International Journal of Health Sciences and Research
www.ijhsr.org ISSN: 2249-9571

Original Research Article

Human Alpha Synuclein, Inflammation and Metabolic Disorders in Obesity, Before and after Dietary Intervention

Salwa M. El Shebini[1], Maha I. A. Moaty[2], Yusr M. I. Kazem[3], Nihad H. Ahmed[4], Suzanne Fouad[5], Atiat M. Arafa[6], Laila M. Hanna[7], Salwa T. Tapozada[8]

[1]Professor of Nutrition and Public Health, [2] Assistant Professor of Nutritional Biochemistry, [3]Professor of Medical Nutrition, [4]Assistant Professor of Applied Nutrition, [5]Researcher, [6]Assistant Professor of Applied Nutrition, [7]Professor of Nutrition, [8]Professor of Nutrition, Department of Nutrition and Food Sciences, National Research Centre, Dokki, Gizza, Egypt.

Corresponding Author: Maha I. A. Moaty

Received: 29/08/2015 *Revised: 21/09/2015* *Accepted: 07/10/2015*

ABSTRACT

Aim: To evaluate the effect of a special dietary therapy on body weight, metabolic profile, and cognitive function in a sample of obese Egyptian women.
Subjects and Methods: Ninety six obese Egyptian women shared as volunteers in this study. The sample was divided into two groups and the study lasted for 8 weeks divided into two phases. In phase (1), each group followed a special dietary therapy composed of a hypocaloric regimen and a kind of dietary supplement, which was omitted in phase (2). Anthropometric, biochemical and dietary evaluations were carried out. Cognitive evaluation was performed by using oral tests and serum alpha-synuclein (α-Syn) determination.
Results: High levels of all the investigated anthropometric and biochemical parameters were detected at the baseline which were improved together with the cognitive tests by the end of phase (1). By the end of phase (2), after omitting the supplement, these parameters increased except α-Syn and Interleukin-6 (IL-6). Significant positive correlation was reported between α-Syn and the inflammatory parameter IL-6 at all periods of the study.
Conclusion: Data of this study give evidence for the healthy effect of using special dietary therapy in the management of obesity, inflammation, and improving the cognitive function.

Key words: obesity, dietary therapy, α-Synuclein, Interleukin-6.

INTRODUCTION

Alpha-Synuclein (α-Syn), a 14.5kD protein, was originally isolated from Alzheimer's disease (AD) plaques and was thought to be a pre-synaptic nerve terminal protein. [(1)] The α-Syn is a member of the synuclein's family of cytoplasmic, predominantly neuron-specific proteins. Considerable amount of α-Syn is found in axons and presynaptic terminals of neurons located in brain areas responsible for emotions and memory. [(2)] The normal function of α-Syn is poorly understood, and the precise mechanisms by which it leads to toxicity and cell death are also unclear. Although α-Syn is a highly soluble, cytoplasmic protein, it binds to a variety of cellular membranes of different properties and compositions. These interactions are considered critical for at least some normal functions of α-Syn, and may well play critical roles in both the aggregation of the protein and its mechanisms of toxicity. [(3)] Synucleins are

small prone to aggregate proteins associated with several neuro-degenerative diseases (NDDs). [4] Normal cellular functions have not been determined for any of the synuclein proteins. Some data suggested a role in the regulation of membrane stability and/or turnover. Mutations in α-Syn are associated with early-onset familial Parkinson's disease, and the protein aggregates abnormally detected in Parkinson's disease, Alzheimer's disease, Lewy body disease, and other neurodegenerative diseases. [5,6] The α-Syn has been found in body fluids, including blood and cerebrospinal fluid, and is likely produced by both peripheral tissues and the central nervous system. Exchange of α-Syn between the brain and peripheral tissues could have important pathophysiologic and therapeutic implications. [7] Recent reports suggest that α-Syn is also widely expressed peripherally, including the macrophages. The expression of α-Syn is enhanced in activated macrophages, suggesting that α-Syn may modulate macrophage function and thereby inflammatory processes. [1] Diet-induced obesity may be an environmental risk factor for the development alpha-synucleinopathies. [8]

The interleukin-6 (IL-6) is a pleiotropic cytokine that plays a key role in the interaction between the immune and the nervous systems. Although IL-6 has neurotrophic properties and beneficial effects in the CNS, its overexpression is generally detrimental, adding to the pathophysiology associated with CNS disorders. [9]

The aim of this study was to evaluate the effect of a special dietary therapy on body weight, metabolic profile, and cognitive function in obese women, by investigating the role of a relatively newly discovered protein α- Syn which appears to be involved in the issues of neurodegenerative disease, inflammation and hence obesity.

