Possible Thermogenesis with Dexfenfluramine

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Abstract

Fifty obese patients with a body mass index greater than 25 kg/m^2 were randomized into 3 groups: control (C=19), placebo (P=18) and dexfenfluramine (D=18). A behavioral modification program which included eating habits, exercise, attitudes, social relationships and six steps to lifetime weight control was taught every week. All patients strictly followed the food manual and recorded their behavior, physical activity and food intake every day through 12 weeks. Placebo and dexfenfluramine 30 mg/day were given in a double blind placebo controlled study. The results showed that all 3 groups had significant decreases in rest times and increased activity times ($p<0.05$) and significant reductions of the average total daily energy, carbohydrate and fat intake ($p<0.05$). They all lost weight. Mean $\pm$ SEM cumulative weight loss was 8.3 ± 0.7 kg in group D, 3.3 ± 1 kg, in group P and 2.9 ± 0.7 kg, in group C. The mean additional weight loss of 5 kg, and 5.4 kg seen with dexfenfluramine being highly significant ($p<0.001$) from group P and C most likely due to increased thermogenesis. Significant ($p<0.05$) and gradual reduction of biceps, triceps skinfold and per cent body fat were constantly observed only in the dexfenfluramine group. There were no significant differences among the 3 groups regarding blood pressure, heart rate, hematologic, lipids and biochemical profiles.

Key word : Thermogenesis, Possible, Dexfenfluramine

Obesity occurs when there is an imbalance between energy intake and expenditure. Although most obese patients firmly believe that their metabolism is at fault, the causes in most cases of obesity are multifactorial. The treatment of obesity includes diet, pharmacotherapy, surgery and behavioral modification. Knowledge of a particular patient's baseline eating and exercise patterns is

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vital to achieve longterm success in weight control. We have developed behavioral weight control programs with special emphasis on the cognitive aspects of food, nutrition, and eating behavior that have been most successful according to recent research[1]. Participant materials, a leader's guide, and lesson plans have been developed to assist the nutrition professional in utilizing the program. The title, "Techniques to eat less, prevent obesity" indicates the emphasis on individual responsibility inherent in the program. The unique aspect of this program is the coordination of nutritional and practical food-savvy information with the Exchange Lists for Meal Planning System. Optional in-session snacks based on the six food exchange groups are used to reinforce the nutritional teaching and to provide opportunities for practicing new eating behaviors[2,3].

In addition to diet, drug therapy has experienced much popularity, although the effectiveness of drugs in the treatment of obesity has not been adequately demonstrated. During the last two years, use of a combination anorectic therapy namely "fen-phen" had previously been linked to increased risk of pulmonary hypertension[4]. It is currently thought to be associated with valvular heart insufficiency[5]. The lesions seen are comparable to those seen in patients with carcinoid syndrome and are thought to be due to elevated levels of serotonin. Dexfenfluramine and fenfluramine have been withdrawn from the market as a precaution which has been reaffirmed by a recent study showing evidence linking use of fenfluramine or dexfenfluramine with valvular lesions[6-8].

Neil.J.Weissman, the Assistant Professor of Medicine and Director of Clinical Echocardiography at Georgetown University Medical Center's Cardiovascular Institute has recently shown the results of a clinical study, the randomized, double-blind, multicenter study involving 1,072 patients, presented at the 47th Annual Meeting of the American College of Cardiology in March 1998 that there was no significant increase in the prevalence of clinically relevant heart valve regurgitation after two to three months of taking dexfenfluramine. The study demonstrates that there is no significant difference in prevalence or severity of valvular regurgitation between patients who took dexfenfluramine and those taking placebo. However, current studies have shown that the use of dexfenfluramine for 4 months or longer is associated with an increased risk of cardiac-valve disorders[7].

Dexfenfluramine is the dextro-rotatory (+) isomer of fenfluramine[9]. Compared with the racemic fenfluramine, dexfenfluramine has a greater selectivity for serotonin (5-hydroxytryptamine : 5HT) receptor. It inhibits reuptake of serotonin and stimulates brain serotonin release, thus, increasing brain serotonin levels. The French Medicine's Agency has restricted the use of appetite suppressant drugs to patients for a maximum of 3 months' treatment[10].

