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The effect of non-exercise activity thermogenesis on subjects with metabolic syndrome – a proof of concept study in Qatar

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ABSTRACT

Metabolic syndrome is a cluster of metabolic abnormalities that increases the risk of cardiovascular disease and type 2 diabetes. Total human energy expenditure is divided into three major components; resting metabolic rate, thermic effect of food, and activity thermogenesis which is divided into exercise and non exercise activity thermogenesis (NEAT). In this study, NEAT was used as a lifestyle intervention on subjects with metabolic syndrome. 200 eligible patients from the Diabetes and Endocrinology Department at Hamad Medical Hospital in Doha, Qatar were assigned to an intervention (n = 100) or control (n = 100) group and followed for one year. The intervention group was advised to practice NEAT enhancing activities, while the control group was not advised about NEAT. Measurements of waist circumference, weight, BMI, blood pressure, glucose and lipid profile were assessed at baseline, six months and 1 year.

After 1 year 52 intervention and 55 control subjects completed the study. The results revealed no statistically significant differences in metabolic syndrome components between the two randomized groups. The amount of recommended NEAT activity appears to have been too small to influence study outcomes. Future studies in similar populations may need to consider the high dropout rate, and use of incentives or other interventions to increase compliance and retention.

INTRODUCTION

Metabolic syndrome is a combination of several abnormalities that increase the risk of cardiovascular disease (CVD) such as increased waist circumference,

lipids, or blood pressure. Each abnormality is associated with cardiovascular disease cases,[1] such as stroke, myocardial infarction, and heart failure.[2] Worldwide, approximately 20 – 25% of the population suffers the burden of symptoms related to metabolic syndrome.[3] The burden is shared among the Qatari population, which suffers from high prevalence rates of obesity and type 2 diabetes.[1] A recent study indicates that the crude prevalence of metabolic syndrome in Qatar is 34% according to the International Diabetes Federation (IDF) criteria.[2] Risk factors associated with metabolic syndrome in the Qatari population include age, ethnicity, obesity and family history of diabetes.[2]

Total human energy expenditure divides into basal metabolic rate, thermic effect of food, and activity thermogenesis. Activity thermogenesis is further divided into exercise, and non exercise activity thermogenesis (NEAT); NEAT is defined as the energy used throughout the day for all non exercise activities.[4] Novak and Levine[5] show an inverse relationship between sedentary behaviors and physical activity; which leads to increased obesity and decreased health at the population level. Structured physical activity may help prevent metabolic syndrome.[6] One way to increase physical activity both on an individual and population level is through increasing NEAT, such as walking instead of driving, or taking the stairs instead of using the elevator.

A lifestyle intervention study was conducted with 200 Qatari subjects identified with metabolic syndrome. This proof of concept study aims to understand whether it is feasible to attempt to reduce the burden of metabolic syndrome in Qatari outpatients by promoting increased NEAT.

METHODS

The study is a one year randomized experiment, with a pretest and posttest intervention and control group. The study was conducted between March 2010 and August 2011. NEAT enhancing activities were used as a lifestyle intervention. Subjects were recruited from the endocrinology and diabetes department clinics at Hamad Medical Corporation in Doha, Qatar. Subjects were asked to sign a written consent form before enrollment. The study was approved by the research ethics committee at Hamad Medical Hospital in Doha, Qatar (research protocol number 9181/09).

The IDF definition for metabolic syndrome was used to establish diagnosis.[3] The inclusion criteria included subjects over the age of 18, who have elevated waist circumference (over or equal to 94 cm for men, over or equal to 80 cm for women), and two or more abnormalities out of four, of the following: (a) elevated triglycerides over or equal to 150 mg/dL (1.7 mmol/L), or drug treatment for elevated triglycerides; (b) reduced HDL cholesterol less than 40 mg/dL (1.0 mmol/L) for males and less than 50 mg/dL (1.3 mmol/L) for females, or drug treatment for reduced HDL cholesterol; (c) elevated blood pressure over or equal to 130 mm Hg for systolic and/or over or equal to 85 mm Hg for diastolic, or diagnosed hypertension; (d) elevated fasting glucose above or equal to 100 mg/dL (5.6 mmol/L), or diagnosed diabetes. The exclusion criteria excluded subjects: (a) diagnosed with major illnesses; (b) taking any type of medication that may affect weight; (c) cannot tolerate study procedures.[7]