MATERIALS AND METHODS

Materials:

Raw Materials: Naked barley grains (giza 129) was purchased from The Ministry of Agriculture. Wheat germ was purchased from the North Cairo Mills Company, Egypt. Turmeric *(Curcuma Longa)* and Ginger *(Zingiber Officinale)* were obtained from a local herbal shop (Dokki, Egypt). Skimmed milk, tomato sauce, corn oil, baking powder and salt were purchased from the local market.

Preparation and Evaluation of Supplements: Basic and modified formulas were prepared by mixing the barley flour with 5% turmeric powder (formula 1), and barley flour with 5% ginger powder (Formula 2) then with the other ingredients according to table (1). 14.7 ml of dextrose solution (5.93%) and a suitable amount of water were added according to AOAC, [10] to be formed as Syrian bread (Table 1). These formulas were baked in a special oven at 200 °C for about 15 minutes.

Table 1: Formula composition of Syrian bread (g/100g)

Raw materials	Formula (1)	Formula (2)
Naked barley	60	60
Wheat germ	15	15
Turmeric	5	-
Ginger	-	5
Skimmed milk	10	10
Tomato sauce	1.5	1.5
Corn oil	5	5
Baking powder	2	2
Salt	1.5	1.5

Analytical Methods: Moisture, ash, fiber, protein and fat of the samples of Syrian bread were determined according to AOAC. [10] Total carbohydrates were calculated by difference. Fatty acids and polyphenols were determined using standard methods. [11, 12]

Subjects: Ninety six Egyptian women suffering from obesity, shared as volunteers in this study which was conducted from March to September, 2014. They were all enrolled in a program for losing weight at the Nutrition Department, National Research Centre.

The study was divided into two phases, phase (1) and phase (2), each one lasted for 4 weeks. The patients were divided into two groups, group (A): 50 patients with mean age of 46.04±1.88 years and had a mean body mass index (BMI) of 37.64±1.11 kg/m², and group (B): 46 patients with mean age of 47.33±2.23 years and mean BMI of 34.83±1.49 kg/m². At phase (1), group (A) followed a low caloric balanced diet (1000- 1200 K calories/ day), accompanied by a supplement composed of naked barley flour mixed with 5% turmeric powder that was baked in the form of Syrian bread (formula 1), two servings were consumed with breakfast (40 g) and one serving with dinner (20 g), instead of Baladi bread. Group (B) consumed another formula of the bread composed of naked barley flour mixed with 5% ginger powder (formula 2) with the same instructions. Phase (2) lasted for 4 weeks during which the volunteers were following only the same low caloric balanced diet. All volunteers were subjected to thorough clinical examination.

The participants were informed about the purpose of the study and their permission in the form of written consent was obtained. The protocol was approved by the "Ethical Committee" of the "National Research Centre".

Anthropometric Parameters and Blood Pressure Measurements: Relevant anthropometric measurements as weight, height and waist circumference were reported. [13] Body fat (BF) as a percent from the body weight was measured by using Geratherm Body Fitness (B-5010), Germany. The BMI was calculated (weight in kg/ height² in meter). Waist to hip ratio (WHR) was also estimated as minimal waist to hip circumferences in cm. Blood pressure for each patient was measured 3 times and the mean was recorded.