The present study aims to evaluate the clinical efficacy and possible thermogenesis effect of a 3-month treatment by dexfenfluramine in conjunction with behavioral programs.

MATERIAL AND METHOD

It was a randomized control trial study which included 68 obese Thai patients. The inclusion criteria were : males or females between 18 and 75 years old, simple obesity with a body mass index (BMI) over 25 kg/m^2. Exclusion criteria were obesity of endocrine origin e.g., hypothyroidism, Cushing's syndrome, type I or type II diabetes, serious systemic or psychiatric illnesses, glaucoma, pregnancy or wishing to become pregnant and lactating women, concomitant medications which could interfere with the activity of dexfenfluramine such as barbiturates, MAO inhibitors, antidepressants, benzodiazepines, neuroleptics, antiserotonergics or serotonergic drugs, reserpine or central-acting antihypertensive drugs, and having taken drug treatment for obesity in the last 3 months. The patients were divided into 2 groups (Group I, n = 36, Group II, n = 32). Patients in group I were randomly stratified into 2 subgroups to receive either placebo (P, n= 18 patients) or 15 mg dexfenfluramine (D, n = 18 patients) twice daily (1 capsule in the morning at breakfast-time and 1 capsule in the evening at dinner-time) for 3 months in a double-blind, placebo-controlled manner. The group II patients who attended the class without any medication served as the control group (C, n= 32). All subjects commenced the behavioral programs[2,3]. All the patients attended the nutrition class as group therapy every Friday afternoon from 1.00 - 4.00 pm. for 8 weeks at Ramathibodi Hospital. After completing the 8-week course, they were followed-up one month later for the last assessment. The total duration of the study was 12 weeks (3 months). The program included the six steps to lifetime weight control, food intake and activity records, dietary

guidelines, the exchange list system of meal planning, mealtime hints for successful weight control, exercise, goal setting, slowing down eating, behavioral chain to inappropriate eating, alternative activities, weight control in the grocery store, nutrition labeling, social support and suggestion for family and friends how you can help, positive self-talk, managing your thinking and maintaining your goal weight.

The diet was designed to be nutritionally sound and conductive to a life long pattern of healthy eating by the subjects. The energy prescription was approximately 1,000 kcal for both male and female subjects, regardless of initial weight. The food plan was based on the Exchange Lists for Meal Planning System (American Diabetes Association and the American Dietetic Association, 1976 modified for Asian food). Exercise was considered to be an important element of weight control[11,12]. We advised aerobic activities as well as exercise for flexibility to the unfit and older subjects. Self-monitoring was emphasized, with subjects keeping a diary of their eating behavior and recording the times and situations in which they had eaten as well as the type of food eaten, the degree of hunger which preceded eating and the feelings that were experienced while eating. They took a lesson from the class in conjunction with the guide book at each visit. They strictly followed the manual and recorded their eating behavior (such as meal frequency, type of food/snacks, amount of food/snacks, estimated calorie intake, etc.) and all physical activities during each period of the visits. Subjects were informed to develop techniques for changes in behavior as well as for weight loss.

To assess the efficacy of dexfenfluramine, we measured body weight which was evaluated weekly in the first 2 months, then at the end of the 3-month study. Anthropometric parameters including triceps, biceps, subscapular and supra-iliac skinfold thickness were measured every month and calculated for per cent body fat from Durnin[13]. To assess the safety profiles we measured heart rate, blood pressure, hematological, biochemistry profiles, serum lipid profiles and urinalyses before and after the program. Each subject was given a questionnaire on frequency of behavioral weight control techniques as a pre-test and post-test to evaluate the efficacy of the program. Compliance and any adverse drug event were recorded at each visit.

Statistical analysis

All the evaluations conducted in the study were recorded in an appropriate case record form for each subject. The statistical analyses were performed concerning efficacy and safety parameters. The results were expressed as rating scores in

Table 1. Characteristics of subjects*.

