Favorable Effects of a 12-week, 500kcal/day deficit diet on endotoxin and cardiometabolic indices in T2DM and overweight Saudi women

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Background

To date, few studies have addressed the effects of life style changes such as dietary intervention involving reduced fat/caloric intake on circulating endotoxin and lipemic marker levels in the Saudi population. In this study, we examined the effects of a reduced caloric dietary intervention program on obesity related chronic diseases by estimating serum endotoxin and markers of obesity and lipemia, among Saudi women with attenuated metabolic status.

Methods

92 Saudi women [18 non-diabetic (ND) (Age 24.4±7.9 yr; BMI 22.2±2.2 kg/m2), 24 overweight+ (age 32.0±7.8 yr; BMI 28.5±1.5 kg/m2) and 50 overweight or obese T2DM patients (age 41.5±6.2yr; BMI 35.2±7.7 kg/m2)], were introduced to a 500 kcal deficit/day diet.

Results

Caloric restriction resulted in significant improvements in BMI and hip circumference of both overweight+ (p<0.05) and T2DM (p<0.01) groups of Saudi females. T2DM group showed decreases in fasting glucose (p<0.05), triglycerides (p<0.05), total- (p<0.01) and LDL-cholesterol (p<0.01), while the HDL-cholesterol increased (p<0.01). In the overweight+ group, serum levels of total- (p<0.01) and LDL-cholesterol (p<0.01) decreased. Levels of fasting insulin, HOMA-IR and endotoxin did not change in either group.

Discussion

Evidence accrued over the years has established the positive role of physical activity in the prevention and treatment of CVDs (1) and T2DM (2). Previous studies with calorie restriction diets have consistently shown beneficial effects in the prevention and management of T2DM (3). Results from our 3-month long restricted diet-induced weight loss intervention indicate significant improvements in cardiovascular disease risk factors, particularly total- and LDL-cholesterol, which are in agreement with several recent clinical trials and intervention studies (4). Adoption of calorie restricted diets has been shown effective in alleviating metabolic, inflammatory and oxidative abnormalities and in improving health in the absence of exercise (5), and this strategy has also been found to be effective in the long run (6). The calorie deficient diet induced improvement in the glucose levels of the T2DM group, and not the overweight+ group, suggests that the type of intervention may have favorable, glucose-lowering effect in the T2DM population as reported before (7).

Conclusion

A 500 kcal deficit/day dietary intervention in the absence of exercise for 3 months resulted in improved glucose levels and lipid profile among Saudi overweight+ and T2DM patients. Endotoxin levels in both groups, which remained unchanged after dietary intervention, were associated with lipid profile, particularly total and LDL-cholesterol in both groups and with BMI and insulin resistance in the T2DM group, reinforcing the exacerbating role of endotoxemia in obese and insulin resistant subjects. Longer term intervention studies in the Saudi population are warranted to confirm the protective effects of the present dietary intervention results in reducing endotoxin associated subclinical inflammation.

Table 1. Anthropometric changes following dietary intervention in the overweight* and T2DM groups

	Overweight*		T2DM	
N	24		50	
Age (years)	32.04±7.78		41.50±6.23	
DM Duration (years)	--		2.04(0-9)	
	Baseline	Follow-Up	Baseline	Follow-Up
BMI (Kg/m ²)	28.54±1.49	27.95±2.25 *	35.24±7.67	35.04±8.07*
Waist (cm)	95.75±7.42	95.87±7.78	112.3±13.43	109.21±12.71 **
Hip (cm)	109.67±5.01	108.07±4.07 *	117.11±11.59	116.7±13.18 **
WHR	0.87±0.05	0.88±0.06 *	0.96±0.07	0.93±0.06 **

Note: p-values given at extreme right denote significance by baseline comparisons in the respective group; * and ** denote significance at p<0.05 and p<0.01 values, respectively.

Table 3. Effects of high-fat meal in T2DM subjects at baseline and 3 months follow up on endotoxin and metabolic parameters.

	0 Hour		1 Hour		2 Hours		3 Hours		4 hours	
	Baseline	Follow-up	Baseline	Follow-up	Baseline	Follow-up	Baseline	Follow-up	Baseline	Follow-up
Glucose	7.9±2.7	7.0±1.8*	7.8±2.5	7.3±2.2	7.5±2.5	7.0±2.2	7.3±2.7	6.9±1.9	7.0±2.8	6.9±1.8
Insulin#	11.7±5.5	10.8±6.0	21.9±17.7	15.8±8.5	19.3±12.6	14.9±9.9	16.2±12.3	15.5±9.0	14.3±8.2	13.5±7.3
HOMA-IR#	3.7±2.0	3.1±2.2	8.7±12.0	5.3±3.3	6.6±6.0	4.7±3.8*	5.6±5.4	4.8±2.7	3.9±2.4	3.9±2.3
Triglycerides#	1.9±1.0	1.6±0.8*	1.8±0.7	1.7±0.8	2.4±0.9	2.2±1.0	2.7±1.1	2.6±1.2	2.7±1.3	2.7±1.3
Total Cholesterol	5.4±1.1	4.6±1.0**	5.3±1.0	4.5±1.0*	5.4±1.1	4.6±1.0*	5.3±1.1	4.6±1.0*	5.4±1.1	4.7±1.0*
HDL-Cholesterol	0.96±0.2	1.0±0.2**	0.96±0.2	0.98±0.2	0.94±0.2	0.97±0.2	0.91±0.2	0.92±0.2	0.89±0.2	0.9±0.2
LDL-Cholesterol	3.7±0.8	2.9±0.8**	3.6±0.8	2.8±0.9*	3.4±0.9	2.6±0.8*	3.2±0.9	2.6±0.8*	3.3±0.9	2.6±0.8*
Endotoxin	3.4±0.9	3.2±1.1	3.0±0.9	3.0±1.0	3.4±0.9	3.0±1.0*	3.5±1.2	3.2±0.7	3.6±1.5	3.4±1.3

Note: Data presented as mean ± standard deviation; * and ** denote significance at 0.01 and 0.05 levels, respectively.