Blood Sampling and Biochemical Analysis: Fasting blood samples (12 hours fasting) were drawn from the patients. Fasting blood glucose (FBG) was determined on fresh samples; other biochemical parameters were performed on the fasting blood sera that were stored at -70 C° until used. The FBG was determined in fresh samples using glucose oxidase method. [14] Serum total cholesterol, high density lipoprotein-cholesterol (HDL-C) and triglycerides (TG) were done using cholesterol proceed No 1010, Stanbio, [15] HDL-C proceed No 0599 StanioLiquicolor, [16] triglycerides proceed No 2100, [17] Enzymatic methods respectively. C-peptide was detected by C-peptide Enzyme Immunoassay Test Kit, catalogue no.E29-071, IMMUNOSPEC Corporation, Netherland. [18] Modified homeostatic model assessment of insulin resistance (M.HOMA-IR) was calculated, where M.HOMA-IR=1.5+fasting blood glucose x fasting c- peptide/2800, [19] in which insulin was replaced by C-peptide so as to be applied on diabetic patients using exogenous insulin. Serum alpha Synuclein (α-Syn) was measured by an enzyme-linked immunosorbent assay performed according to the directions of the supplier (Biosource, Immunoassay Kit #KHB0061, Camarillo, CA 93012). [20] Serum interleukin-6 was determined by AssayMax Human Interleukin-6 (IL-6) ELISA Kit, AssayPro, Catalog Number EI1006-1. [21]

All the measurements and the biochemical analysis were performed at the start of the study (baseline) and by the end of each of the two phases (Phase 1& Phase 2).

Dietary Recalls: Collecting detailed data about nutritional habits and intake was accomplished through 24 hours recall dietary history. Analysis of food items using World Food Dietary Assessment System, (WFDAS), 1995, USA, University of California.

Cognitive and Mental Evaluation: Mini Mental State Examination (MMSE) was performed for evaluation of mental and

cognitive status. Sleep quality and number of sleeping hours and their pattern were evaluated. Exposure to sun: time, duration and clothing. A scoring system of 3 points scale was then put to present the degree of exposure and adequacy. General subjective life stresses, life pattern to evaluate general activity and history of exercising were recorded and put on the 3 points scale. [22]

Statistical analysis: All values were expressed as mean value ±SE. Two tailed student t-test was used to compare between different phases of the same group. Correlation between the different parameters was tested by Pearson's test. P values <0.05 were considered statistically significant. SPSS window software version 17.0 (SPSS Inc. Chicago, IL, USA, 2008) was used.

RESULTS

Table (2) shows the mean values of moisture, protein, fat, crude fiber, ash and the phenolic contents of the two Syrian bread with Turmeric or Ginger.

Table 2: Chemical composition of the two types of the Syrian bread supplements (g/100g).

Samples	Moisture	Protein	Fat	Fiber	Ash	T.CHO	Total phenols (as tannis)
Formula 1 bread (1)	8.22^{b} ±0.22	18.12^{b} ±0.65	8.22^{b}±0.29	6.25^{a} ±0.13	3.16^{a} ±0.19	64.25^{a}±0.74	5.34
Formula 2	9.11^{a}±0.35	20.5^{a} ±0.52	8.92^{a} ±o.41	5.95^{b} ±0.09	3.25^{b} ±0.11	61.38^{b}±0.96	5.46
LSD at 0.05	0.82	1.013	0.026	0.22	0.086	1.032	

T.CHO: total carbohydrate

Table 3: Mean ± SE of age, anthropometric parameters and blood pressure among obese subjects at the baseline and by the end of the two phases of the dietary therapy

	Group (A) (no.=50)			Group (B) (no.=46)		
Parameters	Baseline	Phase 1	Phase 2	Baseline	Phase 1	Phase 2
Ages (year)	46.04±1.88			47.33±2.23		
Height (cm)	159.30±1.17			157.50±1.07		
Weight (kg)	94.79±2.97	$86.47±3.46^{*a}$	$87.46±2.37^{**b}$	86.53±3.55	$83.25±3.43^{**c}$	$82.91±3.64^{**d}$
BMI (kg/m²)	37.64±1.11	34.38±1.36	$35.37±0.88^{**b}$	34.83±1.48	$33.49±1.48^{**c}$	$33.52±1.46^{**d}$
% BF	47.34±0.92	46.32±1.44	45.51±1.42	43.02±1.68	42.65±1.63	41.40±1.90
Waist (cm)	98.79±2.16	$91.97±2.16^{**a}$	$86.64±2.29^{**b}$	91.89±2.80	$86.19±2.56^{**c}$	$83.44±2.88^{**d}$
Abdominal II (cm)	122.00±2.06	$115.08±2.67^{**a}$	$110.54±3.29^{**b}$	115.92±2.76	$109.75±2.72^{**c}$	$107.47±3.19^{**d}$
Hip (cm)	122.53±1.99	$117.25±1.92^{**a}$	$113.66±2.53^{**b}$	117.47±2.85	$112.23±2.71^{**c}$	$110.03±2.97^{**d}$
WHR (cm/cm)	0.81±0.014	$0.78±0.013^{**a}$	$0.76±0.018^{**b}$	0.78±0.01	$0.76±0.01^{**c}$	0.75±0.01
SBP (mmHg)	121.11±2.96	121.11±2.76	$118.21±3.08^{*b}$	124.71±3.32	122.94±1.70	123.21±2.26
DBP (mmHg)	71.11±2.31	71.11±1.96	$71.42±2.53^{*b}$	74.12±1.67	73.53±1.70	$72.31±2.01^{*d}$