	Dexfenfluramine	Placebo	Control
Number	18	18	19
Sex Male	4	3	6
Female	14	15	13
Overweight (BMI = 25-27 kg/m^2)	3	4	4
Severe overweight (BMI = 27.1-30 kg/m^2)	6	10	10
Overt obesity (BMI > 30 kg/m^2)	9	4	5
Age (yrs)	41.8 ± 3	39.6 ± 2	43.9 ± 2
Height (cm)	159 ± 7	156 ± 6	157 ± 6
Weight (kg)	76.4 ± 10.3	70.8 ± 9.1	71.5 ± 8.2
Ideal weight (%)	135 ± 3.8	144.5 ± 4.3	131.9 ± 2.8
Waist circumference (cm)	88.1 ± 2.7	83.1 ± 2.4	87.8 ± 1.5
Hip circumference (cm)	104.9 ± 1.7	103.5 ± 1.3	103.6 ± 1.6
Abdominal obesity			
No	9	11	10
Yes	9	7	9

* Results are expressed as mean ± SEM

There are no significant differences among groups in every parameter. (ANOVA = NS)

Abdominal obesity is determined by waist to hip ratio of ≥ 0.85 in female and ≥ 0.9 in male respectively

absolute values or percentage (%) with the mean and standard error of the mean (SEM). The significant threshold was fixed at 0.05. Specific indices showing the effects of the drug were calculated and analyzed with 2-way analysis of variance (ANOVA) and if significant completed with a Newman Keuls Test. Mc Nemar tests was used to assess the behavioral techniques "before to after" changes.

RESULTS

We excluded 13 patients of group C because they did not return in the second week and refused regular contact. The data which were calculated included group D (n=18), group P (n=18) and group C (n=19) are shown in Table 1.

Mean (±SEM) cumulative weight loss was 8.3 ± 0.7 kg in group D, 3.3 ± 1 kg in group P and 2.9 ± 0.7 kg in group C. The mean additional weight loss of 5 and 5.4 kg seen with dexfenfluramine was highly significant ($P<0.001$) from group P and C respectively. (Table 2)

Only group D showed a gradual decrease in waist/hip ratio, triceps and biceps skinfold thickness and body fat mass with significant differences from those of group P and C (Table 3). Table 4 shows daily activity time, all obese patients spent time resting before the treatment program for more than half a day and showed a significant decrease ($P<0.05$) of rest time and an increase of activity times after the program. According to the program, we emphasized decreasing the total energy from carbohydrate and fat and maintain energy from protein. All the three groups showed the same pattern of significant reduction ($p<0.05$) in the average total daily energy, carbohydrate and fat intake from the beginning (Fig. 1). Table 5 shows behavior modification techniques which changed from "before to after". Table 6 shows consistent weight loss of groups D in 3 consecutive months. Changes in group D included significantly lower serum cholesterol and triglycerides levels after the program (Table 7). For safety profiles, we did not see any change of heart rate, blood pressure, laboratory parameters (hematological, liver and renal function test, electrolytes, minerals and urinary test) among the 3 groups.

DISCUSSION

The present data show a significantly more pronounced weight loss in group D compared to group P and C.

Weight loss in the dexfenfluramine-treated patients resulted from a reduction in body fat mass as assessed by a significant and gradual reduction of biceps and triceps skinfold and waist to hip ratio (Table 3).

Dexfenfluramine has a selective serotonergic effect. It stimulates the release of serotonin and inhibits the re-uptake of serotonin in the synapse (9,13,14). It normalizes the over-consumption of snacks and exerts a qualitative discriminatory action on food intake. The intake of carbohydrates and fats is significantly reduced, while the intake of essential foodstuffs such as protein is maintained by dexfenfluramine(15). However, this phenomenon was not observed in our study because the eating behavior of all patients was modified by our program throughout the 8 week period. All the 3 groups showed a significant reduction in daily energy intake as well as carbohydrate and fat intake with no significant changes in protein intake (Fig. 1).

According to the changes in food intake, activity time and behavioral daily life in all groups, these can explain the weight loss in all groups but it could not explain the consistent weight loss of groups D over 3 consecutive months during the study (Table 6).

