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Effect of Green Coffee Supplement on Autonomic Cardiovascular Functions in Obese Subjects

Kareem M altameemi

(professor of neurology ,college of medicine, kerbala university / Iraq)

Nagham N. Alhamadani

(M.B.Ch.B , Msc Medical Physiology, Merjan medicalcity Babylon / Iraq).

Ekhlas H. Alassady

(PhD Medical Physiology , Dep. Of Medical Physiology , college of Medicine , Babylon University).

Letters correspondence ;**nagham alhamadani**

E.mail: naghamdr71@gmail .com

ABSTRACT

Obesity is a global health issue .It causes many health problems like cardiovascular disease and diabetes mellitus. Obesity can affect the autonomic nervous system, and particularly its sympathetic component which is involved in body weight regulation by modulating energy expenditure. Extended autonomic nervous system dysfunction commonly occur in obese adults affecting several organs systems like kidneys , skeletal muscle , pancreas and liver .There are many options for treatment of obesity which include : exercise , diet , medical remedies and surgical intervention as the last resort . Green coffee proved as an effective option for the treatment of obesity . Furthermore green coffee improves a lot of harmful complications of obesity.

This study aims to test the effect of green coffee on the functions of autonomic cardiovascular system in obese patients before and after treatment with green coffee .

The study designed as cohort study involved 50 obese patients who were enrolled in this study for the period from 1/12/2016 to 1/8/2017. Only 35 patients (24 females and 11 males) were included. The study was done in 3 centers deals with diabetes and obesity in Babylon /Iraq . Any person with body mass index above 25 kg/m^2 was included in this study. All the participants were given 1000mg green coffee as a 2 capsules once daily for 6 weeks. Autonomic function test and catecholamine serum level done for all the patients before starting treatment and after treatment.

The results of the study shows clear and significant improvement of all the autonomic function test battery according to Ewing's scoring system. The patients with normal autonomic functions and early parasympathetic damage shows significant improvement P value <0.001 and <0.002 respectively ,while definite parasympathetic damage and combined sympathetic and parasympathetic damage shows non-significant improvement. Serum catecholamine shows no significant decline .

In Conclusion the green coffee beans is effective in improvement of autonomic function tests. Larger sample is recommended in the future.

Keywords: obesity , green coffee , autonomic function tests.

Introduction

Obesity has recently been recognized to contribute to cardiovascular mortality and morbidity through an increased sympathetic drive leading to end organ damage and hypertension (Lambert *et al.,* 2010). Increased body fat deposition has been specifically correlated to sympathetic overdrive at rest, with resting levels of muscle sympathetic nerve activity in the obese reported as greater than 50% higher in some people. Elevated levels of muscle sympathetic nerve activity are associated with obesity-induced subclinical organ damage to the heart, blood vessels, and kidneys in young subjects, even in the absence of hypertension(Michael and Christopher ,2012).

The autonomic nervous system (ANS) is the part of the nervous system that is responsible for regulation and integration of internal organs' functioning. Together with the endocrine and immunological systems it determines the status of the internal environment of the organism and adjusts it to its current needs, so enabling adaptation of the internal environment to changes in an external environment (Agnieszka and Jerzy, 2010).

Previous reports illustrated extended ANS dysfunction in obese children and adolescents, affecting several organ systems. Both parasympathetic activity and sympathetic activity are reduced. The conspicuous pattern of ANS dysfunction raises the possibility that obesity may give rise to dysfunction of the peripheral autonomic nerves resembling that observed in normal-weight diabetic children and adolescents(Baum *et al.*, 2013).

Caffeine is capable of increasing work capacity while individuals perform strenuous tasks. In one study, caffeine provoked a greater maximum heart rate while a strenuous task was being performed compared to a placebo. This tendency is likely due to caffeine's ability to increase sympathetic nerve outflow. In addition recovery after intense exercise was slower when caffeine was consumed prior to exercise. Caffeine's tendency to inhibit parasympathetic activity in non-habitual consumers. The caffeine-stimulated increase in nerve activity is likely to evoke other physiological effects as the body attempts to maintain homeostasis (Bunsawat *et al.,* 2015).

Due to safety concerns and side effects of many prescription weight loss drugs, herbal remedies are becoming widely popular as alternatives to prescription medications for weight loss(Heather and Brianna, 2014).Tools for obesity management, including caffeine, ephedrine and green tea have been proposed as strategies for weight loss and weight maintenance, they may increase energy expenditure and have been proposed to counteract the decrease in metabolic rate that is present during weight loss(Kristel *et al*.,2006).