BMI: Body mass index, %BF: percent body fat, WHR: waist to hip ratio, SBP: systolic blood pressure, DBP: diastolic blood pressure.
a: Baseline vs. Phase 1 / b :Phase 1vs. Phase 2 for group A.
c: Baseline vs. Phase 1 / d: Phase 1vs. Phase 2 for group B.

*p<0.05, ** p< 0.01.

Table 4: Mean± SE of biochemical parameters of the two groups at the baseline and by the end of the two phases of the dietary therapy

Biochemical Parameters	Group A (no.=50)			Group B (no.=46)		
	Baseline	Phase 1	Phase 2	Baseline	Phase 1	Phase 2
FBG (mg/dl)	112.87±4.66	$99.53±3.89^{**a}$	$114.02±4.84^{**b}$	119.58±5.48	$103.19±4.77^{**a}$	106.38±4.20
Triglycerides (mg/dl)	139.28±13.10	$88.86±8.27^{**a}$	$118.69±7.91^{**b}$	135.24±9.30	$103.87±7.37^{**a}$	102.09±5.41
TC (mg/dl)	243.54±10.18	$185.32±6.62^{**a}$	205.09±10.53	217.01±9.05	$180.57±7.31^{**a}$	183.72±5.99
HDL-C (mg/dl)	47.93±1.53	$54.33±1.74^{**a}$	51.98±1.53	46.39±1.38	$51.81±1.29^{**a}$	51.25±1.64
Non-HDL (mg/dl)	195.61±10.84	$130.98±7.16^{**a}$	$153.11±10.88^{*b}$	170.61±8.93	$128.76±7.87^{**a}$	132.47±6.07
Risk factor (TC/ HDL-C)	5.17±0.29	$3.47±0.18^{**a}$	$3.99±0.26^{*b}$	4.73±0.22	$3.54±0.18^{**a}$	3.63±0.15
C-peptide (ng/ml)	4.93±0.97	$3.72±0.85^{*a}$	$.05±0.91^{*b}$	5.07±0.74	$3.59±0.47^{**a}$	3.72±0.56
M.HOMA-IR	1.69±0.04	$1.63±0.03^{**a}$	$1.67±0.04^{**b}$	1.72±0.04	$1.64±0.02^{**a}$	1.65±0.03
A-Syn (ng/ml)	43.0±2.42	$36.07±1.23^{**a}$	$37.23±1.15^{**c}$	44.18±3.03	$37.71±1.79^{**a}$	$36.27±0.49^{*b,*c}$
IL-6 (pg/ml)	9.56±0.56	$7.77±0.36^{**a}$	$8.27±0.49^{**c}$	8.89±0.39	$7.80±0.47^{**a}$	$7.32±0.21^{**c}$

- FBG: fasting blood glucose, TC: total cholesterol, HDL-C: high density lipoprotein cholesterol, M.HOMA-IR: Modified homeostatic model assessment of insulin resistance, α-Syn: α-Synuclein, IL-6: Interleukin-6.
- a: Baseline vs. Phase 1 / b :Phase 1vs. Phase 2/ c: Baseline vs. Phase 2
- *p<0.05 **p<0.01

Table 5: Pearson's correlation between α-synuclein and interleukin-6 at the baseline and by the end of the two phases of the dietary therapy of the whole sample (no. =96)

Phases	r	p
Baseline	0.343	0.008**
Phase 1	0.611	0.000**
Phase 2	0.359	0.010*

r =correlation coefficient. P=*Correlation is significant at the 0.05 level (2-tailed); **Correlation is significant at the 0.01 level (2-tailed).