The fact that there was a decrease in weight with group P and group C can be interpreted as a sign of good compliance of the patients to diet and behavioral program in the first 2 months of the weekly program. Without reinforcement from the class which they previously attended every week, the patients in group P and C showed much smaller weight reduction during the third month. In group D, since the patients were instructed to maintain their level of calorie intake, the described central effect of the drug in decreasing food intake was minimized during the first 2 months and was obvious in the third month. Thus, weight loss is likely to indicate a direct action of the drug. A report from A.V. Greco et al(16) on the increase of free fatty acid oxidation due to the direct effect of dexfunfluramine can play an important role in the induced weight loss. This suggested an increased cellular lipolytic activity associated with a raised FFA cellular uptake. In group D there was a significant decrease of waist/hip ratio, biceps and triceps skin folds and body fat mass. The drop of serum cholesterol and triglycerides (Table 7) suggests an increase of their peripheral utilization. We suggest that in addition to its well-known central effect,

Table 2. Mean cumulative weight loss during the treatment program*.

Month	Dexfenfluramine	Placebo	Control	ANOVA
1	2.6 ± 0.15	1.5 ± 0.2	1.15 ± 0.3	< 0.001
2	6.5 ± 0.14	3.12 ± 0.4	2.13 ± 0.6	< 0.001
3	8.3 ± 0.9	3.3 ± 1	2.9 ± 0.7	< 0.001

* unit = kg, the results are expressed as mean ± SEM.

Table 3. Anthropometrics data and body composition during treatment.

		Dexfenfluramine	Placebo	Control	ANOVA
Waist/hip ratio	M0	0.84 ± 2.2	0.80 ± 2.3	0.85 ± 1.8	0.048
	M1	0.83 ± 2.2	0.82 ± 2.4	0.87 ± 1.6	
	M2	0.82 ± 2.3	0.80 ± 2.2	0.86 ± 1.3	
	M3	0.81 ± 3.3	0.80 ± 2.2	0.86 ± 1.9	
Biceps skinfold (mm)	M0	17.1 ± 2.0	18.9 ± 1.1	17.7 ± 1.6	0.012
	M1	15.5 ± 1.8	18.5 ± 1.3	16.8 ± 1.8	
	M2	13.2 ± 1.0	15.4 ± 1.0	14.9 ± 1.9	
	M3	11.9 ± 1.3	15.6 ± 1.6	20.4 ± 1.2	
Triceps skinfold (mm)	M0	30.7 ± 1.9	29.9 ± 1.8	30.6 ± 1.7	0.041
	M1	27.9 ± 1.8	29.6 ± 2.3	28.1 ± 2.5	
	M2	25.2 ± 1.7	25.9 ± 2.3	26.2 ± 2.7	
	M3	22.6 ± 2.0	23.9 ± 2.8	30.9 ± 7.4	
Subscapular skinfold (mm)	M0	38.1 ± 2.6	37.2 ± 2.0	14.4 ± 2.3	
	M1	37.9 ± 2.5	40.7 ± 1.8	40.2 ± 2.8	
	M2	34.8 ± 2.9	40.2 ± 2.3	35.7 ± 3.2	
	M3	32.5 ± 3.5	37.1 ± 2.8	41.2 ± 7.1	
Supraliac skinfold (mm)	M0	46.7 ± 2.5	41.4 ± 1.9	40.9 ± 2.2	
	M1	42.2 ± 2.2	43.1 ± 1.7	40.5 ± 2.3	
	M2	39.3 ± 3.1	42.3 ± 1.7	38.8 ± 2.7	
	M3	35.6 ± 2.7	38.9 ± 2.0	46.2 ± 3.8	
Arm circumference (cm)	M0	32.6 ± 0.5	32.5 ± 0.8	32.8 ± 0.7	
	M1	32.4 ± 0.6	32.3 ± 0.8	32.2 ± 0.8	
	M2	32.1 ± 0.6	31.6 ± 0.7	31.6 ± 1.0	
	M3	31.1 ± 0.8	30.2 ± 1.1	34.3 ± 2.1	
Upper arm muscle	M0	22.9 ± 0.6	23.1 ± 0.7	23.2 ± 0.5	
circumference (cm)	M1	23.6 ± 0.7	23.0 ± 0.6	23.4 ± 0.5	
	M2	24.2 ± 0.7	23.4 ± 0.6	23.4 ± 0.8	
	M3	24.0 ± 0.8	22.6 ± 0.7	24.6 ± 1.2	
Arm muscle area (cm)	M0	35.1 ± 2.2	35.8 ± 2.3	35.8 ± 2.0	
	M1	37.7 ± 2.3	35.4 ± 2.0	35.9 ± 1.7	
	M2	39.7 ± 2.4	37.0 ± 2.1	36.1 ± 2.7	
	M3	38.9 ± 2.9	34.2 ± 2.4	40.4 ± 4.1	
Body fat (%)	M0	42.2 ± 0.8	41.6 ± 1.0	40.3 ± 1.3	
	M1	41.2 ± 0.9	42.1 ± 0.8	40.0 ± 1.6	
	M2	39.9 ± 1.2	41.4 ± 1.1	38.6 ± 1.6	
	M3	38.6 ± 1.1	40.6 ± 1.4	40.9 ± 3.2	
Body fat mass (kg)	M0	32.1 ± 1.5	29.5 ± 1.2	20.8 ± 1.1	0.047
	M1	30.3 ± 1.5	29.5 ± 1.2	27.3 ± 1.1	
	M2	28.3 ± 1.4	27.6 ± 1.1	26.3 ± 1.2	
	M3	27.6 ± 1.7	26.4 ± 1.5	29.3 ± 3.3	
Fat free mass (kg)	M0	44.0 ± 1.7	41.5 ± 1.7	42.7 ± 1.5	
	M1	43.2 ± 1.8	40.5 ± 1.5	41.2 ± 1.6	
	M2	42.8 ± 2.0	39.1 ± 1.2	41.6 ± 1.7	
	M3	43.9 ± 2.3	38.5 ± 1.8	42.0 ± 2.9	