The rising in prevalence of the metabolic syndrome has need a greater effort form therapeutic and prevention strategies (Aidilla *et al*., 2013). The world prevalence of obesity has increased considerably in the last decade.

Green coffee extract(GCE) is present in green or raw coffee .It is also present in roasted coffee, but much of the GCE is destroyed during the roasting process. Some GCE constituents, such as chlorogenic acid (CGA) can also be found in a variety of vegetables and fruits (Onkopaya *et al*. ,2010).

Evidence is accumulated from animal and human studies regarding the use of GCE as a weight loss supplement (Cho *et al.*, 2010) . In human subjects coffee intake has been reported to be inversely associated with weight gain (Lopez *et al*., 2006). Consumption of coffee has also been shown to produce changes in several glycaemic markers in older adults (Hiltunen, 2006).

Other researches has indicated that the consumption of caffeinated coffee can lead to some reductions in long-term weight gain, an effect which is likely to be due to the known thermogenic effects of caffeine intake as well as effects of GCE and other pharmacologically active substances present in coffee (Greenberg *et al*., 2006). GCE has also been postulated to modify hormone secretion and glucose tolerance in humans(Johnston *et al*. , 2003) . This effect is accomplished by facilitating the absorption of glucose from the distal, rather than the proximal part of the gastrointestinal tract (Onkopaya *et al*. ,2010).

The study aims to evaluate the functions of autonomic cardiovascular functions in obese patients before and after treatment with green coffee and to test the efficacy of green coffee in decreasing weight.

Patients and Methods

Study Design :

This study is a cohort study done at 3 medical centers in Babylon / Iraq at the period from 1/12/2016 to 1/8/2017 .

The study protocol was approved by the Ethical Committee/college of medicine /Babylon university / Iraq and fully explained to the subjects who gave their written informed consent before participation.

In this study 50 obese patients (16 males and 34 females) their ages range between (20-55) were enrolled in this study . A 35 patients (11 males and 24 females) were included in this study . The diagnosis of obese and overweight patient was done according to the body mass index .It included any person above 25 kg/m^2. Furthermore the patients were divided into four groups according their ages:

1.Age group from 20_29 years.(N= 10) .

2.Age group from30_39 years .(N= 10)

3.Age group from 40_49 years. .(N= 11)

4.Age group from 50_55 years. .(N= 4)

Data base were arranged for all involved patients which include the following : age , sex , job , address , educational level , history of medical disease , duration of obesity according to the formula of questionnaire .

Each participant of the study was instructed to take green coffee capsules for six weeks as 2 cap1000 mg once daily before breakfast (Scott , 2012).

The following variables were studied before and after completion of treatment with green coffee :

1. Measurement of weight , height and body mass index.

2. Autonomic cardiovascular function tests : 5 tests were done according to Ewing's protocol and it involved three parasympathetic tests and two sympathetic tests (heart rate response to valsalva maneuver , heart rate response to standing 30:15 ratio , heart rate response to deep breathing , blood pressure response to standing , blood pressure response to handgrip).

3. Blood sample for measurement of serum catecholamine.

Preparation of capsules :

Capsules prepared manually .First start with grinding crude green coffee beans to form fine powder that can be filled in capsules .Then capsules filled about 500 mg measured by sensitive small scale used for medications .

Assessment:

The same clinical and biochemical assessment were done for all the participants.

History :

Detailed history was taken from each patient regarding personal history , medical history and duration of obesity according to the following questionnaires form.

Questionnaire used in the study of effect of green coffee on weight loss and some blood parameter

Name:	
Age:	**Gender:**
Marital state:	
Educational level:	
Job:	
Address:	
Phone NO:	
Weight : **Height:**	**BMI:**
Medical history:	
Drugs:	
Duration of obesity :	
Appetite change :	

Inclusion criteria

1. Male and female with BMI above 25 kg/m^2.

2. Patients were between 20 -55 years old.

3. Patients who are cooperative and have a desire to decrease their body weight.

4. Patients on no specific diet or specific life style modification.

Exclusion criteria

The following patients were excluded :

1. Patients with hypertension, diabetes, impaired GTT, psychological diseases, head trauma, cardiac abnormalities, IHD, cardiac failure, chronic obstructive lung diseases and thyroid disease .
2. Patients suffering from any clinical diseases likely to affect ANS.
3. Patients with history of smoking, alcohol and drug abuse.
4.Patients taking medication e.g. Vasodilators, α blocker, β blockers, barbiturates, opiates, tricylic antidepressants and phenothiazines that could affect autonomic functions were also excluded from the study(Grewal *et al.*, 2011).
5.Patients were taking any medication or nutritional supplement(Farah *et al.*, 2008).