Table 4. Effects of high-fat meal in overweight* subjects at baseline and 3 months follow up on endotoxin and metabolic parameters.

	0 Hour		1 Hour		2 Hours		3 Hours		4 hours	
	Baseline	Follow-up	Baseline	Follow-up	Baseline	Follow-up	Baseline	Follow-up	Baseline	Follow-up
Glucose	5.15±3.5	4.65±2.8	4.6±0.4	4.3±0.4*	4.6±0.4	4.3±0.6	4.6±0.4	4.5±0.4	4.6±0.8	4.6±0.5
Insulin#	5.0±3.4	12.7±6.6*	15.6±16.2	20.4±20.4	16.9±16.0	19.0±15.3	13.1±8.0	11.4±7.4	10.3±5.3	12.5±7.7
HOMA-IR#	1.1±0.7	0.93±1.9	3.5±4.1	4.2±4.3	3.9±4.1	4.3±3.6	2.8±1.9	2.4±1.7	2.1±1.2	2.8±2.0
Triglycerides#	1.3±0.8	1.4±0.5	1.4±0.8	1.4±0.6	1.7±0.9	1.8±0.9	2.0±1.1	2.0±1.0	1.9±1.3	2.0±0.9
Total Cholesterol	4.5±1.0	3.7±0.8*	4.5±0.9	3.6±0.8*	4.4±0.8	3.4±0.9*	4.4±0.8	3.5±0.8*	4.4±1.0	3.6±0.8*
HDL-Cholesterol	1.2±0.3	0.9±0.2*	1.1±0.3	0.9±0.2*	1.1±0.3	0.82±0.2*	1.1±0.4	0.8±0.2*	1.1±0.4	0.8±0.2*
LDL-Cholesterol	2.8±0.7	2.2±0.6*	2.7±0.6	2.1±0.6*	2.5±0.6	1.9±0.5*	2.4±0.6	1.8±0.5*	2.4±0.6	1.9±0.5*
Endotoxin	3.0±0.5	3.2±1.1	2.9±1.4	3.1±1.3	3.5±0.9	3.2±1.3	3.8±1.6	3.3±0.8	3.5±1.9	3.5±1.7

Note: Data presented as mean ± standard deviation; * denotes significance at 0.05.

Figure 1. Correlations between baseline endotoxin level versus (left) (A) BMI, (B) total cholesterol, (C) LDL-cholesterol, (center) (D) log triglycerides, (E) HDL-cholesterol, (right) glucose, (B) log insulin and (C) log HOMA-IR (right) in total subjects.

Figure 2. Follow-up associations of endotoxin in all subjects versus (left) (A) BMI, (B) total cholesterol, (C) LDL-cholesterol, (center) (D) log triglycerides, (E). HDL-cholesterol, (right) (A). Glucose, (B) insulin, (C) Homa-IR.

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References

- Lavie CJ, Arena R, Swift DL, Johannsen NM, Sui X, Lee DC, Earnest CP, Church TS, O’Keefe JH, Milani RV. Exercise and the cardiovascular system: Clinical science and cardiovascular outcomes. *Circ Res* 2015; 117: 207-219.
- Thent ZC, Das S, Henry LJ. Role of exercise in the management of diabetes mellitus: The global scenario. *PloS One* 2013; 8: e80436.
- Ley SH, Hamdy O, Mohan V, Hu FB. Prevention and management of type 2 diabetes: Dietary components and nutritional strategies. *Lancet* 2014; 383: 1999-2007.
- Brekke HK, Bertz F, Rasmussen KM, Bosaeus I, Ellegard L, Winkvist A. Diet and exercise interventions among overweight and obese lactating women: Randomized trial of effects on cardiovascular risk factors. *PLoS One* 2014; 9: e88250.
- Bekkouche L, Bouchenak M, Malaisse WJ, Yahia DA. The mediterranean diet adoption improves metabolic, oxidative, and inflammatory abnormalities in algerian metabolic syndrome patients. *Horm Metab Res* 2014; 46: 274-282.
- Gotsis E, Anagnostis P, Mariolis A, Vlachou A, Katsiki N, Karagiannis A. Health benefits of the mediterranean diet: An update of research over the last 5 years. *Angiology* 2015; 66: 304-318.
- Juanola-Falgarona M, Salas-Salvado J, Ibarrola-Jurado N, Rabassa-Soler A, Diaz-Lopez A, Guasch-Ferre M, Hernandez-Alonso P, Balanza R, Bullo M. Effect of the glycemic index of the diet on weight loss, modulation of satiety, inflammation, and other metabolic risk factors: A randomized controlled trial. *Am J Clin Nutr* 2014; 100: 27-35.