Table 4. Mean duration of daily activity time before and after treatment program.

Type of activity	Activity time (h) in each group					
	Dexfenfluramine		Placebo		Control	
	Before	After	Before	After	Before	After
Rest	16.0 ± 0.8	11.8 ± 1.1*	15.0 ± 1.1	10.8 ± 0.9*	17.8 ± 0.8	13.5 ± 0.8*
Very light exercise	1.8 ± 0.3	2.8 ± 0.5	3.5 ± 0.5	4.0 ± 0.8	1.6 ± 0.4	2.1 ± 0.5
Light exercise	3.2 ± 0.6	4.8 ± 0.9	3.5 ± 0.7	6.2 ± 0.7*	2.0 ± 0.4	3.4 ± 0.7
Moderate exercise	2.4 ± 0.5	2.3 ± 0.4	1.4 ± 0.3	1.7 ± 0.6	1.9 ± 0.5	3.8 ± 0.8
Strenuous exercise	0.5 ± 0.2	1.8 ± 0.5*	0.6 ± 0.2	1.0 ± 0.2	0.6 ± 0.1	1.3 ± 0.2
Very strenuous exercise	0.02 ± 0.02	0.5 ± 0.2*	0.0 ± 0.0	0.5 ± 0.1	0.05 ± 0.0	0.5 ± 0.1*

The results are expressed as mean ± SEM
* $p < 0.05$ (paired t-test, Before VS After)
Activity rest = sleep or sitting / Very light exercise = standing, talking / Light exercise = typing, strollings
Moderate exercise = house work / Strenuous exercise = swiming, jogging / Very strenuous exercise = tennis, running.

