methods (baked in bread, milling, lignan extracted from flaxseed, etc.) [20-22].

According to scientific literature, the biological processes through which flaxseed reduces BP are still not entirely defined. The most accepted explanation for the phenomenon is that flaxseed contains the lignin compound SDG as phytoestrogen, which is well-known as an Angiotensin-converting enzyme (ACE) inhibitor [23]. In Sprague Dawley male rats, increased BP-induced angiotensin I was reduced when SDG was supplemented by stimulating the guanylate cyclase enzyme [23]. Another important compound in flaxseed, alpha-linolenic acid (ALA), reduces BP by inhibiting the activity of soluble epoxide hydrolases [8]. These soluble epoxide hydrolases develop pro-inflammatory oxylipins, which cause vasodilation loss and inflammatory responses in arterial hypertension [8].

However, a recent analysis on human beings revealed that flaxseedscan reduce inflammation by lowering neutrophil aggregating oxylipin levels [14]. Furthermore, flaxseeds lower C-reactive protein, serum amyloid A, interferon-gamma, and interleukin-1ß, IL-2, IL-4, IL-6, and IL-10 [22,24]. Another component of flaxseeds, protein hydrolysate, which is an isolated fraction (KCl-F1) rich in arginine, has been shown to lower SBP after 2–8 hours of post-oral gavage, mimicking

the anti-hypertensive actions of captopril [25].

Another experimental study showed that flaxseed oil increases vascular responsiveness to phenylephrine by increasing the production of COX-2-derived thromboxane A2 and reactive oxygen species (ROS); this demonstrates the benefits of flaxseeds on vascular functions [26]. The hypotensive effects of flaxseeds may be due to the combined action of strong antioxidants such as lignans and the presence of several bioactive components such as SDG, ALA, and KCl-F1 [27,28].

Although long-term flaxseed consumption can cause lossof weight, it would alsocausea significant reduction in BP and BMI.

The current findings suggest that flaxseed is a major source of dietary nutrition, which is worth being considered for controllingBP and BMI.

Limitations

As far as we know, we followed our methods exactly as we had designed.However, there may always be a few unidentified confounding factors, such as financial constraints, patients avoiding the dose or taking it at a different time than suggested, and a few dropouts due to dehydration and constipation caused due to the consumption of flaxseed powder, which cannot be eliminated. According to our study's stringent inclusion criteria, only patients with metabolic syndromes were considered for thisstudy. Although we have tried in all possible ways to maintain the efficacy of flaxseed powder in all sachets, since our flaxseed powder was received in bulk for the respective months in sachets of 50 gm, few samples' efficacy might have been compromised due to different storage conditions, moisture, and other factors while handling the flaxseed powder.

Conclusion

The study's ultimate finding is that individuals with MetS who were participating in the study and had abnormal blood pressure as well as an elevated BMI have significantly reduced abnormal blood pressure, especially SBP, when given flaxseed at a dose of 30 g per day coupled with lifestyle changes. In addition, a considerable reduction in BMI was observed when using the right dosage of 30 gm of flaxseed powder with a specific LM over an extended period of time, preferably 6-7 months. We included a few additional variables in our study, such as DBP, whose results according to our research didn't reveal any appreciable improvements in MetS patients following dosages of 30 gm in addition to LM advised.

Finally, conclusions in our study, the flaxseed powder recommended group exhibited extremely substantial changes relative to the just LM group, particularly in SBP and BMI. Throughout our trial, the DBS didn't exhibit any differences. Therefore, the recommended dosage of 30gm/day in addition to LM may improve MetS patients' managing average SBP and BMI.

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Reference

1. Mozaffarian D, Capewell S: United nations' dietary policies to prevent cardiovascular disease. BMJ. 2011, 343:5747. 10.1136/bmj.d5747
2. Arjmandi BH, Khan DA, Juma S, et al.: Whole flaxseed consumption lowers serum LDL-cholesterol and lipoprotein (a) concentrations in postmenopausal women. Nutr Res. 1998, 18:1203-14. 10.1016/S0271-531700100-6 [Google Scholar
3. Rad EM, Assadi F, Juma S, et al.: Management of hypertension in children with cardiovascular disease and heart failure. Int J Prev Med. 2014, 5:10-6.
4. MacMahon S, Peto R, Collins R, et al.: Blood pressure, stroke, and coronary heart disease: part 1, prolonged differences in blood pressure: prospective observational studies corrected for the regression dilution bias. Lancet. 1990, 335:765-74. 10.1016/0140-6736(90)90878-9
5. Sarnak MJ, Levey AS, Schoolwerth AC, et al.: Kidney disease as a risk factor for the development of cardiovascular disease a statement from the American Heart Association Councils on kidney in cardiovascular disease, high blood pressure research, clinical cardiology, and epidemiology and prevention. Circulation. 2003, 108:2154-69. 10.1161/01.HYP.0000102971.85504.7c
6. Chobanian AV, Bakris GL, Black HR, et al.: Seventh report of the Joint National Committee On Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension. 2003, 42:1206-52. 10.1161/01.HYP.0000107251.49515.c2
7. Mazza G. OomahB.D.Flaxseed n: flaxseed in human nutrition. 1995.
8. Caligiuri SP, Edel AL, Aliani M, at al: Flaxseed for hypertension: Implications for blood pressure regulation. CurrHypertens Rep. 201416, 499:10.1007/s11906-014-0499-8
9. Dodin S, Cunnane SC, Lemay A, et al.: Flaxseed on cardiovascular disease markers in healthy menopausal women: A randomized, double-blind, placebo-controlled trial. Nutrition. 2008, 24:23-30. 10.1016/j.nut.2007.09.003
10. Cassani RS, Fassini PG, Silvah JH, et al.: Impact of weight loss diet associated with flaxseed on inflammatory markers in men with cardiovascular risk factors: A clinical study. Nutr J. 2015, 14:5. 10.1186/1475-2891-14-5
11. Javidi A, Mozaffari-Khosravi H, Nadjarzadeh A, et al.: The effect of flaxseed powder on insulin resistance indices and blood pressure in prediabetic individuals: A randomized controlled clinical trial. J Res Med Sci. 201621, 10:4103/1735. 10.4103/1735-1995.189660