Clinical examination :

General examination to assess blood pressure , weight and height . Systemic examination include autonomic nervous system examination. The examination consist of :

Anthropometric Measures

Height (m) and weight (Kg) were measured for all patients in the study . Body mass index (BMI) was then calculated using the following standard equation: **BMI (Kg/m^2) = (weight Kg)/(height m)^2** (Revuelta and Al-Dujaili , 2014).

. Examination of Autonomic Nervous System

A- Tests reflecting parasympathetic damage

1.Heart rate response to Valsalva maneuver

The test is performed by asking the patient to blow into mouth-piece connected to aneroid manometer and holding it at a pressure of 40 mm mercury for (15) seconds , while a continuous electrocardiogram (ECG) is recorded. The results are expressed as the valsalva ratio which is the ratio of the longest R-R interval after the maneuver reflecting the overshoot bradycardia to the shortest R-R interval during the maneuver reflecting the tachycardia during the strain. The mean of the three ratio is taken as a final result.

2.Heart rate(R-R interval) variation during deep breathing

The patients sits quietly and breaths deeply at six breaths per minute (5second in and 5 second out) for one minute , an ECG is recorded throughout the period of deep breathing and with a marker used to indicate the onset of each inspiration and expiration .The maximum and minimum R-R interval during each breathing cycle are measured with a ruler and converted to beat/ minute. The results then expressed as the mean of the difference between maximum and minimum HR for the six measured cycle in beats/minute .Heart rate variation has also measured as the ratio of HR of expiration (E) to inspiration (I) .E/I ratio .

3.Immediate heart rate response to standing 30:15 ratios

The test is performed with the patient lying on a couch while the HR is recorded continuously on ECG. The patient then asked to standup unaided and the point at standing is marked on ECG. The shortest R-R at or around the 15^{th} beat and the longest R-R at or around the 30^{th} beat ,after the standing ,is measured .This is expressed by the 30:15 ratios(R-R interval of the 30^{th} to the R-R interval of the 15^{th}).

B. Tests reflecting the sympathetic damage

1.Bloood pressure response to standing

The test is measured by measuring the patient blood pressure while he is lying down quietely and again when he is stands up after three minutes supine position .The postural fall in blood pressure is taken as the difference between systolic Bd-p lying and systolic Bd-p standing.

2.Blood pressure response to sustained handgrip

The maximum voluntary contraction is first determined using a handgrip dynamometer .Hand grip is then maintained at 30% of the maximum as long as possible for up to 5 minutes .Blood pressure is measured three times before , and one minute interval durig hand grip ,the result express as the difference between the highest diastolic blood pressure during hand grip and the mean of the three reading before handgrip begun.

C- Results of Autonomic testing

The result of each of the five tests are classified into normal , borderline , abnormal according to Ewing scoring table (1) .

The results can be categorized and usually falls into one of the four groups :

1.Normal.

2.Early parasympathetic damage : with results of only one of the three tests of the parasympathetic function is abnormal.

3.Definite parasympathetic damage : with results of at least two of the tests of parasympathetic function abnormal.

4.Combined parasympathetic and sympathetic damage : in addition to abnormal parasympathetic functions , finding in one or both of the sympathetic tests are abnormal.(Ewing *et al* .,1982).

Instruments used in the study :

The instruments used are shown in Table (2).

Blood collection

Venous blood samples were aspirated at about 9 a.m. from anticubital fossa after a 12 hours overnight fast. From each person 5 ml of blood aspirated , collected in tubes containing gel , centrifuged for 10 mimutes after waiting for 45 minutes to separate serum from whole blood . Serum samples stored in refrigerator (-20 C) .Serum samples were used for measurement of catecholamine

Measurement of serum catecholamine :

Catecholamine measured by ELISA .

Statistical Analysis:

Computerized SPSS program software 24 was used to analyze data which were expressed by means ± standard deviation (SD) . Correlation between different parameters where done using T –test and Chi square whenever it is applicable. The statistical difference considered to be significant when p value < 0.05 and highly significant when p value < 0.01 (Daniel , 2013).

Results

Demographic Data:

The study group were 35 obese patients .They were 24 (68.6%) females and 11(31.4%) males. The age of patients in this study ranged from 20 -55 years and the mean and SD was 36 ±9.7.

