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ALTERNATIVE MEDICINE ALERT™

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Metabolife 356® for Weight Loss

By E-P. Barrette, MD

OBESITY IS ALL TOO COMMON. UNLIKE DIABETES AND HYPERTENsion, few drugs work well for this condition. The available prescription agents have significant adverse effects and meager, temporary benefit, if any. Frustrated by diet drugs' ineffectiveness, physicians often avoid discussing obesity altogether. Many patients have lived with years of frustration themselves—failed diets, failed diet pills, and failed attempts to exercise enough to see a benefit.

It is not surprising that many have looked to herbal supplements for an answer. Supplement stores have expansive sections devoted to weight loss products. Metabolife 356® has become the most successful herbal product for weight loss and has garnered some publicity, having been recently featured on a prime time TV news program.[1] To providers, however, the primary issues remain safety and effectiveness. Although some trials suggest modest weight loss with ephedrine and caffeine, the main components of Metabolife 356, legitimate concerns regarding the safety of ephedrine products exist. Also, the benefit of Metabolife 356, a complex mixture of many herbs, remains undocumented.

Background—Rx Agents

With the failure of dietary modification and exercise in many obese patients, pharmacologic agents have been the hoped-for solution. When weight loss was noted as a side effect of dextroamphetamine, prescriptions of amphetamines for weight control increased. Serious problems with tolerance and dependence resulted in a movement away from these and other agents. Although several drugs (phentermine and mazindol, among others) remained available in the 1980s, lingering concerns regarding their long-term safety and efficacy kept them out of the mainstream of medicine.

In the early 1990s two events reawakened the interest in the pharmacologic management of obesity: the long-term success of phentermine/fenfluramine combination (phen-fen) in a single trial and a greater understanding of the genetic basis of obesity (e.g., leptin). The use of phen-fen increased dramatically. However, with the discovery of valvular abnormalities in users of fenfluramine and dexfenfluramine, along with the development of primary pulmonary

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hypertension in users, both drugs were withdrawn in 1997. The release of newer agents (e.g., sibutramine and orlistat) has not persuaded many physicians to prescribe drugs for obesity again.[2]

Background—Metabolife

With the absence of substantial competition from prescription agent manufacturers, supplement suppliers aggressively market products for weight reduction. Metabolife 356 projects retail sales for this year of $850-900 million. Mike Ellis, CEO of Metabolife International, Inc., developed this supplement to increase energy levels in his father who had bone cancer. The combination of herbs, minerals, and vitamins was selected to decrease adverse effects and improve quality of life.

Ellis states that he was "dumbfounded" when others taking the supplement, which contains ephedrine, caffeine, and other compounds, noticed weight loss.[3] While it is not generally known in the United States, ephedrine combined with caffeine has been used for more than 25 years in Denmark for weight loss. In 1972, a general practitioner there noted that asthmatic patients taking a combination of ephedrine, caffeine, and phenobarbitol had unexplained weight loss.[4] By 1977 the "Elsinore pill," named after the town where the association was found, was used by 70,000 patients for weight control.

An increased number of dermatological reactions, some serious, among users resulted in a warning by the Danish Institute of Health. The skin reactions were attributed to phenobarbitol, which is known to cause dermatologic reactions in 1-2% of users. In 1981, researchers at the University of Copenhagen published the first trial of the "Elsinore pill" minus the phenobarbitol.[4] Since then, they have published a series of weight control trials involving ephedrine and caffeine, both alone and together.

Pharmacology

Ephedrine is a sympathomimetic drug, structurally similar to epinephrine and methamphetamine. It has fewer CNS effects than do amphetamines because it has a lower lipid solubility than amphetamines. It has both alpha (nasal decongestion, increase blood pressure) and beta (increased cardiac contraction, bronchodilator) receptor effects. Caffeine, a methylxanthine, is structurally similar to theophylline. It is a CNS stimulant and a diuretic. The half-life of ephedrine is six hours; for caffeine, it is three to seven hours.

Mechanism of Action

Ephedrine stimulates the metabolic rate via norepinephrine released from sympathetic nerve endings. The proposed mechanism involves both an anorectic effect via adrenergic pathways in the hypothalamus and a thermogenic effect via increased metabolic rate. Both animal and human studies of ephedrine alone demonstrate a thermogenic effect. The addition of caffeine to ephedrine appears to blunt the negative feedback control on the release of norepinephrine in two ways. Caffeine turns off self-regulation at two points, as it both inhibits phosphodiesterase (therefore slowing the degradation of cyclic AMP within the cell) and inhibits adenosine release into the synaptic junction.[5] Ephedrine plus caffeine increased the fasting metabolic rate twice as much as ephedrine alone in a human study.[6]

Animal Studies

The manufacturer of Metabolife states that acute, subacute, toxicology, and histopathology studies on animals showed Metabolife 356 to be safe. These studies are unpublished.