Subjects were divided to an intervention (n = 100) and a control group (n = 100). The randomized list was

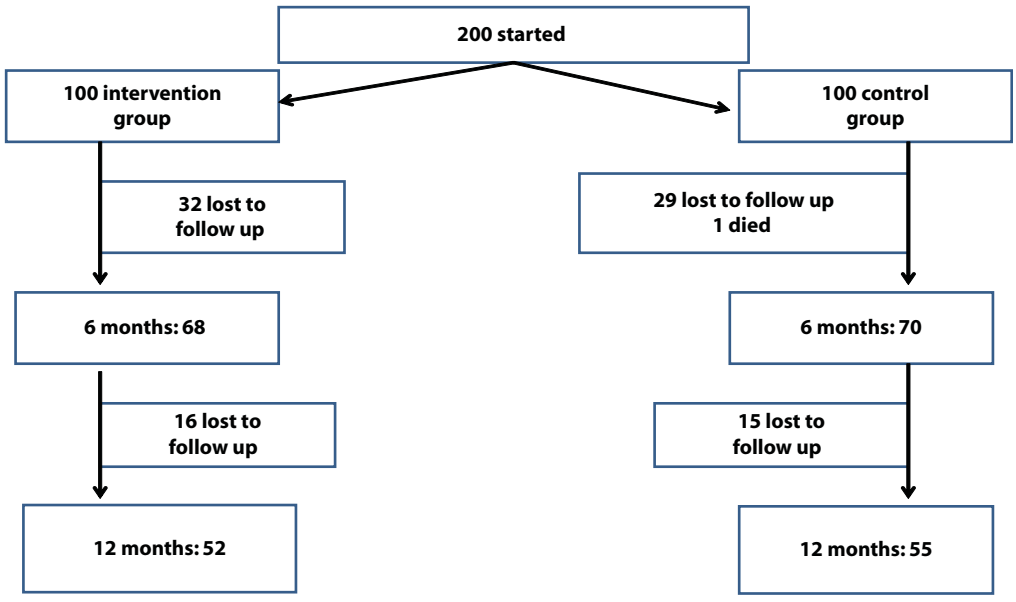

Figure 1. Flow chart showing study progress.

Table 1. Patient demographics, metabolic syndrome components, and anthropometrics (Quantitative values expressed as mean ± SD/ *p* value derived using independent t test, qualitative values expressed as number (percentage)/ *p* value derived using chi square test).

Variable	Intervention	Control	*p* value
Gender	(n = 100)	(n = 100)	
Male	58 (58%)	62 (62%)	0.564
Female	42 (42%)	38 (38%)	
Age (years)	(n = 100)	(n = 100)	
Mean ± SD	57.1 ± 13.44	55.9 ± 12.32	0.490
Median (Range)	56.5 (20-84)	57.5 (18-85)	
Marital Status	(n = 100)	(n = 100)	
Married	83 (83.0%)	88 (88.0%)	0.195
Single	9 (9.0%)	10 (10.0%)	
Widowed	7 (7.0%)	1 (1.0%)	
Divorced	1 (1.0%)	1 (1.0%)	
Height (cm)	(n = 100)	(n = 100)	
Mean ± SD	162.7 ± 8.71	162.3 ± 9.29	0.772
Median (Range)	162.0 (139-182)	161.0 (143-185)	
Weight (kg)	(n = 100)	(n = 100)	
Mean ± SD	86.9 ± 18.48	87.0 ± 19.25	0.952
BMI (kg/m^2)	(n = 100)	(n = 100)	
Mean ± SD	33.0 ± 7.04	33.1 ± 7.66	0.935
Waist circumference (cm)	(n = 100)	(n = 100)	
Mean ± SD	108.2 ± 12.26	108.4 ± 14.13	0.902
Glucose (mmol/L)	(n = 94)	(n = 93)	
Mean ± SD	8.4 ± 3.15	8.5 ± 3.5	0.762
High-density lipoprotein cholesterol (mmol/L)	(n = 92)	(n = 94)	
Mean ± SD	1.1 ± 0.28	1.1 ± 0.35	0.595
Low-density lipoprotein cholesterol (mmol/L)	(n = 92)	(n = 94)	
Mean ± SD	2.7 ± 0.94	2.7 ± 0.89	0.872
Triglyceride (mmol/L)	(n = 92)	(n = 94)	
Mean ± SD	1.6 ± 0.94	1.6 ± 1.1	0.970
Cholesterol (mmol/L)	(n = 92)	(n = 93)	
Mean ± SD	4.6 ± 1.1	4.6 ± 1.0	0.965
Systolic blood pressure (mmHg)	(n = 100)	(n = 99)	
Mean ± SD	145.1 ± 18.51	140.5 ± 20.18	0.096
Diastolic blood pressure (mmHg)	(n = 100)	(n = 99)	
Mean ± SD	76.8 ± 10.65	76.3 ± 10.77	0.744
Medications	(n = 90)	(n = 88)	
Anti-diabetic			
Yes	65 (72.2%)	64 (72.7%)	0.940
No	25 (27.8%)	24 (27.3%)	