Examination Results :

Results of BMI:

The study showed significant decrease in the BMI after 6 weeks treatment with green coffee with a mean of 36.026 ,33.871 pre and post respectively .The p-value was 0.0001.Table 3.

Distribution of body mass index in the studied group

according to age pre and post intervention:

Distribution of BMI according to age showed highly significant correlation between BMI and all age group with the least significant being above 50 years old as summarized in table (4)

The Results of Autonomic function test Pre and Post according to autonomic function test Battery:

The effect of green coffee on the studied autonomic function test showed clear and significant improvement of all the autonomic function test battery. The number of normal AFT pre treatment increased from 11 to 28post treatment. the number of patients with early parasympathetic damage pre treatment also showed significant decrease in the number from 18 to only 6 after treatment involved patients. (Table 5, Table 6).

Distribution of Autonomic Function Test battery(Pre and Post treatment with green coffee) according to Age :

Distribution of AFT battery according to age showed improvement of all the parameter after treatment with green coffee for 6 weeks in all age groups as detailed in table 7.

Distribution of Autonomic Function Test battery(Pre and Post treatment with green coffee) according to Gender :

Distribution of Autonomic Function Test battery(Pre and Post treatment with green coffee) according to gender showed no effect of gender on the result of AFT battery .both males and females demonstrate the same significant improvement of both sympathetic and parasympathetic functions after treatment with green coffee.(Table 8)

Distribution of Autonomic Function Test battery(Pre and Post treatment with green coffee) according to BMI :

In a trial to know the correlation between decrease of BMI and improvement of AFT ,we found that there is strong and significant improvement in the AFT(Table 9)

Results of Catecholamine in the present study :

The result of catecholamine was not changed in this study . There is very little decrease in the mean amount of this neurotransmitter(10)

Discussion

Autonomic Function Test

AFT battery disclosed clear and significant improvement after treatment with green coffee for 6 weeks. This improvement in the AFT results clearly reflect the reduction in BMI and improvement of fitness. Improvement in AFT may reflect improvement of other parameters such as glycemic state , lipid profile and general wellbeing of the participant and their mood after successful reduction their weight .The AFT contribute to the modulation of the energy expenditure of the human organism (Koenig *et al*., 2014). A previous short communicating published in European journal of clinical nutrition provided the first evidence of an association between sympatho -vagal balance and BMI .Providing evidence for a prominent role of the vagus nerve in the regulation of energy expenditure .Decrease HRV reflect an abnormal autonomic sinus node activity featured by a dominating sympathetic and reduced parasympathetic control(Molfino *et al.,* 2009). ANS activity plays an important role in regulation of BMI (Rajashree *et al*., 2015). In this study green coffee caused significant weight reduction and hence improvement of the sympathetic part and returning the sympatho- vagal balance which in turn regulate the energy expenditure. This improvement reflect the advantage of this herbal on improvement of cardiovascular disease.

The effect of green coffee on catecholamine

The present study showed non- significant changes in the catecholamine .It is well known that green coffee increased the levels of catecholamine and this in turn increased the duration of alertness and exercise tolerance (Bunsawat *et al.,* 2015). This study failed to demonstrate an increase in catecholamine because habitual consumers of caffeine usually shows an increase in parasympathetic and decrease in sympathetic activity. Some of our patients were probably habitual consumers of other caffeinated drinks likes black tea , green tea or roasted coffee .

Conclusions and recommendations

There is a clear improvement of some autonomic cardiovascular functions after 6 weeks treatment with green coffee .

We recommend to repeat this study on a larger sample , multicentric, team work and longer duration to confirm our preliminary results.

And also to use chlorogenic acid extract instead of crude green coffee to increase the effectiveness . and to repeat the study with different doses of the extract to look for different results.

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Tables

Table 1 .The scoring of the five Ewing tests(Ewing *et al*., 1982).

Test	Normal	Borderline	Abnormal
Heart rate response to Valsalva maneuver	≥1.20	1.11 -1.20	≤1.0
Heart rate variation during deep breathing	≥15 beats Beats/minute	11-14 Beats/minute	≤10Beats/minute
Immediate heart response to standing	≥1.04	1.01 – 1.03	≤1.00
Blood pressure response to standing (decrease)	≤ 10 mmHg	11- 29 mmHg	30 mmHg
Blood pressure response to sustained handgrip(increase)	≥16 mmHg	11 -15 mmHg	≤10 mmHg

Table 2 : The instruments used in this study .