Clinical Studies

There are no published trials of Metabolife 356. Metabolife International posted on a Web site the full text of a 20/20 interview concerning its product,[3] including an abstract of a 24-hour metabolic study done at

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Conflict of Interest Disclosure

Physicians have reported the following relationships with companies related to the field of study covered by this CME program. Dr. La Puma is Director of C.H.E.F. Research. Dr. Ofman has the following relationships: Consultant for Zynx Health, Inc., Cedars-Sinai Health System; Research for Astra USA, Johnson & Johnson, Janssen. Dr. Barrette, Dr. Cirigliano, Dr. deLeon, Dr. Schiedermayer, Dr. Sorrentino, and Dr. Szapary have no relationships with companies related to the field of study covered by this CME program.

Table 1

Controlled trials of ephedrine with caffeine for weight loss

Study	# Enrolled/ # Completed	Duration (Weeks)	Intervention (mg)	Weight Loss (kg)
Astrup[13]	180/141	24	P	13.2 +/-6.6
			E/C 20/200 tid	16.6 +/-6.8, P < 0.01
			E 20 tid	14.3 +/-5.9, P > 0.2
			C 200 tid	11.5 +/-6.0, P > 0.2
Daly[12]	29/24	8	P	0.7 +/-0.6
			E/C/A 75-150/150/330 tid (E dose increased after 4 weeks)	2.2 +/-0.7, P = 0.004
Malchow-Moller[4]	132/108	12	P	4.1
			E/C 40/100 tid	8.1, P < 0.01
			Diethylpropion 25 tid	8.4, P < 0.01
Cesari[10,21]	22/20	16	P	7.6 +/-4.8
			E/C 50/100 tid	9.2 +/-4.2, P > 0.05
			E 50 tid	10.2 +/-3.3, P > 0.05
Mancini[11]	41/31	8	P	2.2 +/-2.8
			E/C/Am 22/20/50 tid	4.5 +/-3.7, P < 0.05
Breum[14]	103/86	15	E/C 20/200 tid	8.3 +/-5.2, P = 0.12
			Dexfen 15 bid	6.9 +/-4.3

Abbreviations: P = placebo, E = ephedrine, C = caffeine, A = aspirin, Am = aminophylline, Dexfen = dexfenfluramine

Vanderbilt University. This double-blind, placebo-controlled crossover study included 17 moderately obese subjects who took two tablets of Metabolife 356 tid or placebo for one day. The 24-hour energy expenditure was 4.1% greater with Metabolife 356 than placebo (P = 0.02).[3] This appears to confirm the study of Astrup, discussed below.[7] The Web site also refers to an unpublished eight-week randomized, double-blind, placebo-controlled study measuring weight loss.

Although minimal evidence exists for the effectiveness of synthetic ephedrine with caffeine, which are in ma huang and guarana respectively, multiple searches of PubMed, MEDLINE, and references for CAM and herbal therapies were unsuccessful in finding any adequate clinical data supporting the use of any other ingredient (including chromium) in Metabolife 356, either alone or in combination, for weight loss.[8] Trials of synthetic ephedrine with caffeine are discussed below.

Astrup et al performed a double-blind, placebo-controlled trial in 16 obese women to monitor changes in body composition and energy expenditure. Over eight weeks all maintained a 1,000 Kcal/d diet while half received either placebo or ephedrine (20 mg) with caffeine (200 mg) tid. Weight loss occurred equally in both arms (mean loss ephedrine/caffeine 10.1 +/-0.4 kg, placebo 8.4 +/-1.2 kg, P = NS). However, the ephedrine/caffeine group lost 4.5 kg more body fat and 2.8 kg less fat-free mass. Respiratory chamber measurements of the 24-hour energy expenditure in the placebo group decreased 13% but only 8% (P = 0.044) in the ephedrine/caffeine group. The authors estimated that 20% of the weight loss with ephedrine/caffeine was because of increased energy expenditure while 80% was because of the anorectic effect.[7] In another study, this group of investigators demonstrated synergistic effects when the doses of ephedrine and caffeine were 20/200 mg but only additive effects if the doses were 10/200 mg or 20/100 mg.[9]