Table 1 – *continued*

Variable	Intervention	Control	*p* value
Lipid-lowering			
Yes	62 (68.9%)	62 (70.5%)	0.820
No	28 (31.1%)	26 (29.5%)	
Anti-hypertensive			
Yes	69 (76.7%)	66 (75.0%)	0.795
No	21 (23.3%)	22 (25.0%)	

produced using random allocation software. The control group received general dietary and physical activity guidelines. The intervention group received additional information on how to increase their daily NEAT. This information was given by the nurse, on a one to one basis, over a 10 min period of time. Participants also received a one page handout explaining different NEAT options and how it works. Subjects were asked to practice the following NEAT enhancing activities recommended by Levine et al.[4] standing instead of sitting, gum chewing, fidgeting, using the stairs instead of the elevator, walking instead of using the car. This information along with the frequency was reported by subjects on weekly report sheets that were turned in at their six and 12 month visit.

Subjects were followed for one year, during which the waist circumference, blood pressure, weight, glucose and lipid profile were assessed at baseline, six, and 12 months. Subjects in the intervention group received reminders, via text messages, to practice NEAT at 2, 4, 8, and 10 months.

MEASUREMENTS

A Seca digital medical weighing scale was used to obtain body weight. Waist circumference was assessed using a measure tape at the level of the superior iliac crest with the person lightly clothed. The fasting glucose and lipid profile were assessed by drawing blood samples. This included information on the blood levels of total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, and glucose (Roche/Hitachi modular p chemistry analyzer using enzymatic in vitro assay) at the facility laboratory. LDL cholesterol was calculated unless triglycerides were >4.5 mmol/L, when it was measured directly. The blood pressure was measured using an electronic sphygmomanometer after the patient was seated for 10 min.

STATISTICAL ANALYSIS

Power analysis revealed that based on Cohen's estimation of a medium effect size ($f = 25$), power = 80%, and $\alpha = 0.05$, 64 subjects were needed for each group, for a total of 128.[8] Categorical and continuous data were expressed as frequency (percentage) and mean ± SD. Descriptive statistics were used to summarize all demographic and clinical characteristics of the participants. Baseline participant characteristics in the two independent groups were compared using an unpaired t test for continuous variables and a chi-square test for categorical variables. For the primary outcome variable i.e., average number of components of metabolic syndrome, data from the baseline, 6 months and 12 months were compared using repeated measure analysis of variance (ANOVA). The results were presented with the associated 95% confidence interval. Where an overall group difference was found statistically significant, pair-wise comparisons were made using the appropriate post-hoc test. All statistical tests were two-sided and the *p* value smaller than 0.05 was considered to be statistically significant. All statistical analyses were done using statistical packages SPSS 19.0 (SPSS Inc. Chicago, IL).

STUDY PROGRESS

A total of two hundred individuals were recruited between March and August of 2010. These were randomized using random allocation software into two groups, an intervention and control group. At the 6 month visit, 62 were lost at follow up; 32 of the intervention and 29 of the control group. Additionally one person died from the latter group. At the 12 month visit, 31 additional subjects were lost at follow up, 16 and 15 of the intervention and control group respectively. The following flow chart shows the overall study progress (Figure 1).

