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The Beneficial Effect of 12-Hour Fasting, 45 Minutes Exercise Thrice Weekly and Their Combination on Weight Loss, Anthropometric Measures and Metabolic Syndrome

Kamel El-Reshaid[1*], Shaikha Al-Bader[2], Samah Ghanem[3]

[1]Department of Medicine, Faculty of Medicine, Kuwait University, Kuwait City, Kuwait
[2]Department of Nephrology, Amiri Hospital, Ministry of Health, Kuwait City, Kuwait
[3]Qutaina Medical Center, Mubarak Al-Kabeer, Kuwait
Email: *kamel@hsc.edu.kw

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Abstract

Background: Obesity is the leading preventable cause of death worldwide. It is associated with significant increases in morbidity and mortality. Few studies have addressed, prospectively, the impact of life-style modification in weight-reduction in 1) morbidly obese patients with BMI > 35 kg/m^2 and 2) on its associated co-morbid risk factors for metabolic syndrome viz. high blood pressure, diabetes, hyperlipidemia and steatohepatitis as well as psychiatric disorders. **Patients and Methods**: We prospectively evaluated the role of 1) two meals daily with in between 12-hour fasting, 2) thrice weekly 45-minute active-walk, and 3) their combination, in management of ambulant obese patients, at BMI of 35 to 39.9 kg/m^2 who had such multiple acquired metabolic disorders. The study was conducted over 3 years with 45 patients in 3 matched groups with regards to gender, age, BMI, waist circumference, lipid profile (LDL and TG), fibroscan steatosis grade, psychiatric assessment, antidiabetic drugs and antihypertensive ones. **Results**: At 6 and 12 months, the 3 regimens were well tolerated and were effective in weight loss, improvement in anthropometric measures and management of metabolic syndrome yet the combined one was significantly better in all endpoints. **Conclusion**: Our protocols of exercise and dieting were effective measures in managing obesity and its associated co-morbidities and their combination is synergetic.

Keywords

Hyperlipidemia, Hypertension, Metabolic Syndrome, Obesity, Psychiatric Disorders, Type 2 Diabetes, Weight Reduction

1. Introduction

Obesity is a medical disorder in which excess body fat leads to negative effects on health. It is defined as a body mass index exceeding 30 kg/m^2. The latter is a measurement obtained by dividing a person's weight by the square of the person's height [1]. In 2013, obesity was classified as a disease [2]. In adult population, the worldwide prevalence of overweight and obesity has tripled with overweight reaching 39% and obesity at 13% by 2016 compared to 1975 [3]. Obesity is associated with significant increases in morbidity (especially type 2 diabetes) and mortality (especially from cardiovascular disease). Retrospective studies have shown that reductions in body weight, even 5% - 10%, were associated with a significant reduction in risk factors for chronic disease viz. metabolic syndrome, high blood pressure, atherosclerosis, heart disease, diabetes, high blood cholesterol, cancers, knee osteoarthritis and sleep disorders [4]. Four management modalities, alone or in combination, have been proposed for obesity: diet, lifestyle change, medications and bariatric surgeries. The latter has been advocated for patients with body mass index (BMI); 1) ≥40 kg/m^2, 2) BMI 35 up to 39.9 kg/m^2 which is associated with obesity-related comorbidity (e.g., diabetes, hypertension, gastroesophageal reflux disease, osteoarthritis, among many others), and 3) BMI of ≥30 kg/m^2 with difficult-to-control type II diabetes mellitus, dysmetabolic syndrome X and hypertension [5]. In this study, we evaluated prospectively for 12 months the role of life-style modifications with 1) practical 12-hour fasting dieting, 2) thrice/weekly 45-minute walk, and 3) the combination of both, in management of ambulant obese patients, with a BMI of 35 to 39.9 kg/m^2 with multiple acquired metabolic disorders.

2. Patients and Methods

2.1. Study Design

Obese adult patients, with BMI ≥ 30 kg/m^{2,}, who attended Dr. El-Reshaid clinic from 1st January 2019 to 31st December 2022, were analyzed prospectively for the impact of 3 regimens on weight loss and its metabolic syndrome. The 3 weight loss regimens were; 1) special diet with 12-hour fasting, 2) 45 minutes active-walk thrice weekly, and 3) combination of both. Dr. El-Reshaid clinic was established in 1997 in the center of Kuwait City. It is a tertiary referral center and is equipped with adequate diagnostic as well as therapeutic facilities to care for both in- and out-patients with all medical diseases.