Instruments	**Company and /or Country**
Deep Freeze	Liebhe (Austria)
Micropipette	Glison (France)
Centrifuge	PLC series (USA)
Plane tube	Afma-Dispo-(Jordan)
Disposable syringe	Witeg(Malaysia)
Spectrophotometer	Cambridge (England)
SPOTECHEM	ARKRAY (Japan)
Electronic balance	Seca (Germany)
Electrocardiogram	GE Healthcare (Germany)

Sphygmomanometer	United kingdom
Stethoscope	Littmann (U.S.A)
Modified sphygmomanometer	China

Table 3 Mean difference of BMI pre and post treatment (Mean ± SD):

Variable	Pre treatment N= 35	Post treatment N= 35	p-value
BMI kg/m^2	36.026 ± 5.14	33.871± 4.69	0.0001**

Table 4. Distribution of body mass index in the studied group according to age pre and post intervention (Mean ± SD).

Age group(N0.)	BMI kg/m2 Pre treatment	BMI kg/m2 Post treatment	P- value
20-29years (10)	35.99 ± 4.44	33.68 ± 4.86	< 0.001**
30-39 years (10)	38.02 ± 8.81	35.42 ± 5.98	< 0.001**
40-49 years (11)	35.6 ± 4.07	33.66 ± 4.18	< 0.001**
>50 years (4)	32.3 ± 8.81	31.05 ± 8.43	< 0.023*

* significant ** highly significant** highly significant

Table 5. Results of autonomic nervous system function test according to Ewing protocol (Mean ± SD)

Test	Patients Pre treatment N=35	Patients post treatment N=35	P value
1.Heart rate (HR) response to Valsalva maneuver	1.24± 0.1	1.3 ± 0.13	0.9*
2. Herat rate variation to deep breathing (beat/min)	17.29 ± 9.96	18.03 ±6.29	0.9*
3.Immediate heart rate response to standing	1.15 ± 0.16	1.2 ± 0.21	0.9*
4.Blood pressure response to standing (mmHg)	7.43 ± 5.05	6.37 ± 4.81	0.9*
5. Blood pressure response to handgrip (mmHg)	16.63 ± 4.59	14.86 ±5.84	0.9*

*non significant <0.05

Table 6 . The result of Autonomic function tests (pre and post treatment with green coffee) According to the Ewing's scoring system:

AFT battery*	Pre treatment N=35	Post treatment N=35	P- value
Normal (No. ,%)	11 (26.2%)	28 (66.7%)	0.001**
Early parasympathetic damage (No. ,%)	18 (42.9%)	6 (14.3%)	0.002**
Definite parasympathetic damage (No. ,%)	3 (7.1%)	0	0.289
Combined sympathetic parasympathetic damage (No. ,%)	3 (7.1%)	1 (2.4%)	0.149

*AFT autonomic function test ** highly significant

Table 7 Distribution of Autonomic Function Test battery(Pre and Post treatment with green coffee) according to Age group :

Age group (No.)	AFT*	Pre treatment(No.)	Post treatment(No.)	P value
20-29 years (N=10)	Normal	7	10	0.3
	Early	3	0	
	Definite	0	0	
	Combined	0	0	
30-39 years (N=10)	Normal	0	8	0.003**
	Early	6	1	
	Definite	2	0	
	Combined	2	1	
40-49 years	Normal	4	8	0.8

(N=11)	Early	5	3	
	Definite	1	0	
	Combined	1	0	
>50 years (N=4)	Normal	0	2	0.6
	Early	4	2	
	Definite	0	0	
	Combined	0	0	

** highly significant * AFT autonomic function test

Table 8. Distribution of Autonomic Function Test battery(Pre and Post treatment with green coffee) according to Gender :

Gender (No.)	AFT**	Pre treatment (No.)	Post treatment (No.)	P- value
Male (N=11)	Normal	2	9	0.03*
	Early	9	2	
	Definite	0	0	
	Combined	0	0	
Female (N=24)	Normal	9	19	0.02*
	Early	9	4	
	Definite	3	0	
	Combined	3	1	

* significant ** AFT autonomic function test

Table 9 Improvement in autonomic function Before and after treatment:

Variable(No.)	Pre treatment	Post treatment	P –value

	N=35	N=35	
Normal AFT**	**11**	**28**	**0.0001*** **
Abnormal AFT	**24**	**7**	

*** very high significant ** AFT autonomic function test

Table 10. Results of Serum Catecholamine Mean ± SD :

Variable	Pre Treatment **N =35**	Post treatment **N= 35**	P- value
Catecholamine ng/ml	63.82 ± 13.33	63.67 ± 10.35	0.95 *

*non significant < 0.05