12. Caligiuri SP, Aukema HM, Ravandi A, et al.: Flaxseed consumption reduces blood pressure in patients with hypertension by altering circulating oxylipins via an α-linolenic acid-induced inhibition of soluble epoxide hydrolase. Hypertension. 2014, 64:53-9. 10.1161/HYPERTENSIONAHA.114.03179

13. Bloedon L.T. Szapary P.O: Flaxseed and cardiovascular risk Nutr Rev. 2004, 62:18-27. 10.1111/j.1753-4887.2004.tb00002.x

14. Caligiuri S.P, Aukema H.M, Ravandi A, et al.: Elevated levels of pro-inflammatory oxylipins in older subjects are normalized by flaxseed consumption. Exp Gerontol. 2014, 59:51-57. 10.1016/j.exger.2014.04.005

15. Castro IA, Barroso LP, Sinnecher P, et al.: Functional foods for coronary heart disease risk reduction: A meta-analysis using a multivariate approach. Am J Clin Nutr. 2005, 82:32-0. 10.1093/ajcn.82.1.32

16. Epaminondas PS, Araújo KLGV, de Souza AL, et al.: Influence of toasting on the nutritious and thermal properties of flaxseed. J Therm Anal Calorim. 2011, 106:551-5. 10.1007/s10973-011-1638-y

17. Sargi S.C, Silva B.C, H. M. C Montanher, et al.: Antioxidant capacity and chemical composition in seeds rich in omega- 3: chia, flax, and perilla. Food Sci Technol. 2013, 33:541-548. 10.1590/S0101-20612013005000057

18. Stuglin C, Prasad K: Effect of flaxseed consumption on blood pressure, serum lipids, hemopoietic system and liver and kidney enzymes in healthy humans. J Cardiovasc PharmacolTher. 2005, 10:23-7. 10.1177/107424840501000103

19. Paschos GK, Magkos F, Panagiotakos DB, et al.: Dietary supplementation with flaxseed oil lowers blood pressure in dyslipidaemic patients. Eur J Clin Nutr. 2007, 61:1201-6. 10.1038/sj.ejcn.1602631

20. Rhee Y, Brunt A: Flaxseed supplementation improved insulin resistance in obese glucose intolerant people: a randomized crossover design. Nutr J. 2011, 10:44. 10.1186/1475-2891-10-44

21. Hutchins AM, Brown BD, Cunnane SC, et al.: Daily flaxseed consumption improves glycemic control in obese men and women with pre-diabetes: A randomized study. Nutr Res. 2013, 33:367-75. 10.1016/j.nutres.2013.02.012

22. Pan A, Demark- Wahnefried W, Ye X, et al.: Effects of flaxseed derived lignan supplement on C-reactive protein, IL-6 and retinol-binding protein 4 in type 2 diabetic patients. Br J Nutr. 2009, 101:1145-9. 10.1017/S0007114508061527

23. Prasad K: Secoisolariciresinol diglucoside (SDG) isolated from flaxseed, an alternative to ACE inhibitors in the treatment of hypertension. Int J Angiol. 2013, 22:235-8. 10.1055/s-0033-1351687

24. Lemos JR, Alencastro MG, Konrath AV, et al.: Flaxseed oil supplementation decreases C-reactive protein levels in chronic hemodialysis patients. Nutr Res. 2012, 32:921-7. 10.1016/j.nutres.2012.08.007

25. Doyen A, Udenigwe CC, Mitchell PL, et al.: Antidiabetic and antihypertensive activities of two flaxseed protein hydrolysate fractions revealed following their simultaneous separation by electrodialysis with ultrafiltration membranes. Food Chem. 2014, 145:66-76. 10.1016/j.foodchem.2013.07.108

26. Nunes DO, Almenara CC, Silva MA, et al.: Flaxseed oil increases aortic reactivity to phenylephrine through reactive oxygen species and the cyclooxygenase-2 pathway in rats. Lipids Health Dis. 2014, 13:107. 10.1186/1476-511X-13-107

27. Bassett CM, Rodriguez-Leyva D, Pierce GN, et al.: Experimental and clinical research findings on the cardiovascular benefits of consuming flaxseed. Appl PhysiolNutrMetabol. 2009, 34:965-74. 10.1139/H09-087

28. Austria JA, Richard MN, Chahine MN, et al.: Bioavailability of alpha-linolenic acid in subjects after ingestion of three different forms of flaxseed. J Am Coll Nutr. 2008, 27:214-21. 10.1080/07315724.2008.10719693