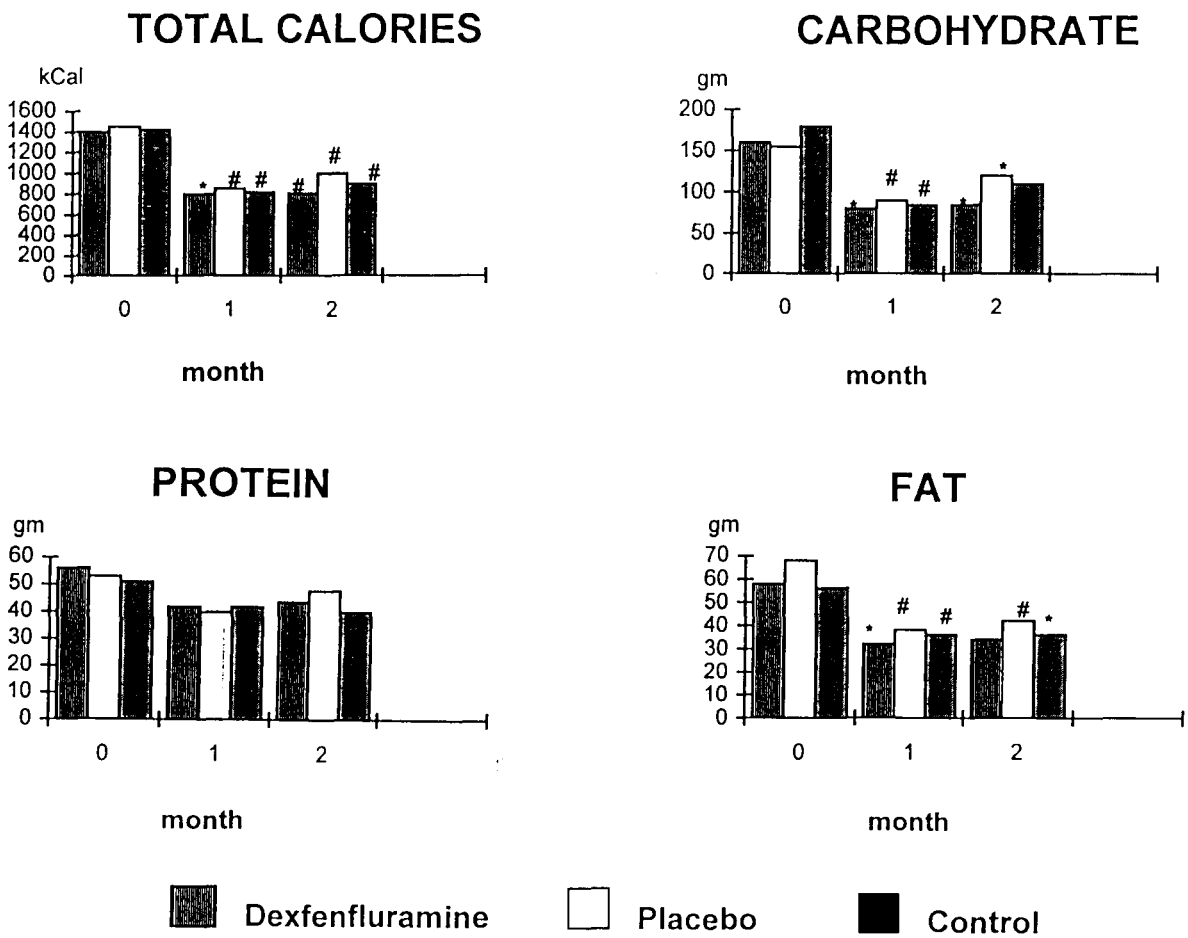

Fig. 1. Daily nutrient intake of the patients during the program.

Table 5. Changes of behavior in each group after treatment program.

Behavior modification	Group		
	Dexfenfluramine	Placebo	Control
1. Eating habits			
- keep a food diary		Y	
- avoid problem food	Y		Y
- leave the table immediately after eating	Y		
- put down fork between mouthful	Y		Y
- use smaller plates or bowls	Y		
- substitute an alternate activity for eating	Y		Y
- food selection			
a. meat - 5 servings / day			Y
b. fruits and vegetables - 3 servings/day			Y
c. grain (rice) - 6 serving/day	Y		
2. Exercise			
- take a long walk	Y	Y	
- 15 minute vigorous exercise, at least 3 times a week	Y		
3. Planning and problem solving			
- plan ahead what to eat	Y		
- try to change eating behavior rather than to lose weight	Y		Y
- "Failure is a lesson" attitude			Y
- self evaluation and alter the method if unsuccessful	Y		

y = significant changes of behaviors at the end of program assessed by Mc Nemar test

Table 6. Number of patients and mean different weight loss between months.