2.2. Inclusion and Exclusion Criteria

Patients were included, in the study, if they had acquired chronic obesity and with BMI ≥ 30 kg/m^2. The latter was defined as obesity lacking; genetic-susceptibility, mental disorders, uncontrolled endocrine diseases and obesity-promoting drugs. Hence; exclusion criteria were:

1) Childhood genetic syndromes associated with obesity viz. Prader-Willi syndrome, Pseudohypoparathyroidism, Laurence-Moon-Biedl (Bardet-Biedl) syn-

drome, Cohen syndrome, Down syndrome, and Turner syndrome.

2) Endocrinal obesity due to hypothyroidism, insulin resistance, polycystic ovary syndrome, and Cushing's syndrome.

3) Mentally disturbed patients.

4) Those on antipsychotics, antidepressants, antiepileptics, gabapentin, oral contraceptives, and corticosteroids. Moreover, none of the patients was on medications promoting weight loss.

5) Patients with creatinine clearance ≤ 60 ml/minute.

6) Patients with liver cirrhosis or (+) fibroscan for fibrosis.

7) Patients with unstable effective intravascular volume *i.e.*, heart failure, renal failure, nephrotic syndrome and liver disease.

2.3. Interventional Design

All patients were subjected to special diet characterized by; 1) avoidance of excessive sodium, sugar, sweats, potato, fruits, dates; 2) low trans fats and shrimps; 3) limited amount of rice and bread; 4) limited cold-juices to unsweetened lemonade; 5) limited amount of red-meat yet permission of chicken breasts and fish, with 6) permission of coffee, low-fat dairy products, salads and vegetables. The total amount of calories was limited to 15 kcal/kg in the diet and diet/exercise group and 22 Kcal/kg in the exercise group. Carbohydrates, fats and proteins constituted 45%, 30% and 25% of the total calory counts, respectively. The daily protein intake was planned at 0.8 g/kg to maintain lean muscle mass [6]. All patients were supplemented daily with 1 multivitamin tablet (Centrum with lutein). Patients in the diet (D) as well as diet and exercise (D + E) groups had only 2 meals/day viz. adequate breakfast and adequate dinner meal separated by 12 hours. Water, unsweetened lemonade, low-fat milk and coffee were permitted ad lib. Those in the exercise (E) as well as D&E groups were subjected to 45-minutes active walk thrice weekly. The activity refers to walking with the addition of: 1) side-waddling gait, 2) upper & lower belly tucking technique and 3) side-bends. Moreover, there was an intermission of 5-minute stoppage periods for squeezing and pinching of belly-fat. The calculated calory-loss with such active walking was 350 - 400/session.

2.4. Initial Assessment

All obese patients, willing to participate in the study, had clinical assessment, laboratory and radiological testing to satisfy inclusion and exclusion criteria. The laboratory ones included: 1) serum urea, creatinine and 24-hour urine collection for creatinine clearance and protein output, 2) serum electrolytes viz. sodium, potassium and bicarbonate content, uric acid 3) urine routine and microscopy, 4) serum TSH, free T3 & 4, cortisol, ACTH, catecholamines, and testosterone. Radiological investigations included; 1) ultrasound of the abdomen for liver, spleen, kidneys sizes and abnormality as well as the presence of ascites, and 2) echocardiogram to assess for pericardial, valvular disease and left ventricular

ejection fraction.

2.5. Study Groups

Patients were allocated into either of the 3 groups at random yet to satisfy; 1) 45 patients in each group, and 2) a matched initial assessment with regards gender, age, BMI, waist circumference, lipid profile (LDL and TG), fibroscan steatosis-grade, psychiatric assessment, antidiabetic drugs and number of minor psychiatric disorders (anxiety, depression and libido/erectile dysfunction in males).

2.6. Follow Up

Patients were evaluated every 2 months for the following parameters; 1) anthropometric measurements (BMI and waist circumference), 2) hyperlipidemic indicators (LDL-cholesterol and TG level serum levels), 3) number of antihypertensive and anti-diabetic drugs, and 4) number of psychiatric defects. Antihypertensive therapy was recorded as 0, 1, 2, ≥ 4 according to number of antihypertensive drug combinations. Similar grading was used for anti-diabetic therapy with (0) if controlled with diet alone and 1, 2, 3, 4 for patients with added classes of Biguanides, DPP-4 inhibitors, SGLT2 inhibitors, second-generation Sulphonylurea, and insulins. Moreover, Fibroscan testing was used to measure steatosis (fatty changes) in the liver at 6 and 12 months. The latter was graded according to CAP scores (dB/m) into S1 (238 - 260), S2 (>260 - 290) and S3 (>290).

