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Modulation of Serum Vaspin Level by Diet Regimen in Obese Diabetic Female Patients

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Abstract

Background: High serum vaspin concentrations and increased vaspin mRNA expression in human adipose tissue were associated with obesity, insulin resistance, and type II diabetes. However, the mechanisms how vaspin secretion may be linked to deterioration of glucose metabolism and insulin sensitivity are not understood.

Objectives: The aim of this work is to explore the effect of dietary regimen for 6 months on serum vaspin levels in obese diabetic and non-diabetic female patients.

Patients and Methods: The study was carried out in Zagazig University Hospital and Obesity management and research unit. The sample size was 40 obese female patients. All participants were screened to determine the eligibility for participation in the study according to specific inclusion and exclusion criteria. Control groups didn't follow any diet plan while mediterrnean diet group followed mediterrnean diet for 6 months. The following parameters were assessed at the beginning and after 6months: body mass index (BMI), waist circumference (WC), Homeostatic model assessment (HOMA), Atherogenic index (AI), creatinine clearance and circulating levels of vaspin, vitamin D, Low density lipoprotein (LDL), High density lipoprotein (HDL), Triglyecrides (TG), Total cholesterol (TC), glucose, insulin, ALT, AST, Superoxide dismutase (SOD) and Malondialdehyde (MDA).

Results: Mediterrnean diet life style for 6 months resulted in a significant decrease in BMI, WC, HOMA, AI, vaspin, LDL, TG, TC, glucose, insulin and MDA with a significant increase in HDL, SOD and vitamin D.

Conclusion: Elevated serum vaspin and low VitD levels are encountered in obesity. So, vaspin may be used as a novel biomarker for obesity, insulin resistance and Type II DM management.

Keywords: Vaspin; Adipokines; Obesity; Type II DM

Abbreviations: BMI: Body Mass Index; WC: Waist Circumference; HOMA: Homeostatic Model Assessment; AI: Atherogenic Index; LDL: Low Density Lipoprotein; HDL: High Density Lipoprotein; TG: Triglyecrides; TC:

Total Cholesterol; SOD: Superoxide Dismutase; MDA: Malondialdehyde; VAT: Visceral white Adipose Tissues; OLETF: Otsuka Long-Evans Tokushima Fatty; Mets: Metabolic syndrome; NGT: Normal Glucose Tolerance; MD: Mediternean Diet; SFAs: Saturated Fats; MUFAs: Monounsaturated Fatty Acids; PUFAs: Polyunsaturated Fats; HbAc1: Glycated Haemoglobin; Hk7: Human Kallikrein 7.

Introduction

Vaspin was initially isolated from visceral white adipose tissues (VAT) of abdominal obesity with type II diabetes mellitus Otsuka Long-Evans Tokushima fatty (OLETF) rats [1]. The unique mechanism of vaspin is not known [2].

Many studies found a positive correlation between Vaspin gene expression and metabolic syndrome (Mets) components [3,4], while others found no association between Vaspin and insulin resistance [5-8]. Data on serum vaspin levels in Type II DM are conflicting [8]. While Ye, et al. described higher Vaspin levels in patients with Type II DM and a positive correlation between postprandial blood glucose levels and Vaspin [9], others found no difference between subjects with and without glucose abnormalities [10,11] or lower Vaspin levels in Type II DM [12,13]. Elevated Vaspin levels was found in obese patients with normal glucose tolerance (NGT) and prediabetes [13,14]. Vaspin levels were lowered, and glycemic control and insulin sensitivity improved in newly diagnosed Type II diabetic patients after 2 weeks of intravenous insulin infusion [15]. Gulcelik, et al. found lower Vaspin levels in Type II DM females with good glycemic control, and the development of microvascular complications was found to further reduce Vaspin levels [12]. However Vaspin levels were reduced in subjects with BMI < 25 kg/m^2 and in those with long-term physical activity [10,16]. Blüher revealed permanent decrease in vaspin levels after 2-year Mediterranean low-carbohydrate, or low-fat diet [17]. Weight loss after bariatric surgery caused a significant decrease in vaspin levels [18]. Meanwhile, Koiou, et al. and Martos-Moreno, et al. did not find variation in vaspin level in different weight loss interventions [19,20]. Kim, et al. described no change in vaspin levels after a 10-month program of life style modification in MetS patients [21]. Also, Kang, et al. reported that acute starvation didn't affect Vaspin level [22]. The intimate relation between vaspin, obesity and diabetes is not clearly understood so our study was designed to determine the role of vaspin in obesity and insulin sensitivity and its relation with weight loss or exercise and diet regulating glucose metabolism.