RESULTS

Among those recruited 120 (60%) were men, and 80 (40%) were women. The number of males was higher in both groups, 58 in the intervention and 62 in the control groups. All subjects were of the same ethnicity as they were all Qatari nationals. The mean height for the intervention group was 162.7 cm ± 8.71

Table 2. Patients' metabolic syndrome components (*p* value derived using chi square test).

Components of metabolic syndrome	Intervention	Control	*p* value
Elevated waist circumference	(n = 100)	(n = 100)	
Yes	95 (95.0%)	92 (92.0%)	0.390
No	5 (5.0%)	8 (8.0%)	
Elevated triglycerides	(n = 94)	(n = 98)	
Yes	63 (67.0%)	63 (64.3%)	0.690
No	31 (33.0%)	35 (35.7%)	
Elevated blood pressure	(n = 100)	(n = 99)	
Yes	91 (91.0%)	88 (88.9%)	0.620
No	9 (9.0%)	11 (11.1%)	
Reduced HDL cholesterol	(n = 94)	(n = 96)	
Yes	70 (74.5%)	80 (83.3%)	0.134
No	24 (25.5%)	16 (16.7%)	
Elevated glucose	(n = 97)	(n = 96)	
Yes	86 (88.7%)	82 (85.4%)	0.502
No	11 (11.3%)	14 (14.6%)	

(range: 139 – 182), and for the control group162.5 cm ± 9.29 (range: 143 – 185). Patient demographics, metabolic syndrome components and anthropometrics are listed in Table 1 below. Information regarding the number of components of metabolic syndrome among each group is summarized in Table 2 below.

The results showed no significant difference over time between the groups in regard to weight, BMI, waist circumference, glucose, HDL cholesterol, triglycerides, diastolic and systolic blood pressure, and the number of metabolic syndrome components as well as total and LDL cholesterol. The detailed results are presented in Table 3.

NEAT ACTIVITY

In regard to the frequency of NEAT practiced, among the 40 participants that did report their activity, 24 (60%) were found to have practiced NEAT enhancing activities 1 – 2 times a week, 10 (25%) practiced it 3 – 4 times a week, and 3 (7.5%) did it more than 4 times a week, while 3 (7.5%) reported no activity.

DISCUSSION

The increasing prevalence of metabolic syndrome in Qatar is just one indication among many that this population is suffering as a result of major lifestyle changes that have occurred in the past four decades. In this study on 200 subjects, there was no significant difference between the groups on the measures of metabolic syndrome after a 1-year intervention study.

We are unaware of previous studies using NEAT as an intervention in patients with metabolic syndrome. Most of the patients were middle aged or older, and already had established type 2 diabetes. Such interventions may be effective in younger patients, and work better for prevention rather than cure.

Factors that play an important role in the development of metabolic syndrome include genetics, sedentary lifestyle, cigarette smoking, progressive weight gain, and a Western diet.[9,10] Lifestyle plays a major role in the etiology of metabolic syndrome either through low physical activity or excess caloric intake or both. The most common risk factor seems to be abdominal obesity which majorly justifies lifestyle modification. The American Heart Association states that "in the long run, the greatest benefit for those with metabolic syndrome will be derived from effective lifestyle intervention".[11] Levine et al.[4] show that NEAT plays an important role in overall energy balance because it may vary as much as 2000 kcal/day between individuals. Moreover, they indicate that highly active people may expend as much as three times more than inactive people.

Components of metabolic syndrome showed no significant difference between the groups in this study. This can be due to many reasons. Non compliance is one of the major influencing factors, which can be due to social norms, or lack of local convincing evidence on the effectiveness of NEAT, or lack of awareness. It appears that not enough NEAT was accomplished per week to influence the results. It is possible that NEAT should be

carried out and practiced on a daily basis to the point where it becomes a personal habit or part of one's lifestyle before one might expect to see significant results.

While the results were disappointing they provide a basis for future studies. To increase NEAT, more significant activities that expend more energy than others may be emphasized like walking. Furthermore, specific goals to

Table 3. Comparison of anthropometric and metabolic parameters at baseline, 6 months, and 12 months in completers in the intervention and control group (*p* value derived using repeated measures ANOVA test).