2.7. Statistical Analysis

SPSS statistical package version 26 was used for data entry and processing. The p-value ≤ 0.05 was used as the cut-off level for significance. Since only age data were normally distributed; they were expressed as Mean ± SD while other anthropometric measurements were expressed as Median (IQR). Comparison of age between groups was done using ANOVA while others by Kruskal-Wallis's test. Moreover; comparison of anthropometric changes in at different times (start, 3 months, and 12 months) was done using Wilcoxon Signed Rank test.

3. Results

A total of 158 motivated and dedicated patients fulfilled the inclusion criteria. By testing they did not have evidence of significant heart failure, kidney disease, endocrine defect and cirrhosis. Patients with locomotor disability that limits exercise maneuvers were allocated to diet group. A total of 45 matched patients, in each group, had completed the study. Drop out were due to; poor compliance with diet in general (n = 5), diet in D group (n = 7), exercise regimen in E group (n = 5) and diet and/or exercise in D + E group (n = 6).

3.1. Demographical Data of the Study Groups

The baseline characteristics of the participants in each group are summarized in

Table 1. The groups had matched adults with mean age 42 ± 4 years and insignificant difference in female/male ratio. All patients were obese with medians of weight at 108 kg, BMI at 38 and waist at 118 cm. They had severe multiple co-morbid conditions with hypertension grade ≥ 4: >33%, DM grade ≥ 5: >57%, liver steatosis grade 3 (S3): ≥82%, psychiatric disorders grade 3: >71%. Moreover, they had severe hyperlipidemia with LDL-cholesterol at 4.5 mmol/L (Normal: <3 mmol/L) and triglycerides at 2.9 mmol/L (Normal: 0.4 - 2.5) as well as gamma GTT at 57 U/L (Normal: 9 - 40). Moreover, at start, there was no statistical difference in the measurements of morbidity and prevalence of co-morbidity between the 3 groups.

3.2. Global Impact of Interventions

As shown in Table 2; all patients had significant improvement with time at 6 and 12 months. Such improvement was a reflection of; 1) decrease in anthropometric measurements (weight, BMI, waist circumference), 2) hyperlipidemic parameters and 3) co-morbid conditions. Overall, the changes were best seen in the D + E group followed by E then the diet group.

Table 1. Comparison of demographical characteristics, anthropometric mesurements, biochemical data and prevalnce of metabolic syndrome in the 3 weight reduction groups.

Study group	Diet + exercise	Exercise alone	Diet alone	Statistical significance
	(n = 45)	(n = 45)	(n = 45)	(P < 0.05)
Demographical characteristics:				
Gender (M/F)	25/20	24/21	26/19	NS
Age (years)	41 + 4	42 + 3	42 + 5	NS
Anthropometric measurements:				
Weight (kg)	108 (4)	108 (5)	108 (4)	NS
BMI	38 (2)	38 (2)	38 (4)	NS
waist (cm)	118 (4)	118 (3)	118 (2)	NS
Biochemical data:				
LDL	4.5 (0.7)	4.5 (0.6)	4.5 (0.6)	NS
TG	2.9 (0.3)	2.9 (0.2)	2.9 (0.2)	NS
GGT	57 (5)	57 (7)	57 (7)	NS
Prevalance of metabolic syndrome:				
Hypertension	37% on 4 drugs	36% on 4 drugs	34% on 4 drugs	NS
DM	63% on 4 drugs	62% on 4 drugs	60% on 4 drugs	NS
Steatosis	82% grade 3	84% garde 3	84% grade 3	NS
Psychiatric disorders	76% were 3	73% were 3	71% were 3	NS

Abbreviations: M: male; F: female; BMI: body mass index; LDL: LDL-cholesterol; TG: triglycerides; GGT: gamma-glutamyl transferase; DM: diabetes mellitus.

Table 2. Time-related changes in patients', nutritional and metaboilc parameters, with weight-reduction intervention in the 3 treatment groups.