	Dexfenfluramine	Placebo	Control
During the first month	2.6 ± 0.2 (15)	1.6 ± 0.2 (15)	1.1 ± 0.3 (15)
During the second month	3.9 ± 0.3 (14)	1.1 ± 0.2 (12)	1.6 ± 0.3 (13)
During the third month	2.8 ± 0.2 (9)	0.6 ± 0.8 (8)	0.2 ± 0.5 (4)

Unit = kg; Results are expressed as mean ± SEM

Table 7. Serum cholesterol, triglycerides, HDL and LDL in obese subjects during the program.

	Dexfenfluramine	Placebo	Control
Cholesterol (mg/dl)			
M0	213.8 ± 16.1	217.5 ± 9.9	209.9 ± 7.6
M2	188.9 ± 10.3*	204.0 ± 11.0	217.9 ± 8.3
Triglycerides (mg/dl)			
M0	142.3 ± 22.1	132.7 ± 9.1	131.0 ± 17.7
M2	108.9 ± 16.9*	129.7 ± 13.2	137.9 ± 17.7
HDL-cholesterol (mg/dl)			
M0	54.5 ± 3.5	54.2 ± 3.2	48.4 ± 1.9
M2	48.6 ± 4.6	47.9 ± 2.9	55.2 ± 3.4
LDL-cholesterol (mg/dl)			
M0	134.0 ± 11.5	130.1 ± 10.5	139.6 ± 5.7
M2	111.5 ± 11.2	132.1 ± 9.3	133.8 ± 7.3

Results are expressed as mean ± SEM.
* $p < 0.05$ as compared with M0

dexfenfluramine also acts by inducing increased peripheral utilization. A possible way to explain this phenomenon could be the effects of dexfenfluramine on increasing thermogenesis[16-22].

There were no significant differences in the changes of blood pressure, heart rate, and the laboratory parameters among the patients in all 3 groups (fasting blood sugar, uric acid, hematological, renal and liver function test). It is apparent that dexfenfluramine displays a favorable acceptability profile in regard to the laboratory parameters.

Fifty per cent of the subjects in the control group dropped-out predominantly in the first week. They decided not to enroll in the program right after they became aware of details of the program. Some problems identified included the classes were held during the normal working hours, unable to attend class regularly or vacations had already been planned during the program period. A few thought that it was useless without pharmacotherapy and they had no will power to carry out the program. However, those who continued the program without any drug were partly successful in terms of weight reduction and behavioral change and were even better than the placebo group. This study was conducted before the discovery of cardiac valvulopathy in association with dexfenfluramine therapy. It was on a short term (3 months) basis according to the recommendation[10]. Two years after the completion of the study, there have been no complaints or complications reported by any subject receiving dexfenfluramine.

Table 8. Per cent drug's compliance of obese patients.

Month of treatment	Dexfenfluramine	Placebo
1	86 ± 5	88 ± 4
2	92 ± 4	91 ± 5
3	87 ± 9	88 ± 3

Unit = %; Results are expressed as mean ± SEM

Attrition and compliance

At the end of the program, there were 4 patients in group D and 5 patients in group P who prematurely discontinued the drugs and the reasons were nausea, fatigue, insomnia, diarrhea, personal problems or inadequate response. Most of them had the symptoms and discontinued the drugs within 1 month. 30 per cent, 35 per cent and 50 per cent of the patients in group D, P and C respectively were lost to follow-up. Placebo effect has the beneficial effect for the patient to better adhere to the program than the control group. The effective anoretic drug makes the patient both adhere and practice the program more effectively.

The per cent drug compliance and incidence of side effects is shown in Table 8 and 9 respectively.