	Time Points			
	Baseline	6 months	12 months	
Variable	(Mean ± SD)	(Mean ± SD)	(Mean ± SD)	*p* value
Weight (kg)				
Intervention (n = 48)	84.2 ± 18.51	84.6 ± 18.46	84.9 ± 19.16	0.677
Control (n = 49)	86.5 ± 20.19	85.9 ± 20.34	86.3 ± 21.23	
Body mass index (kg/m^2)				
Intervention (n = 47)	32.15 ± 7.62	32.26 ± 7.42	32.38 ± 7.74	0.611
Control (n = 49)	33.21 ± 8.32	32.99 ± 8.37	33.12 ± 8.77	
Waist circumference (cm)				
Intervention (n = 40)	104.5 ± 13.21	104.6 ± 11.38	104.6 ± 11.44	0.159
Control (n = 47)	108.5 ± 13.21	108.1 ± 13.24	108.4 ± 13.38	
Glucose (mmol/L)				
Intervention (n = 45)	8.78 ± 3.54	8.86 ± 3.83	8.62 ± 3.47	0.501
Control (n = 39)	9.42 ± 3.93	9.29 ± 4.42	9.09 ± 4.33	
High-density lipoprotein cholesterol (mmol/L)				
Intervention (n = 43)	1.14 ± 0.29	1.10 ± 0.25	1.15 ± 0.28	0.396
Control (n = 38)	1.05 ± 0.31	1.03 ± 0.28	1.15 ± 0.51	
Low-density lipoprotein cholesterol (mmol/L)				
Intervention (n = 43)	2.57 ± 0.81	2.63 ± 0.71	2.58 ± 0.68	0.789
Control (n = 39)	2.53 ± 0.79	2.56 ± 0.70	2.58 ± 1.05	
Triglyceride (mmol/L)				
Intervention (n = 43)	1.64 ± 0.93	1.47 ± 0.68	1.51 ± 0.65	0.124
Control (n = 39)	1.79 ± 1.45	2.02 ± 1.66	1.87 ± 1.35	
Cholesterol (mmol/L)				
Intervention (n = 43)	4.55 ± 0.90	4.40 ± 0.73	4.38 ± 0.82	0.889
Control (n = 39)	4.41 ± 1.09	4.45 ± 0.82	4.54 ± 1.42	
Systolic blood pressure (mmHg)				
Intervention (n = 43)	144.77 ± 19.60	137.49 ± 18.76	137.21 ± 16.64	0.456
Control (n = 46)	142.07 ± 19.94	143.59 ± 18.82	141.24 ± 19.19	
Diastolic blood pressure (mmHg)				
Intervention (n = 43)	75.79 ± 9.03	75.12 ± 9.39	72.72 ± 9.46	0.218
Control (n = 46)	75.70 ± 11.76	78.22 ± 10.81	76.15 ± 10.43	
Number of components of metabolic syndrome				
Intervention (n = 50)	3.64 ± 0.77	3.68 ± 0.79	3.78 ± 0.76	0.059
Control (n = 45)	3.98 ± 0.78	3.96 ± 0.85	4.02 ± 0.86	

be attained in regard to frequency and duration of activity should be promoted. Another suggestion would be to use pedometers or other physical activity sensors as an incentive to increase NEAT as Gardner and Campagna show that such devices help increase motivation and aid in raising awareness to different activity patterns.[12] Also, self-report was used as a reporting method, where subjects may tend to over report, or simply forget. Only 40% of participants in the intervention group filled out the report forms.

Other factors may include the high dropout rate and missing data. To improve the dropout rate, one may consider shortening the time between follow up visits or by providing incentives at each visit. Other possible options include increasing the frequency and type of reminders, such as using phone follow ups on regular basis. Additionally the quality of training of personnel who gave the advice may be improved, as well as the quality of advice given. Many other factors may have influenced participants of this study, such as the limited physical activity outlets considering the overall hot weather, which also contributes to the common sedentary lifestyle, which is quite prevalent in the area, as well as the occurrence of the month of fasting during the final evaluation of some participants.

Due to the high rate of metabolic syndrome locally, it would be beneficial to conduct future studies learning from the experience of this study, to help curb the epidemic of metabolic syndrome and its hazardous outcome. Such studies should take into consideration the high dropout rate which occurred in this study, and should be constructed to minimize such occurrences.

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