		Time *			% improvement with time
		At start	6 months later	12 months later	
Anthropometric measurements:					
Weight					
	D + E	108 (4)	98 (4)	87 (5)	19.4
	E	108 (5)	99 (3)	95 (3)	12
	D	108 (4)	100 (4)	96 (5)	11.1
BMI					
	D + E	38 (2)	34 (2)	31 (2)	18.4
	E	37 (2)	34 (2)	33 (2)	10.8
	D	38 (4)	35 (3)	34 (3)	10.5
Waist					
	D + E	118 (4)	109 (5)	98 (14)	16.9
	E	118 (3)	112 (3)	106 (5)	10.2
	D	117 (2)	112 (2)	109 (2)	6.8
Biochemical data:					
LDL-C					
	D + E	4.5 (0.7)	3.7 (0.4)	2.6 (0.3)	42.2
	E	4.5 (0.6)	3.8 (0.4)	2.9 (0.3)	35.5
	D	4.5 (0.6)	3.8 (0.3)	3.4 (0.3)	24.4
TG					
	D + E	2.9 (0.3)	2.6 (0.4)	2.2 (0.5)	24.1
	E	2.9 (0.2)	2.8 (0.2)	2.3 (0.1)	20.7
	D	2.9 (0.2)	2.7 (0.2)	2.6 (0.2)	10.3
GGT					
	D + E	56 (7)	48 (3)	29 (7)	48.2
	E	57 (7)	51 (6)	39 (1)	31.6
	D	57 (7)	50 (6)	44 (3)	22.8
Prevalence of metabolic/psychiatric syndromes:					
Hypertension					
	D + E	3 (2)	2 (2)	1 (1)	66.7
	E	3 (2)	2 (1)	2 (0)	33.3
	D	3 (2)	2 (1)	2 (1)	33.3
DM					
	D + E	4 (1)	3 (1)	2 (0)	50
	E	4 (1)	3 (0)	2 (1)	50
	D	4 (1)	3 (1)	2 (2)	50

Continued

Steatosis				
D + E	3 (0)	2 (1)	1 (0)	66.7
E	3 (0)	2 (0)	1 (0)	66.7
D	3 (0)	3 (1)	2 (1)	33.3
Psychiatric disorders				
D + E	3 (1)	2 (1)	0 (1)	100
E	3 (1)	2 (2)	1 (0)	66.7
D	3 (1)	3 (1)	2 (0)	33.3

Abbreviations: Groups: Diet: D, Exercise: E and combination of both: D + E; BMI: body mass index, LDL-C: LDL-cholesterol, TG: triglycerides, GGT: gamma-gluamyl transferase and DM: diabetes mellitus; Normal levels of 1) LDL-C: <3 mol/L; 2) TG: 0.4 - 2.4 mmol/L, and 3) GTT: 9 - 40 U/L. *Significant change, with time, in all 3 treatment' groups.

3.3. Changes in Anthropometric Measures

Marked reduction in weight, BMI and waist (19%, 18.4 and 16.9%, respectively) were evident in the D + E group. The 2 other groups had modest decrease in weight and BMI yet E group had better decrease in waist circumference (10.2 vs 6.8%).

3.4. Improvements in Biochemical Parameters

Similar trend was seen in all groups which were marked in D + E group followed by E than D groups.

3.5. Impact on Metabolic Syndrome

All patients had improvements in number of antihypertensive and antidiabetic drugs as well as in the degree of steatohepatitis and psychiatric disorders. Again; D + E group had the best results. However, decrease in; 1) anti-diabetic drugs were equal in the 3 groups and 2) antihypertensive agents were similar in E & D groups and 3) steatosis was similar in D + E and E group. Hence further sub analysis of those data, using % changes in grading, was done to assess that and the results are summarized in Table 3. When the combination of the highest grades was considered, similar pattern of improvement was seen and with the highest in the D + E group, followed by E then D groups. Fortunately, control of hypertension with drugs < 4 was achieved in all patients except for 1 in the D group. Moreover, discontinuation of insulin was achieved in all patients. Steatosis and psychiatric disorders had improved significantly in D + E and E groups yet improvement in psychiatric ones was less in D group.

4. Discussion

The causes of obesity are multi-factorial. Genetic susceptibility (monogenic obesity) is rare and accounts for <5% of severe obesity. It is due to autosomal-recessive

Table 3. Details of % grading changes of co-morbid conditions with time after weight reducion in the 3 treatment groups.

Time:	At start	6 months	12 months	% improvement with time *
		Diet + Exercise		
Hypertension	4/25/34/37	10/42/42/6	22/70/8/0	88.7
DM	0/0/2/9/26/63	0/2/8/20/70/0	0/4/18/72/8/0	91.5
Steatosis	0/18/82	22/36/42	82/8/0	92
Psychiatric disorders	0/26/74	18/34/48	62/30/8	62
		Exercise		
Hypertension	2/30/32/36	8/42/40/10	18/58/33/0	51.5
DM	0/0/0/12/26/62	0/0/0/28/72/0	0/0/2/74/24/0	72.7
Steatosis	0/16/84	16/36/48	84/16/0	84
Psychiatric disorders	0/28/72	14/36/50	54/38/8	54
		Diet		
Hypertension	2/30/34/34	6/43/41/10	9/58/32/1	51.5
DM	0/0/0/10/30/60	0/0/0/11/84/5	0/0/56/44/0	51.1
Steatosis	0/16/84	2/30/68	40/48/12	40
Psychiatric disorders	0/26/74	4/36/60	10/52/38	10