Five double-blind randomized, controlled clinical trials comparing ephedrine/caffeine combinations vs. placebo in obese subjects for weight loss have been published. (*See Table 1.*) Two are reported in abstract form only[10,11] and three enrolled very small numbers. Study duration ranged from eight to 24 weeks. Doses varied widely: ephedrine 20-150 mg tid, caffeine 20-200 mg tid. One trial included aspirin with ephedrine/caffeine, while another added aminophylline to ephedrine/caffeine. Only 15% of the subjects in the combined trials were male. Mean body mass index (BMI) at entry was 33.1-38.5 kg/m^2. Only one trial attempted to control dietary caffeine intake by limiting subjects to two cups a day.[12]

Four of the five trials showed a benefit of ephedrine/caffeine over placebo, including the largest and longest study. In this study,[13] patients were instructed to maintain a 1,000 Kcal/d diet. They also continued to consume their baseline five to seven cups of caffeine a day, which may have added up to 500 mg of caffeine daily. In this well-designed trial, ephedrine/caffeine achieved 3.4 kg of weight loss beyond the placebo arm. An additional double-blind randomized trial compared ephedrine/caffeine combination to dexfenfluramine without a placebo control.[14] Weight loss was similar at 15 weeks but a subgroup analysis of patients with a BMI > 30 kg/m^2 at entry showed a slight benefit with ephedrine/caffeine (ephedrine/caffeine 9.0 +/-5.3 kg vs. dexfenfluramine 7.0 +/-4.2 kg, $P < 0.05$).

Adverse Effects

Ephedrine acts as a sympathomimetic and has many known adverse effects: increased blood pressure (which can be dramatic), palpitations, tachycardia, chest pain, coronary spasm, psychosis, mania, tremor, insomnia, nervousness, vertigo, headache, diaphoresis, urinary retention, dry mouth, and nasal mucosa. Chronic use has been linked to cardiomyopathy. Caffeine may cause nervousness, insomnia, tremors, palpitations, dyspepsia, and gastroesophageal reflux.

In the clinical studies listed in Table 1, most of these adverse effects were observed. In two of the larger trials, side effects were reported in 60% and 54% of the ephedrine/caffeine arm compared to 24% in the placebo arm.[13,14] Among the total of 507 subjects from the studies in Table 1, syncope was seen in two subjects and severe hypertension (185/125 mm Hg) in one. Note that subjects with hypertension, cardiovascular disease, diabetes, psychiatric disorders, pregnancy, and lactation were excluded from these studies. After stopping ephedrine/caffeine, withdrawal symptoms of headache and fatigue were seen in 65%.

The FDA has received hundreds of reports of adverse events associated with ephedrine supplements including several deaths.[15] In 1997, after an extensive review, the FDA proposed to limit ephedrine to less than 8 mg per tablet, less than 24 mg per day, for no more than seven days.[16] The supplement industry has ignored these limitations, and no limit exists today. Notably, some supplement labels are self-contradictory, with some recommending up to six tablets of their preparation daily, providing more than the daily limit of 100 mg of ephedrine stated elsewhere in a warning on the same bottle.

There are concerns regarding the other ingredients in Metabolife 356:

- Nettle leaf and sarsaparilla are diuretics.[17]
- Several adverse events with Siberian ginseng, which is not a ginseng but more accurately called eleuthero, are now felt to be caused by other plants incorrectly labeled as Siberian ginseng.
- Damiana has been reported to have aphrodisiac properties for more than 100 years.[18] However, there is no evidence to support this claim, and the Commission E lists it as an unapproved herb.
- Both royal jelly and bee pollen are associated with many claims and few clinical trials. Bee pollen products have been reported to result in severe allergic reactions.
- Chromium picolinate use and renal failure may be related.[19,20]

Contraindications

Ephedrine is contraindicated in those with hypertension, cardiovascular disease, and hyperthyroidism and in pregnant and nursing women. Its use in those with benign prostatic hyperplasia, glaucoma, diabetes, anxiety disorders, and seizures should be closely monitored.

Drug and Herb Interactions

Willow bark may decrease the renal excretion of ephedrine. MAO inhibitors and yohimbine may greatly increase the sympathomimetic effect of ephedrine and should not be used together with ephedrine or Metabolife.

Formulation

Metabolife 356 is a complex blend of many ingredients. Its active ingredients are most likely the alkaloids from ma huang (primarily ephedrine) and from guarana seed (primarily caffeine). Metabolife 356 also contains chromium picolinate, plus 15 other ingredients. (*See Table 2.*) Its supply of vitamin E, magnesium, zinc, and chromium is modest and easily achieved with a multivitamin or mineral supplement. The remaining ingredients are noted to add up to 728 mg but exact amounts are not provided, which makes it difficult for competitors to duplicate and for consumers to analyze.