Subjects and Methods

This study was carried out on 40 adult female patients (We started our study with 60 patients but only 40 of them completed the study) matched for age and BMI: 18 obese type II diabetic patients and 22 obese non diabetic control subjects attending the outpatient clinic of Obesity Management and Research Unit and Internal medicine department, faculty of medicine Zagazig university hospitals, Egypt.

Inclusion criteria

- Sex (Non pregnant female patients).
- Age (20 up to 45 years old).
- Obese patients.
- Type II diabetic patients treated by biguanides and sulphonylurea.

Exclusion Criteria

- Male patients.
- Patients younger than 20 years old or older than 45years old.
- Patients with other endocrinal disorders as myxodema.
- Pregnant females.

Patients are Classified Into

Obese non diabetic female patients (obese group): n=22

It was subdivided into 2 subgroups:

- Control subgroup(group 1): n=10
- Mediternean diet (MD) subgroup(group 2): n =12

Obese diabetic female patients (obese diabetic group): n=18

It was subdivided into 2 subgroups:

- Control subgroup (group 3): n=8
- Mediternean diet subgroup (group 4): n=10

All patients were followed for about 6 months. Mediternean diet subgroups in both groups followed a specially designed dietary regimen with specific macronutrient distribution.

Macronutrient distribution

- Carbohydrates 45-60 % of total caloric intake.
- Protein 1-1.5 gram/kg body weight.
- Fat: saturated fatty acids (SFAs) < 7% of total caloric intake.
- Mono-unsaturated fatty acids (MUFAs) 10%- 20% of total caloric intake.

- Poly-unsaturated fatty acids (PUFAs) up to 10 % of total caloric intake.
- Fibers form about 25 -50 gram/day or 15-25 gram / 1000 Kcal [23,24].

The principal aspects of this diet include:

- High olive oil consumption.
- High consumption of legumes (eat one serving of beans per day).
- High consumption of whole grains (about 5-6 servings per day).
- High consumption of unrefined sugar.
- High consumption of fruits , salads and vegetables (about 5 servings fruits per day and about 5 servings vegetables per day) to make the back bone of each meal and choose the brightly colored ones of each season and green leafy vegetables.
- High consumption of fish.
- Moderate consumption of dairy products especially low fat milk products (mostly as cheese and yogurt) [25].
- Low consumption of meat, meat products and poultry (limit to one serving per week).

The following parameters were assessed at the beginning and after 6 months: BMI, WC, serum Vaspin level, serum vitamin D level, random blood sugar level, glycosylated haemoglobin A1c, ALT, AST, creatinine clearance, insulin level, TC, HDL-C, LDL, TG, SOD and MDA levels.

Results

Results are illustrated in the following tables.

		Obese			
		Group I (n= 10)		Group n2(n=12)	
		Before (G1a)	After (G1b)	Before (G2a)	After (G2b)
Vaspin	Mean ± SD	820.17	820.8	830.5	479.6
		92.9	98.01	132.6	122.4
	tt (P value)	0.04		10.4	
		NS		<0.001	
Vit D	Mean ± SD	46.85	46.19	45.5	67.33
		7.55	7.73	7.91	7.74
	tt (P value)	0.474		10.641	
		NS		<0.001	
HbAc1	Mean ± SD	5.33	5.36	5.12	4.8
		0.53	0.45	0.54	0.51
	tt (P value)	0.232		2.258	
		NS		<0.05	
Insulin	Mean ± SD	9.99	11.22	10.13	8.97
		1.07	2.99	1.01	0.55
	tt (P value)	1.5		3.05	
		NS		<0.05	
Glucose	Mean ± SD	88.5	88.4	94.25	83.5
		6.74	6.87	11.07	7.39
	tt (P value)	0.041		3.67	
		NS		< 0.01	
HOMA-IR	Mean ± SD	2.13	2.46	2.33	1.81
		0.33	0.78	0.27	0.17
	tt (P value)	1.849		9.838	
		NS		<0.001	
TC	Mean ± SD	251.8	252.3	254.67	180.83
		20.01	21.16	29.14	20.17
	tt (P value)	0.074		15.54	
		NS		<0.001	