*Significant improvement, with time, considering combination of last highest grades.

mutations in genes of the leptin-melanocortin pathway which controls hypothalamic food intake [7]. However, nearly a third of the population have failure to maintain energy balance after low levels of physical activity and energy dense diets that unmasks a polygenetic susceptibility to obesity [fat mass and obesity-associated (*FTO*) gene] [8]. On the other hand; acquired causes of obesity include; socioeconomic, and environmental causes, including diet, physical activity, automation, urbanization, medications, mental disorders, economic policies, endocrine disorders and exposure to endocrine-disrupting chemicals [1]. Management of acquired causes entails: 1) dietary restrictions, and 2) weight-reducing exercises. Multiple diets have been proposed viz. low-calorie (intermittent fasting and weight watchers), very low calorie (<800 calories/day), low-carbohydrate/high protein and fat (Atkins, Dukan, South beach), McDougall's low fat/high calorie, Mayo Clinic (high complex carbs and low saturated fat and salt), Crash, Detox, Dash, Vegan (vegetarian) and Mediterranean. All have shown variable success yet most were risky for patients with heart, renal and liver disease as well as expensive and intolerable on long-term [9]. On the other hand, exercise is indicated to lose and maintain calorie-deficient state. The key ones are; cardio, strength-training and multi-joint compound movement which are risky to some patients, intolerable on long-term and require expensive devices [2]. In our study we proposed 2 tolerable weight reduction techniques viz. diet and exercise. Our dietary regimen consisted of; 1) a minimum number of calories and limited

portions of protein and fat to ease its future-use in patients with heart, renal and liver diseases without muscle wasting [10], and 2) 12-hour meals-separation to surpass the 8-hours 50% liver-ability of glycogenolysis and hence shift to muscle glycogenolysis and subcutaneous lipolysis using their lactate, pyruvate, glycerol, and amino acids [11]. On the other hand, our exercise technique consisted of; 1) acceptable protocol of 45 minutes thrice-weekly active walk rather than rigid daily practice to ease compliance and avoid injuries, 2) active straight walking without knee twisting to avoid its common injury in obese patients, 3) active abdominal movement and belly-fat squeezing to ease central obesity, and 4) after-burn (avoiding food for 1 hour after exercise) to assist in further breakdown of muscle fats by avoiding food-induced insulin lipogenesis [12]. Such calculated calory-loss of 350 - 400/session is an acceptable muscle training to catabolize more fats and proteins [13]. In our study, we confirmed, in a prospective fashion, the beneficial effect of weight reduction on multiple obesity-associated metabolic derangements viz. control of hyperglycemia, hypertension, hyperlipidemia, fatty liver, psychiatric disorders. Improvement in diabetic control was associated with decrease requirement of insulin, and other hypoglycemic drugs which excludes pancreatic exhaustion, in type II DM, and is in favor of reversible obesity-induced insulin resistance [14]. Our patients had significant amelioration of their severe hypertension with decrease requirements of anti-hypertensive drugs. The latter may have a reflection of decrease in counter regulatory mechanisms induced by obesity [15]. In our patients, weight reduction, was associated with significant reduction of waist, severity of hypertension and diabetes as well as LDL and TG measurement which has been shown to be associated with premature atherosclerosis and long-term cardiovascular risk [16]. Moreover, our study has shown dramatic and prospective decrease of hyperlipidemic parameters (LDL, TG, GGT) and steatosis which can ameliorate NASH and its associated-risk of cirrhosis and cancer [17]. Finally, our study confirmed, prospectively, the beneficial role of weight reduction on anxiety, depression and erectile dysfunction. Such improvement will reflect positively in the quality of life of obese patients and the community health [18]. A major finding in our study was the significant synergism between dietary restriction and exercise with best results in the combination group [19]. Twenty-one (19%) weight reduction was achieved by 1 year that was translated into >60% reduction in all health parameters. Hence, health strategies should encourage such combination rather than isolated programs.

5. Conclusion

The study has shown that 1) the combination of dieting and exercise resulted in significant benefits across a variety of important anthropometric health measurements compared to modest ones in isolated intervention; 2) the three protocols were not associated with negative health outcomes or harmful side effects; 3) their ease and application-practicality can maintain weight loss over the long

term; and 4) such improvements could translate into a long-term reduction in mortality and morbidity.

Conflicts of Interest

The authors declare that there were no conflicts of interest regarding the publication of this paper.

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