Cost

Retail price, advertised on the company's Web site, is $49.95 for a bottle of 90 tablets, although those taking it for weight loss and weighing more than 180 lbs will likely use six tablets a day. Many Web pages of Metabolife 356 distributors advertise a price of $35.95 per bottle. A visit to a supplement store will reveal a score of products containing some combination of ma huang, guarana, chromium picolinate, willow bark (presumably to boost the serum level of ephedrine), and *Garcinia cambogia* along with many other herbs, vitamins, and minerals.

Several companies are clearly trying to reproduce Metabolife's formula. Cost comparisons are not possible.

Conclusion

A serendipitous clinical observation in 1972 by a Danish general practitioner led to a series of publications on ephedrine and caffeine, both alone and together, as a thermogenic agent. These studies do suggest that ephedrine/caffeine support weight loss. However the sum of all the trials yielded only 507 subjects; two trials have been reported in abstract form only; and three had very low enrollment. Various doses and additives make comparison difficult. The best evidence suggest that six months of ephedrine/caffeine, 20/200 mg tid, will result in 3.4 kg (7.5 lbs) beyond a 1,000 Kcal diet alone in a motivated obese patient without most major medical problems.

The adverse effects of ephedrine are well known and may be serious. Some patients appear to be especially sensitive to ephedrine. Many common medical conditions associated with obesity may be worsened with ephedrine. At present there is no evidence that the additional ingredients in Metabolife 356 will provide any additive clinical benefit toward weight loss or will protect from any adverse effect. No adequate data exist to support its chronic use as a weight loss agent. Although Metabolife International claims its product is safe, these claims are based on unpublished animal studies.

Table 2

Metabolife 356® ingredients

Ingredient	Amount per tablet
Ma huang	equivalent 12 mg ephedrine
Guarana seed	equivalent 40 mg caffeine
Vitamin E	6 IU
Magnesium chelate	75 mg
Zinc chelate	5 mg
Chromium picolinate	75 mcg
Lecithin	*
Damiana leaf	*
Ginger root	*
Goldenseal aerial part	*
Gotu kola aerial part	*
Nettle leaf	*
Sarsaparilla root	*
Siberian ginseng root	*
Bee pollen	*
Bovine complex	*
Royal jelly	*
Spirulina algae	*

*proprietary information

Source: FAQ. Web site presented by Metabolife International, Inc. Available at: www.metabolife.com/b_356_faq.html. Accessed: December 6, 1999.

Recommendation

Although the currently available prescription agents for obesity have their own limitations, e.g., costs, meager benefit, and significant adverse effects, there is no evidence that Metabolife is any better and may be worse. Ephedrine products should not be used in patients with hypertension, cardiovascular disease, hyperthyroidism, benign prostatic hyperplasia, glaucoma, diabetes, anxiety disorders, seizures, or by women who are pregnant or lactating. Based on the modest benefit, the known risks, and the lack of long-term safety data, Metabolife 356 is not recommended. ❖

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Plant Sterols and Stanols in the Treatment of Hypercholesterolemia

By Philippe O. Szapary, MD and Michael D. Cirigliano, MD, FACP

CARDIOVASCULAR DISEASE (CVD) IS THE NUMBER ONE cause of death in industrialized nations, and within CVD, coronary artery disease (CAD) is still the leading cause of death, especially in men over 45 years and women over 65 years old. Serum cholesterol is a potent marker for the development of clinical CAD: A 10% reduction in cholesterol reduces the risk of a coronary event by 18%, and the risk of CAD death by 10%.[1] The most recent National Cholesterol Education Program (NCEP) estimates that 30% of American adults have elevated serum cholesterol levels that require non-pharmacologic intervention, while 7% merit cholesterol-reducing drugs.[2] Naturally-occurring plant sterols (phytosterols) and their derivatives (stanols and stanol esters) represent a class of biologically active compounds that have been shown to reduce serum cholesterol. Many clinical trials have shown a reduction in low-density lipoprotein (LDL-C) levels by up to 14%.[3] Based on current evidence, phytosterols and their derivatives are useful, non-pharmacologic adjunctive agents in reducing elevated serum cholesterol levels, especially in those who do not need to reduce their total calorie intake.