Table 6: Cognitive variables in percentage at the baseline and after intervention

Variable	Score (1) (%)		Score (2) (%)		Score (3) (%)	
	Baseline	Phase 2	Baseline	Phase 2	Baseline	Phase 2
MMSE	16.7	13.3	72.9	76.2	10.4	10.5
Sleeping hours	33.4	33.4	60.4	60.2	6.2	6.4
Sleeping quality	27.1	24.9	31.3	33.3	41.6	41.8
Eposure to sun	41.6	40.7	31.3	31.2	27.1	28.1
Stress	8.3	7.9	36.6	39.2	52.1	52.9
General activity	42.0	30.0	33.0	40.0	25.0	30.0
Exercising	31.2	28.0	56.3	58.5	12.5	13.5

MMSE: mini mental state examination 22-25 =1, 26-28=2 and 29=3, Sleeping hours: 4-5 =1, 6-8 =2 and 9-10 = 3, Exposure to sun, Sleep quality, Stress, General activity, Exercising 1=low, 2=medium and 3 =high.

Table 7: Mean ± SD & % Recommended dietary allowances (RDA_s) of nutrient intakes and different types of diet among the obese women.

Nutrient intake	Habitual diet	Diet with Baladi Bread	Diet with Turmeric bread (formula 1)	Diet with Gingerbread (formula 2)	RDA_s
	Mean ± SD %RDS				
Energy (kcal)	2717.53±235.01 123.52%	974.25±152.11 44.28%	904.28±70.59 41.10%	901.02±67.20 40.96%	2200
Protein (g)	91.23±27.30 182.46%	52.63±19.17 105.26%	52.23±14.67 104.46%	53.05±11.34 106.10%	50
Fat (g)	123.57±37.08	30.17±16.31	28.04±13.20	27.18±12.37	
Carbohydrate (g)	310.12±60.96	123.05±32.51	110.75±28.71	111.05±24.61	
Dietaryfiber (g)	18.83±9.97	29.19±10.02	35.47±8.91	35.60±7.84	30
Vit. A (µg)	598.12±20.97 74.77%	771.54±23.11 96.44%	775.31±21.98 96.91%	778.51±20.31 97.31%	800
Vit. D (µg)	2.16±0.65 43.20%	3.61±0.52 72.20%	3.78±0.35 75.60%	3.75±0.28 75.00%	5
Sodium (mg)	655.25±50.30 131.05%	385.20±30.25 77.04	320.89±14.27 64.18%	309.78±11.37 61.96%	500
Potassium (mg)	3231.78±45.50 161.59%	1638.89±60.35 81.94%	1645.82±30.69 82.29%	1630.71±26.30 81.54%	2000
Calcium (mg)	624.37±70.61 62.44%	804.61±36.25 80.46%	835.13±26.91 83.51%	852.73±27.32 85.27%	1000
Iron (mg)	7.35±1.26 49.00%	11.20±1.62 74.67%	11.30±2.64 75.33%	11.26±3.01 75.07%	15
Zinc (mg)	8.49±2.08 70.75%	9.76±1.54 81.33%	10.19±1.84 84.92%	10.22±1.37 85.17%	12
SFAs (g)	41.6023±13.59	9.29±2.39	9.03±1.28	9.02±1.39	
MUFAs (g)	37.3715±11.75	10.46±2.14	10.95±1.89	10.88±1.94	
PUFAs (g)	34.89±11.69	7.77±2.58	5.39±1.94	5.36±1.87	
Cholesterol (mg)	390.58±44.06	89.20±11.74	87.35±4.58	87.65±3.46	

SFAs; Saturated Fatty acids MUFAs: Mono-Unsaturated Fatty acids PUFAs: Poly-Unsaturated Fatty acids

Table (3) shows the mean± SE of age, anthropometric and blood pressure measurements of group (A) and group (B) at the start of the study and at the end of the two phases of the regimen. All the anthropometric measurements of the two groups decreased significantly at p<0.05-0.01 at the end of the two phases except the BMI and %BF in group (A) which showed numerical decreases at the end of phase (1) and significant increases at the end of phase (2). Both systolic blood pressure in group (A) and diastolic blood pressure in group (B) showed a significant decrease at the end of phase (2).