TG	Mean ± SD	193.3	194.25	177.5	99.17
		36.84	36.65	18.03	19.19
	tt (P value)	0.182		13.132	
		NS		<0.001	
LDL	Mean ± SD	162.46	162.66	163.5	117.5
		17.18	16.64	18.03	18.03
	tt (P value)	0.04		9.649	
		NS		<0.001	
HDL	Mean ± SD	44.2	42.2	43.67	65
		6.41	6.41	8.39	7.21
	tt (P value)	1.732		7.74	
		NS		<0.001	
AI	Mean ± SD	4.81	5.1	5.09	1.84
		1.02	1.07	1.7	0.51
	tt (P value)	2.66		7.91	
		<0.05		<0.001	
CC	Mean ± SD	124.57	120.55	120.03	132.57
		15.09	16.19	24.18	20.52
	tt (P value)	1.466		2.055	
		NS		NS	
BMI	Mean ± SD	37.3	37.49	37.63	28.73
		3.34	3.39	3.8	3.61
	tt (P value)	0.398		9.166	
		NS		<0.001	
WC	Mean ± SD	1.574	105.4	110.58	90.08
		NS	8.63	10.5	7.7
	tt (P value)	1.574		7.678	
		NS		<0.001	

Table 1: All parameters measured in obese subjects at the beginning of experiments (G1a and G2a) and after of ordinary diet or MD (G2a & G2b respectively).

		Obese Diabetic			
		Group I (n= 8)		**Group n (n=10)**	
		Before (G3a)	**After (G3b)**	**Before (G4a)**	**After (G4b)**
Vaspin	Mean ± SD	995.1	1000.6	1015.8	643.8
		139.5	139.4	218.2	174.5
	tt (P value)	0.08		5.36	
		NS		< 0.001	
Vit D	Mean ± SD	38.03	35.39	39.2	66.5
		7.29	4.91	6.41	9.08
	tt (P value)	1.571		15.366	
		NS		<0.001	
HbAc1	Mean ± SD	10.08	10.45	11.17	6.67
		1.96	1.82	2.16	0.86
	tt (P value)	1.156		8.441	
		NS		<0.001	
Insulin	Mean ± SD	26.4	29.07	27.14	12.95
		8.66	10.13	9.42	2.99
	tt (P value)	1.72		5.31	
		NS		<0.001	

Glucose	Mean ± SD	337.13	353.38	330.5	188.1
		111.8	101.37	109.13	72.36
	tt (P value)	0.9		6.718	
		NS		<0.001	
HOMA-IR	Mean ± SD	23.57	27.21	24.09	5.97
		15.996	17.04	17.08	2.92
	tt (P value)	1.341		3.979	
		NS		<0.01	
TC	Mean ± SD	280.88	275.75	305.5	188.5
		22.67	40.45	48.45	33.3
	tt (P value)	0.366		9.61	
		NS		<0.001	
TG	Mean ± SD	172.5	175.5	245.7	164
		12.25	22.05	57.86	36.33
	tt (P value)	0.256		4.393	
		NS		<0.01	
LDL	Mean ± SD	174.5	164	174.7	136.5
		16.74	19.59	15.48	15.14
	tt (P value)	0.913		8.605	
		NS		<0.001	
HDL	Mean ± SD	43.63	43.5	34	49.5
		7.56	12.25	6.06	9.08
	tt (P value)	0.075		6.337	
		NS		<0.001	
AI	Mean ± SD	5.63	5.74	8.42	3.01
		1.31	1.79	2.96	1.34
	tt (P value)	0.337		7.29	
		NS		<0.001	
CC	Mean ± SD	119.04	120.01	103.82	152.42
		12.76	15.13	7.92	27.34
	tt (P value)	0.461		6.949	
		NS		<0.001	
BMI	Mean ± SD	36.63	37.31	37.02	27.27
		4.91	4.08	4.02	3.81
	tt (P value)	0.239		11.069	
		NS		<0.001	
WC	Mean ± SD	113.13	114.25	110.5	90.5
		14.88	15.22	18.02	18.33
	tt (P value)	0.132		3.956	
		NS		<0.01	

Table 2: All parameters measured in obese diabetic subjects at the beginning of experiments (G3a and G4a) and after 6 months of ordinary diet or MD (G3b & G4b respectively).