History

Since the 1950s, it has been recognized that adding the phytosterol ß-sitosterol to the diet of cholesterol-fed chickens and rabbits lowered their cholesterol levels.[4] Since then, more than 100 reports describing the cholesterol-lowering efficacy of plant sterols and stanols in more than 18,000 human subjects have been published.[4]

Source and Identification

At least 44 sterols from seven different plant classes have been identified. The most abundant are ß-sitosterol and campesterol.[5] Phytosterols are found in trees (especially pine), soybeans, corn, squash, vegetable oils, and grains. Currently, the largest source of commercial sterols comes from "tall oil," a byproduct of the paper pulping industry. The typical Western diet contains approximately 160-180 mg/d of phytosterols, compared to vegetarian diets, which contain approximately 370-400 mg/d of phytosterols.[5]

While initial studies used large doses of naturally-occurring plant sterols, more recent studies have focused on lower doses of processed sterols called stanols and their esters. Unlike sterols, stanols are virtually absent from typical diets. Both esterified sterols and stanols have been incorporated into fatty foods such as mayonnaise, margarine, and salad dressing. In general, these fatty foods contain < 1 g/serving of unsaturated trans fatty acids, which are associated with an increased risk of CAD. Processed food products containing sterol and stanol esters are often marketed in the United States and Europe as cholesterol-lowering functional foods.

Pharmacology

Structurally, phytosterols are very similar to cholesterol. They differ in their chemical structure only by the presence of an additional ethyl group (sitosterol) or methyl group (campesterol) at the C-24 position of the side chain.[6] These phytosterols can then be saturated by hydrogenation to yield the 5 α-stanols such as sitostanol and campestanol. Hydrogenation produces primarily cis fatty acids, but a small amount of trans fatty acids is also formed (< 1.5% of the total fat per serving). Finally, both sterols and stanols can be esterified with fatty acids from vegetable oils (usually canola) to form sterol esters and stanol esters, which can then be more readily incorporated into foods.

Thus, there are two major classes of hypolipidemic compounds: sterols and stanols. The major difference between them are that sterols are found in nature and are systemically absorbed. Stanols on the other hand, because of hydrogenation, are not systemically absorbed and are not found in nature in substantial amounts. Most of the published research has been done with stanols.

Mechanism of Action

The primary mode of action by which sterols and stanols reduce serum cholesterol is by decreasing cholesterol absorption from the small intestine.[7] Both these agents have a higher affinity than cholesterol for mixed bile salt micelles formed in the small bowel. By displacing cholesterol from these micelles, sterols and stanols decrease cholesterol absorption and subsequently, serum cholesterol as well.[7]

One recent study quantified this effect, showing that 3 g of sitostanol ester decreased both dietary and biliary cholesterol absorption by 44% and 37% respectively.[8] This same study found that the increased fecal excretion of cholesterol was accompanied by a compensatory increase in cholesterol synthesis by 39%. Other studies have shown that patients with high intestinal cholesterol absorption and low endogenous cholesterol synthesis respond best to phytosterols.[9] To date however, there are no readily available serum markers to distinguish patients whose hypercholesterolemia is secondary to enhanced absorption of intestinal cholesterol vs. increased synthesis of cholesterol.

Clinical Trials

Searching MEDLINE, PubMed, the Cochrane Collaboration database, and CINAHL, we identified more than 20 randomized, controlled trials (RCT) since 1976 evaluating the safety and efficacy of various sterols, stanols, and stanol esters in the treatment of hyperlipidemia. The majority of RCTs used plant stanol esters (PSE) incorporated into margarine. Of note, some of these studies dealt specifically with children, pre- and postmenopausal women, diabetics, patients with known CAD, and patients already taking HMG-CoA reductase inhibitors (i.e., statins).

The largest and longest trial was a double-blind RCT of 153 subjects with mild hypercholesterolemia defined as total cholesterol (TC) > 216 mg/dL.[3] In this primary prevention trial, subjects were randomized into three groups: control margarine, margarine + 1.8 g sitostanol ester, or margarine + 2.6 g of sitostanol ester. After 12 months of therapy, the average TC decreased by 0%, 9%, 11% in the control, 1.8 g, and 2.6 g groups, respectively. More importantly, LDL-C decreased by 1%, 12%, and 16%, respectively, over the same period without any significant change in high density lipoprotein (HDL-C) or triglycerides (TG).