Table (4) shows the mean± SE of biochemical parameters of the two groups at the baseline and at the end of the two phases of the dietary therapy. At the end of phase (1), in spite of the slight elevation in the level of the FBG at the start of the study as the diabetic participants were under medical treatment, yet the mean level of the FBG decreased significantly in both groups. The lipid profile disorders that were detected at the basal examination

were improved significantly in both groups. Non- HDL-C (total cholesterol – HDL-C) was an important marker in such condition. C-peptide concentration, M.HOMA-IR values, IL-6 and α-Syn decreased significantly in both groups at p<0.05-0.01. By the end of phase (2) the levels of these parameters increased in group (A), and decreased in group (B) with different ranges, while HDL-C concentration decreased.

Table (5) shows the correlation coefficient between α-Syn and IL-6 in the whole sample. Positive significant correlations were detected between the two parameters at p <0.05-0.01 at the baseline and at the end of the two phases of dietary therapy.

Table (6) shows the baseline results of the mini mental state examination (MMSE)) which evaluates the cognitive functions. The results show that 16.7 % had mild cognitive impairment, 72.9 % had good mental functions with no signs of cognitive impairment, while 10.4 % had excellent mental and cognitive functions. 33.4 % had very low hours of sleep, 60.4 % got moderate sufficient hours of sleep, while 6.2% got more than average hours of sleep. Sleep quality was low in 27.1 %, moderate in 31.3% and high in 41.6%. What was clear, was that exposure to sun and general activity was low in general, and stress was very high in more than 50% of the sample. Moderate exercising was practiced by 56.3 % of the sample, low exercising in 31.2% and high in 12.5%. The percent distribution of the sample as regard the MMSE, sleeping quality, general activity, exercising and exposure to sun were improved by the end of the intervention.

Table (7) shows the mean± SE of the macro and micro nutrients of the habitual diet of the obese women, the three hypo-caloric regimens; with Baladi bread and with the two types of the Syrian bread. The habitual diet of the patients showed a high rate of consumption of protein, fat and carbohydrate which reflected a high caloric intake (123.52% of the RDA). The mean intake of vitamin A and D, and the mean mineral intake of calcium, iron and zinc were below the RDA. The three recommended regimens showed low caloric intake with sufficient protein, fat and carbohydrate and a better intake of the vitamins and the minerals.

DISCUSSION

In this study we aimed to fight obesity and the associated complications especially the inflammatory processes, and their deleterious effects on the cognitive functions in obese women.

At the basal level, the patients were complaining of obesity, dyslipidemia and mild elevation of FBG, IL-6 and α-Syn, in addition to a significant positive correlation between serum IL-6 with serum α-Syn. Furthermore, analysis of their usual nutrients intake revealed high macronutrients intake especially lipids. It has been stated that life-long high fat diet (HFD) induces obesity and glucose intolerance in a transgenic mouse model for α-synucleinopathy and thereby leads to decreased life span as well as accelerated onset of age of the terminal phenotype. This is accompanied by increased neuroinflammation and premature α-synucleinopathology in the brain stems of the HFD-fed mice. [8]

Dietary therapy that was prescribed in this study consisted of functional ingredients that have proved to contain bioactive components, (barley, and either curcumin or ginger). It has been stated that the addition of barley to a healthy diet may be effective in lowering total and LDL cholesterol in both men and women. [23] Furthermore, Shehzad et al. [24] reported that the interactions of curcumin with several signal transduction pathways reverse insulin resistance, hyperglycemia, hyperlipidemia, and other inflammatory symptoms associated with obesity and metabolic diseases. Generation of free

radicals or reactive oxygen species (ROS) during metabolism beyond the antioxidant capacity of a biological system results in oxidative stress which plays an essential role in heart diseases, neurodegenerative diseases, cancer, and in the ageing process. [25,26] The bioactive molecules of ginger, like gingerols have shown antioxidant activity in various modules. [27]