Parameters	**Correlation with Vaspin levels (pg/mL)**		**Correlation with Vit D levels (ng/ml)**	
	r	**P**	**r**	**P**
Vaspin (pg/ml)			0.945	<0.001
BMI (kg/m²)	0.967	<0.001	0.994	<0.001
WC (Cm)	0.935	<0.001	0.995	<0.001
Vitamin D (ng/ml)	0.945	<0.001		

C.C (ml/minute)	0.979	<0.001	0.964	<0.001
MDA (nmol/L**)**	0.961	<0.001	0.995	<0.001
SOD (nmol/L**)**	0.476	NS	0.385	NS
HGA1c (gm/dL)	0.904	<0.001	0.959	<0.001
Glucose (mg/dl)	0.573	NS	0.688	<0.05
Insulin (mIU/ml)	0.308	NS	0.218	NS
HOMA-IR	0.87	<0.001	0.937	<0.001
TC (mg/dL)	0.667	<0.05	0.695	<0.05
TG (mg/DL)	0.945	<0.001	0.991	<0.001
HDL (mg/DL)	0.803	<0.01	0.829	<0.01
LDL (mg/DL)	0.939	<0.001	0.984	<0.001
AI	0.895	<0.001	0.929	<0.001

Table 3: Correlations between each of serum vaspin and vitamin D levels with all studied parameters in group 2A "obese non diabetic group before 6 months of following mediterenean diet".

Parameters	**Correlation with Vaspin levels (Pg/mL)**		**Correlation with Vit D levels (ng/ml)**	
	r	**P**	**r**	**P**
Vaspin(pg/ml)			0.959	<0.001
BMI (kg/m²)	0.975	<0.001	0.98	<0.001
WC (Cm)	0.894	<0.001	0.954	<0.001
Vitamin D (ng/ml)	0.959	<0.001		
C.C (ml/minute)	0.929	<0.001	0.985	<0.001
MDA (nmol/L**)**	0.957	<0.001	0.98	<0.001
SOD (nmol/L**)**	0.793	<0.01	0.825	<0.01
HGA1c (gm/dL)	0.904	<0.001	0.961	<0.001
Glucose (mg/dl)	0.553	NS	0.703	<0.05
Insulin (mIU/ml)	0.522	NS	0.375	NS
HOMA-IR	0.866	<0.001	0.919	<0.001
TC (mg/dL)	0.665	<0.05	0.781	<0.01
TG (mg/DL)	0.893	<0.001	0.937	<0.001
HDL (mg/DL)	0.75	<0.01	0.743	<0.01
LDL (mg/DL)	0.791	<0.01	0.821	<0.01
AI	0.883	<0.001	0.951	<0.001

Table 4: Correlations between each of serum vaspin and vitamin D levels with all studied parameters in group 2B "obese non diabetic group after 6 months of following mediterenean diet".

Parameters	**Correlation with Vaspin levels (Pg/mL)**		**Correlation with Vit D levels (ng/ml)**	
	r	**P**	**r**	**P**
Vaspin (pg/ml)			0.673	<0.05
BMI (kg/m²)	0.656	<0.05	0.972	<0.001
WC (Cm)	0.646	<0.05	0.958	<0.001
Vitamin D (ng/ml)	0.673	<0.05		
C.C (ml/minute)	0.732	<0.05	0.982*	<0.001
MDA (nmol/L**)**	0.678	<0.05	0.997	<0.001
SOD (nmol/L**)**	0.691	<0.05	0.996	<0.001
HGA1c (gm/dL)	0.629	NS	0.984	<0.001
Glucose (mg/dl)	0.852	<0.01	0.786	<0.01
Insulin (mIU/ml)	0.787	<0.01	0.846	<0.01
HOMA-IR	0.891	<0.01	0.821	<0.01
TC (mg/dL)	0.622	NS	0.858	<0.01

TG (mg/DL)	0.634	<0.05	0.814	<0.01
HDL (mg/DL)	0.681	<0.05	0.928	<0.001
LDL (mg/DL)	0.688	<0.05	0.794	<0.01
AI	0.798	<0.01	0.953	<0.001

Table 5: Correlations between each of serum vaspin and vitamin D levels with all studied parameters in group 4A "obese diabetic group before 6 months of mediterenean diet".