In a smaller RCT, 22 postmenopausal women with angiographically documented CAD who were not taking other cholesterol-lowering medication were randomized in a crossover fashion to 3 g sitostanol ester-containing margarine or placebo for seven weeks each.[8] In this study, PSE decreased TC by 13% and LDL-C by 20%. The authors also reported 10 other similar women who had been on a stable dose of simvastatin for one year who received 3 g of PSE for 12 weeks in an open trial. Combination therapy augmented the LDL-C lowering effect by 16% compared to simvastatin alone, which decreased LDL-C by 35%.[8] Although the number of statin-treated subjects was small and the subset not randomized, another small RCT in type II diabetics confirmed the added benefit of PSE in combination with statins. In this RCT, the addition of 3 g of PSE to 40 mg of pravastatin in controlled diabetics decreased LDL-C by a modest additional 4% (46% statin + PSE vs. 42% statin alone) after seven weeks.[10]

Finally, a European RCT of 95 subjects directly compared the efficacy of a PSE margarine (Benecol®) against soybean, rice bran, and shea nut-enriched margarines.[11] The soybean margarine primarily contained esterified sterols, making it similar to the American product Take Control™. At the end of only 3.5 weeks, both Benecol and the soybean margarine when used twice daily significantly and equally reduced LDL-C by 13%, while the other test margarines had no significant lipid lowering effect. These results imply that when used twice a day, both Benecol and Take Control margarines are probably equally effective.

Adverse Effects and Drug Interactions

In all RCTs, sterol and stanol enriched foods at up to 6 g/d were well tolerated, without significant side effects

and little dropout at up to 12 months. Over 90% of study participants in one study rated the palatability and texture of a PSE margarine as "good" or "all right."[12] In addition, these studies do not report laboratory abnormalities. There are no known drug-PSE interactions. In vitro and in vivo animal studies inconsistently suggest that sitosterol has estrogenic effects and may affect fertility.[12] There are no data on its use in pregnancy. Studies have shown that ß-sitosterol is effective in treating benign prostatic hypertrophy, raising the possibility of an estrogenic effect in humans.[13] The use of sterols and stanols has been associated with a decrease in serum measures of fat soluble vitamins D, E, A, and K.

These findings however, have not been consistent across RCTs, primarily because tested products have not always been fortified with vitamins. Because these vitamins are transported by lipoproteins, a decrease in cholesterol may also decrease the absolute vitamin levels, while lipid standardized values remain stable. However, Weststrate and Meijer found a decrease of both absolute and lipid-standardized α- and ß-carotenes by 22% and 19% respectively despite vitamin A fortification.[11] Another eight-week RCT using vitamin A-fortified margarine found a decrease in absolute values of ß-carotene but not in the carotene/cholesterol ratio.[14] Since carotenoids themselves may have positive health effects, this slight decrease of carotene levels needs to be addressed in longer studies.

Studies have not found significant decreases in levels of vitamins D and E when standardized for the reduction in serum cholesterol. A rare, autosomal recessively inherited dyslipidemia called sitosterolemia is characterized by markedly increased absorption of phytosterols in the gut, leading to elevated serum sterol levels, and is clinically manifest by xanthomatosis and premature atherosclerosis. While there are fewer than 50 reported cases, affected patients should limit their dietary intake of sterols. In these patients, unabsorbed stanols should not cause a problem. In normal individuals, one epidemiologic study suggested that high serum phytosterol levels were associated with premature CAD.[15] However, a recent analysis of the Scandinavian Simvastatin Survival Study found that higher serum levels of phytosterols did not increase the incidence of coronary events in those patients with CAD assigned to placebo.[16]

Formulations

In the United States, plant sterols and stanols are currently available in margarine spreads, salad dressings, and tablets. (*See Table 1.*) Soybean-derived sterol esters are the active ingredient in Take Control, while nonabsorbable wood-derived stanol esters are the active ingredient in Benecol products. Currently, Take Control comes only in one regular spread and three salad dressings, with a soybean/canola and sunflower oil base. Benecol is available as a regular and light spread with a

Table 1

Comparison of commercially available sterol and stanol products

Product	Serving Size and Active Ingredient	Manufacturer's Suggested Use	Retail Cost	Calories Per Serving	Total Fat /% Daily Value from Fat
Benecol® Spread (McNeil)	1.5 tsp (1.5 g sitostanol ester)	1 pat tid	$4.99/21 servings	45	5 g/14%
Take Control™ Spread (Lipton)	1 tbsp (1.12 g sitosterol ester)	1 tbsp qd to bid	$3.79/16 servings	50	6 g/9%
Benecol® Light Spread	1 tsp (1.5 g sitostanol ester)	1 pat tid	$4.99/21 servings	30	3 g/5%
Benecol® Ranch Salad Dressing	2 tbsp (1.5 g sitostanol ester)	2 tbsp	$4.99/8 oz	130	13 g/20%
Take Control™ Reduced Fat Ranch Dressing	2 tbsp (1.12 g sitosterol esters)	2 tbsp	$3.79/8 oz	100	8 g/13%
Cholestatin™ (Futurebiotics)	380 mg phytosterols/ tablet	1 pill with each of three daily meals	$12.95/90 tablets	0	NA