In the present study, by the end of phase, [1] the mean levels of α- Syn and IL-6 in the obese patients decreased significantly after following the dietary therapy with the two different supplements. In addition, both parameters showed significant positive correlation with each other. Mina et al. [1] stated that α-Syn's function is not exclusive to the central nervous system, but it is also involved in modulating inflammatory responses associated with obesity and glucose intolerance. Moreover, these decreases in the two parameters were accompanied by similar decreases in most of the anthropometric measurements including the percent of body fat; decrease of the dietary fat intake, in addition to the improvements of the metabolic profile as indicated by the different biochemical parameters. Detection of α-Syn in the body fluid differs from α-Syn in solid tissue samples of the enteric and autonomic nervous system, but offers some potential as a surrogate marker of brain synucleinopathy. [28]

In spite of the obese patients did not show any neurological symptoms, yet the oral cognitive functions of the patients' revealed good degree of improvement after the dietary therapy. Cann et al. [29] reported that α-Synucleinopathies are neurodegenerative diseases characterized by the abnormal accumulation of α-Syn aggregates in neurons, nerve fibres or glial cells. While small amounts of these α-Syn pathologies can occur in some neurologically normal individuals who do not have associated neurodegeneration, the absence of neurodegeneration in such individuals precludes them from having a degenerative α-synucleinopathy, and it has yet to be established whether such individuals have a form of preclinical disease.

In addition, the healthy beneficial anti-inflammatory protection effects of this dietary therapy proved by the decrease in the mean levels of IL-6. The source of the increase in peripheral IL-6 remains to be established and varies among different pathologies, but has been found to be associated with cognitive dysfunction in several pathologies. [9]

CONCLUSION

Data of this study give further support for the healthy beneficial effects of using functional food containing bioactive components in the management of the obese subjects; as all the detected improvement in most of the studied parameters started to increase by the end of phase. [2] However, the concentration of α-Syn and IL-6 continued to decrease in group (B) who were consuming ginger supplement during the phase, [1] which could emphasized its long lasting therapeutic effects as compared to the turmeric supplement. Therefore, we can conclude that intervention by using dietary therapy as a strategy for reducing adiposity, inflammation and neurodegeneration in the obese patients, might serve as neuroprotectors and disease-modifying tools.

REFERENCES

1. Mina EW, Perera TJ, Chen Z, Chou J, Lin JC. Novel Roles of alpha-Synuclein in Energy and Glucose Homeostasis. American Diabetes Association 75th Anniversary, 2009.
2. Kokhan VS, Afanasyeva MA, Van'kin GI. α-Synuclein knockout mice have cognitive impairments. Behav Brain Res. 2012 May 16; 231(1): 226-30.
3. Snead D, Eliezer D. Alpha-synuclein function and dysfunction on cellular membranes. Exp Neurobiol. 2014; 23(4): 292-313.