Parameters	Correlation with Vaspin levels (pg/mL)		Correlation with Vit D levels (ng/ml)	
	r	P	r	P
Vaspin(pg/ml)			0.884	<0.01
BMI (kg/m²)	0.884	<0.01	0.984	<0.001
WC (Cm)	0.9	<0.001	0.996	<0.001
Vitamin D (ng/ml)	0.884	<0.01		
C.C (ml/minute)	0.859	<0.01	0.984	<0.001
MDA (nmol/L)	0.959	<0.001	0.97	<0.001
SOD (nmol/L)	0.833	<0.01	0.891	<0.01
HGA1c (gm/dL)	0.871	<0.01	0.969	<0.001
Glucose (mg/dl)	0.779	<0.01	0.768	<0.05
Insulin (mIU/ml)	0.421	NS	0.497	NS
HOMA-IR	0.907	<0.001	0.903	<0.001
TC (mg/dL)	0.825	<0.01	0.879	<0.01
TG (mg/DL)	0.844	<0.01	0.939	<0.001
HDL (mg/DL)	0.823	<0.01	0.891	<0.01
LDL (mg/DL)	0.871	<0.01	0.988	<0.001
AI	0.932	<0.001	0.932	<0.001

Table 6: Correlations between each of serum vaspin and vitamin D levels with all studied parameters in group 4B "obese diabetic group after 6 months of meditrenean diet".

Discussion

No significant difference was found in serum vaspin levels in control groups after six months of ordinary diet. However, a significant decrease in serum vaspin level in both obese and obese diabetic groups after following mediternean diet for 6 months.

This came in accordance with li and youn et al. who found a decrease in serum vaspin level following long-term physical activity and in subjects with a BMI < 25 kg/m² [15,10]. Moreover, weight loss after following healthy life style resulted in diminished serum vaspin level [26]. Similarly, a significant decrease in serum vaspin levels occurred in subjects who lost ≥2% of their base line weight after orlistat administration for 12 weeks [4]. Moreover, a reduction in serum vaspin level in extremely obese subjects with acute weight loss after gastric bypass [18]. However, an increase in serum vaspin level occurred in weight loss resulting from sharp increase in exercise in lean subjects [16]. Nevertheless, different weight loss interventions didn't affect serum vaspin level [19]. No change in serum vaspin level occurred in prepubertal children following dietary intervention [20]. Moreover, acute starvation had no effect on serum vaspin level [22]. Additionally, no alteration in serum vaspin levels after life style modification for about 10 months in MetS patients [21].

We suggest that this decrease in serum vaspin level after following mediterrnean diet for six months occurred as a result of chronic adaptation mechanism of its secretory level, and fat mass reduction and also healthy life style and that it increase in obesity as an adipokine hormone that increases when fat mass becomes greater as supported by Youn, et al. who stated that fat mass expansion was associated with high circulating vaspin levels or as a compensatory mechanism against obesity- and insulin resistance-stimulated expression of certain proteases synthesized in abdominal fat [4,10,27,28]. It can be postulated that vaspin, inhibits a protease which plays a role in the degradation of a hormone or molecule with direct or indirect glucose and lipid lowering effects [13,29,30]. These proteases blunt insulin action. Dimova and Tankova supposed that human kallikrein 7 (hK7) was a vaspin target [8] Heiker has isolated vaspin-hK7

complexes in human plasma, established co-expression of both proteins in murine pancreatic β-cells, and exhibited the ability of hK7 to cleave human insulin within A- and B-chain. However, receptor for the vaspin–protease complexes, KLK7, or yet unidentified proteases, is currently not known [31].

Our results revealed a significant increase in vitamin D after 6 months of mediterrnean diet. In addition to a significant positive correlation between VitD and SOD, HDL and CC with a significant negative correlation between VitD and MDA, LDL, TG, TC, AI, BMI, WC, glucose, insulin and HOMA.

Noteworthy, our study was conducted on female sample and this could explain the low base line level of Vit D as decrease mobility and sun exposure (due to cultural reasons) and inadequate consumption of animal based food stuff rich in VitD (due to economic reasons) are more common in females as they spend most of their time indoor and they use sun screens more [32].

Low vitamin D level in obesity can be explained by: First; diminished sun exposure among obese people. Second, the reduction of 25 (OH) D by negative feedback stemming from increased 1,25(OH)D2. Third, increased the uptake of vitamin D in adipose tissues. Fourth, the volumetric dilution of low 25 (OH) D concentrations [33].

Conclusion

Elevated serum vaspin and low VitD levels are encountered in obesity. So, vaspin may be used as a novel biomarker for obesity, insulin resistance and Type II DM management. Several studies are needed to clarify the link between obesity, vitamin D and vaspin. Further studies are needed for a better understanding of the molecular mechanisms regulating vaspin, providing new insights into the pathogenesis of diet induced metabolic derangement and also to determine whether VitD supplementation in obesity and DM could improve these conditions.

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