Source: Based on authors' phone conversations wtih company representatives and information from the following Web sites: www.benecol.com, www.takecontrol.com, www.futurebiotics.com, online mail-order sites

soybean/canola oil base, as well as four salad dressings. More products such as PSE snack bars are anticipated later next year.

To avoid potential fat-soluble vitamin deficiencies, all products are fortified with vitamins A and E. Although it is possible to sauté and fry with the regular PSE margarine products (Benecol), the plant sterol products (Take Control) and the lower calorie PSE spread (Benecol Light) are not recommended for this purpose, as plant sterols and PSE in the low-fat product break down with extremes of temperature.

Studies of up to one year's duration have shown that sterol and PSE-containing margarines, when substituted for regular margarine, have not resulted in weight gain.[3,8,11,14] This may not be true with the higher fat salad dressings which have never been studied in RCTs. The enriched spreads used in these studies contained low levels of saturated fat (0.5-1 g/serving) and trans fatty acids (0.3-0.8 g/serving), values that are similar to commercially available soft margarines such as Promise™.

Dosage

Recommended dosages and available formulations are summarized in Table 1. Esterified sterols are also available in pill form to be ingested with meals. At the recommended doses of 1,200 mg/d, some studies have shown a benefit to these agents, although no published RCTs have specifically addressed the value of sterols in pill form.[9] In the United States, there are no currently available stanols in pill form.

Conclusion

Plant sterols and stanols actively and reliably reduce TC and LDL-C by 10-15% in a variety of patient populations. Sterol esters and stanol esters when used bid or tid are probably equally effective and well-tolerated. Because of their proven efficacy and excellent safety profile, sterols and stanols deserve to be incorporated into future NCEP guidelines as part of Step I and II diets or patients with above-target LDL-C. More data are needed on the long-term effects of these agents on carotenoid levels. The potential hormonal effects of sterols, and the possible relationship between serum sterol levels and the development of CAD needs to be studied further in larger clinical trials. Promising early data suggest that PSEs are also safe and effective in combination with statins in lowering serum cholesterol levels.

Recommendation

Plant sterols and stanols should be first-line non-pharmacologic adjuncts to diet and exercise in all patients who do not need to lose weight and who have mild-to-moderate hypercholesterolemia. Because stanols are not absorbed, they might provide an advantage over sterols whose systemic hormonal effects are not yet known. Neither plant sterols nor the low-fat PSEs can be used in cooking. Like other fatty foods, sterol and stanol enriched foods are calorie-dense, and should be substituted for currently used fatty foods. Simply adding these functional foods to a diet already high in fat will likely negate the cholesterol lowering effect of these products. ❖

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Note to Readers

American Health Consultants is pleased to introduce a new monthly addition to *Alternative Medicine Alert*—Clinician Fact Sheets, edited by Mary L. Hardy, MD, Medical Director at Cedars-Sinai Integrative Medicine Medical Group in Los Angeles, CA. These two-page quick-reference sheets will cover a variety of topics related to complementary and alternative medicine.

The 1999 *Alternative Medicine Alert* index is now available. You may download the full index by going to http://www.altmednet.com/titles/ama.html and select "Browse 1999 Topic Index." ❖

CME Questions

1. The most likely active ingredients in Metabolife 356® for weight loss are:
   a. ma huang and guarana.
   b. ma huang, guarana, and damiana.
   c. ma huang and bee pollen.
   d. ma huang, guarana, and chromium picolinate.

2. An obese patient comes to you for advice regarding herbal weight loss products. Her BMI is 32 kg/m^2. She has no significant medical problems and is taking no prescription medications or supplements. Her blood pressure is 115/85. Her physical examination is notable for her obesity. She used phen-fen for five months and lost 30 lbs but has regained this. She asks how much an average woman can expect to lose with ma huang. After explaining the lack of adequate trials of ma huang for weight loss, you review the evidence for ephedrine with caffeine. You tell her after six months on a 1,000 Kcal/d diet the average weight loss for those taking ephedrine with caffeine compared to placebo was:
   a. 10.5 kg (23.1 lb).
   b. 8.2 kg (18.0 lb).
   c. 5.5 kg (12.1 lb).
   d. 3.4 kg (7.5 lb).