4. Surgucheva I, He S, Rich MC, Sharma R, Ninkina NN, Stahel PF, Surguchov A. Role of synucleins in traumatic brain injury - An experimental in vitro and in vivo study in mice. Mol Cell Neurosci. 2014;63C:114-23.
5. Mezey E, Dehejia A, Harta G, Papp MI, Polymeropoulos MH, Brownstein MJ. Alpha synuclein in neurodegenerative disorders: murderer or accomplice? Nat Med. 1998; 4 (7): 755–757.
6. Goedert M. Alpha-synuclein and neurodegenerative diseases. Nat. Rev Neurosci. 2001; 2 (7): 492–501.
7. Sui YT, Bullock KM, Erickson MA, Zhang J, Banks WA. Alpha synuclein is transported into and out of the brain by the blood-brain barrier. Peptides. 2014; 62: 197-202.
8. Rotermund C, Truckenmüller FM, Schell H, Kahle PJ. Diet-induced obesity accelerates the onset of terminal phenotypes in α-synuclein transgenic mice. J Neurochem. 2014; 131(6): 848-58.
9. Trapero I, Cauli O. Interleukin 6 and cognitive dysfunction. Metab Brain Dis. 2014; 29(3): 593- 608.
10. AACC 2000. Approved Method of the AACC. 10th ed., American Association of Cereal Chemists, INC. st., Paul, Minnesota, USA.
11. Association of Official Analytical Chemists (AOAC) (1990). Official methods of analysis (15th ed.) Washington, D.C.
12. AOCS, 1998 Official Methods and Recommended Practices of the American Oil chemist's Society (5th Edn.). AOCS press, Champaign Washington.
13. Jelliffe DB. The assessment of the nutritional status of the community. World Health Organization, Geneva Monograph, 1966; 35: 63-9.
14. Barham D and Trinder P. An improved color reagent for determination of blood glucose by oxidase system. Analyst. 1972; 97: 142-5.
15. Allain CC, Poon LS, Chan CS, Richmond W, Fu PC. Enzymatic determination of total serum cholesterol. Clin Chemo. 1974; 20: 470- 5.
16. Wornick DF, Albers JJ. A comprehensive evaluation of the heparin-manganese precipitation procedure for estimating high density lipoprotein cholesterol. J Lipid Res. 1978; 19: 65-76.
17. Seidel J, Klos S, Ziegenhorn T.ACC Meeting Abstract 34.Clin. Chem. 1993; 39: 1127.
18. Bonger A, Garcia-Webb P. C-Peptide Measurement: Methods and Clinical Utility. CRC Critical Reviews in Clinical Laboratory Sciences. 1984; 19: 297.
19. Li X, Zhou ZG, Qi HY et al. Replacement of insulin by fasting C-peptide in modified homeostasis model assessment to evaluate insulin resistance and islet beta cell function. Zhonghua Yi Xue Yi ChuanXueZaZhi (Chinese). 2004; 29(4): 419–23.
20. Lee PH, Lee G, Park HJ, Bang OY, Joo IS, Huh K. The plasma α-synuclein levels in patients with Parkinson's disease and multiple systems atrophy. J Neural Transm. 2006; 113: 1435–1439.
21. Feldmann M, Brennan FM, Maini RN. Role of cytokines in rheumatoid arthritis. Annu Rev Immunol. 1996; 14: 397- 440.
22. Dean PM, Feldman DM, Morere D, Morton D. Clinical evaluation of the mini-mental state exam with culturally deaf senior citizens. Arch Clin Neuropsychol. 2009; 24(8): 753–60.
23. Behall KM, Scholfield DJ, Hallfrisch J. Diets containing barley significantly reduce lipids in mildly hypercholesterolemic men and women. Am J Clin Nutr. 2004; 80 (5): 1185-9.
24. Shehzad A, Ha T, Subhan F, Lee YS.New mechanisms and the anti-inflammatory role of curcumin in obesity and obesity-related metabolic diseases. Eur J Nutr. 2011; 50(3):151-161.
25. Zheng W, Wang SY. Antioxidant activity and phenolic compounds in selected herbs. J Agric Food Chem. 2001; 49: 5165–70.

26. Astley SB. Dietary antioxidants past, present and future. Trends Food Sci Technol. 2003; 14: 93–8.
27. Dugasani S, Pichika MR, Nadarajah VD, Balijepalli MK, Tandra S, Korlakunta JN. Comparative antioxidant and anti-inflammatory effects of [6]-gingerol, [8]-gingerol, [10]-gingerol and [6]-shogaol. J Ethnopharmacol. 2010; 127: 515–20.
28. Malek N, Swallow D, Grosset KA, Anichtchik O, Spillantini M, Grosset DG. Alpha-synuclein in peripheral tissues and body fluids as a biomarker for Parkinson's disease - a systematic review. Acta Neurol Scand. 2014; 130 (2): 59-72.
29. Cann HM, Stevens CH, Cartwright H, Halliday GM. α-Synucleinopathy phenotypes. Parkinsonism & Related Disorders. 2014; 20 (1): S62–S67.

How to cite this article: Shebini SME, Moaty MIA, Kazem YMI et al. Human alpha synuclein, inflammation and metabolic disorders in obesity, before and after dietary intervention. Int J Health Sci Res. 2015; 5(11):304-312.

****