We, therefore, conclude that the treatment of overweight or obese patients particularly those with no will power with dexfenfluramine for 3 months in addition to a behavioral program leads to a considerable additional weight loss, most likely due to increased thermogenesis. Exaggerated weight loss by dexfenfluramine shows body composition changes to decreased fat composition, decreased cholesterol and triglycerides levels and a drive from higher body weight loss which acts as a reward. It makes them appreciate the efforts and

Table 9. Side effects of drug.

Symptoms	Dexfenfluramine		Placebo	
	N	%	N	%
Dry mouth	6	30	4	23.5
Diarrhea	2	10	1	5.8
Insomnia	3	15	1	5.8
Palpitation	-	-	2	11.8
Headache	-	-	1	5.8
Fatique	2	10	2	11.8
Polyuria	-	-	2	11.8
Nausea	1	5	-	-

boosts them to practice the program. The medication must be restricted to no longer than 3 months to avoid any consequences.

The differences in minor side effects between group D and P are negligible. The absence of serious side effects renders dexfenfluramine an efficient component of weight management for overweight / obese patients.

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ผลเพิ่มความร้อนในร่างกายจากยาเด็กซ์เฟ็นฟูรามีน

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ศึกษาคนอ้วน 50 รายที่มีดัชนีมวลสารของร่างกายมากกว่า 25 กก/ตารางเมตร^2 แบ่งออกเป็น 3 กลุ่ม แบบไม่ทราบทั้งสองฝ่าย โดยกลุ่ม (ดี) ได้ยา dexfenfluramine 30 มก./วัน กลุ่ม (พี) ได้ยาหลอก และกลุ่มควบคุม (ซี) ไม่ได้รับยาอะไรทั้งสิ้น จำนวนผู้ป่วยในกลุ่ม ดี, พี และซี คือ 18, 18, 19 ตามลำดับ โดยผู้ป่วยทุกคนได้เข้าโครงการปรับพฤติกรรมในช่วง 2 เดือนแรก ซึ่งมีการบันทึกทุกวันเกี่ยวกับลักษณะนิสัยการกิน ออกกำลังกาย ความคิด สังคมกับคนรอบข้างและโภชนาการ ตลอด 3 เดือน โดยผู้ป่วยต้องพบผู้วิจัยเพื่อส่งบันทึกให้กับผู้วิจัยในการติดตามผลการรักษาและปรับปรุงพฤติกรรมทุกสัปดาห์ ผลการรักษาเมื่อครบ 3 เดือนพบว่าทั้ง 3 กลุ่ม ลดกิจกรรมแบบพักผ่อนและเพิ่มการออกกำลังกาย ($P < 0.05$) และลดการกินอาหารประเภทคาร์โบไฮเดรตและไขมัน ($P < 0.05$) ทั้ง 3 กลุ่มมีน้ำหนักลดลง ค่าเฉลี่ยสะสมที่ลดน้ำหนักในกลุ่มดี พี, และซี คือ 8.3 $\pm$ 0.7, 3.3 $\pm$ 1 และ 2.9 $\pm$ 0.7 น้ำหนักที่ลดในกลุ่มดีมากกว่ากลุ่มพีและซี คือ 5 ก.ก. และ 5.4 ก.ก. น่าจะมาจากการเพิ่มความร้อนในร่างกายของยา มีเพียงคนไข้ในกลุ่มดีเพียงกลุ่มเดียวเท่านั้นที่แสดงว่ามีการลดลงของไขมันใต้ผิวหนังบริเวณไบเซพ ไตรเซพและไขมันร่างกายอย่างสม่ำเสมอและมีนัยสำคัญที่ $P < 0.05$ ไม่พบการเปลี่ยนแปลงอย่างมีนัยสำคัญในแง่ความปลอดภัยเกี่ยวกับความดันโลหิต, การเต้นของหัวใจ, ผลข้างเคียง, โลหิตวิทยา, ไขมัน และการตรวจทางชีวเคมีอื่น ๆ ในผู้ป่วยทั้ง 3 กลุ่ม

คำสำคัญ : เพิ่มความร้อนในร่างกาย, ความเป็นไปได้, เด็กซ์เฟ็นฟูรามีน

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