3. You review with the patient your concerns regarding ephedrine/caffeine weight loss products. Which of the following have been documented in published trials?
   a. Fifty-five to 60% of those taking ephedrine/caffeine experience some side effect.
   b. Severe side effects have been seen, .e.g., syncope, marked hypertension.
   c. Withdrawal symptoms of headache and fatigue are seen in 65% of those who used ephedrine/caffeine for six months.
   d. All of the above.

4. The following statements about plant stanols are correct except:
   a. stanols are absorbed by the GI tract.
   b. stanols can lower LDL-C by 14%.
   c. stanols are the active ingredient in Benecol® products.
   d. stanols are effective in reducing serum cholesterol in diabetics.
   e. stanols have a synergistic effect when used with statins.

5. Which of the following statements about plant sterols is/are true?
   a. There are more than 44 naturally occurring plant sterols.
   b. Sterols are found in pine trees.
   c. Sterols are structurally similar to cholesterol.
   d. Sterols can improve BPH symptoms.
   e. All of the above.

6. Which of the following statements is/are true about phytosterols and stanols?
   a. They decrease total cholesterol.
   b. They decrease HDL-C.
   c. They decrease LDL-C.
   d. They decrease triglycerides.
   e. Both a and c.

Licorice and Serum Testosterone Levels

Source: Armanini D, et al. Reduction of serum testosterone in men by licorice. *N Engl J Med* 1999;341:1158.

WE EVALUATED THE EFFECT OF licorice on gonadal function in seven normal men, 22 to 24 years of age. The men were given 7 g/d of a commercial preparation of licorice in the form of tablets (Saila, Bologna, Italy) containing 0.5 g of glycyrrhizic acid, as determined by gas chromatography-mass spectrometry; the effect on the metabolism of mineralocorticoids in these men was reported previously.

Serum testosterone, androstenedione, and 17-hydroxyprogesterone were measured by radioimmunoassay before and after four and seven days of administration of licorice and four days after it was discontinued. During the period of licorice administration, the men's serum testosterone concentrations decreased and their serum 17-hydroxyprogesterone concentrations increased.

These results demonstrate that licorice inhibits both 17-ß hydroxysteroid dehydrogenase and 17,20-lyase, which catalyzes the conversion of 17-hydroxyprogesterone to androstenedione. Men with decreased libido or other sexual dysfunction, as well as those with hypertension, should be questioned about licorice ingestion.

■ COMMENT

Real licorice is hard to come by, but those seeking the distinct wet leaves, dark tobacco, thickly bitter flavors that the root offers will be disappointed by these results. These Italian investigators studied the effects of licorice, extracted from real licorice root, on hormone levels. The effects of testosterone, androstenedione, and 17-hydroxyprogesterone are of real interest to men. The investigators demonstrated a progressive drop in testosterone level (which rebounded 4 days after licorice discontinuation); a progressive rise in 17-hydroxyprogesterone (which dropped 4 days after licorice discontinuation); and an uncertain effect on androstenedione, which is normally converted to testosterone (see *Alternative Medicine Alert*, September 1999, pp. 97-100).

The mineralocorticoid-like, blood pressure-raising effect of licorice is well known: Licorice is known to inhibit 11-ß hydroxysteroid dehydrogenase, which catalyzes the conversion of cortisol to cortisone. Less well established are the inhibitory effects proposed above. Nevertheless, the fall in testosterone level and rise in 17-hydroxyprogesterone level were significant at the $P < 0.001$ level.

The fact that there were only seven men; that they were all young; that the commercial preparation likely cannot be found in the United States; and that red licorice Twizzlers (with lots more sugar than licorice) are far more popular than glycyrrhizic acid will ever be make this study an interesting hors d'oeurve instead of a main course.

Recommendation

Sustained licorice use has its downside for men. Though the connection to libido and sexual performance is still modest, a question about supplements (and candies) of all kinds is much cheaper than Viagra. ❖

"Alternatives" for Fibromyalgia

Source: Rossy LA, et al. A meta-analysis of fibromyalgia treatment interventions. *Ann Behav Med* 1999;21:180-191.

TO EVALUATE AND COMPARE THE EFFIcacy of pharmacological and non-pharmacological treatments of fibromyalgia syndrome (FMS), we performed a meta-analysis of 49 fibromyalgia treatment outcome studies assessing efficacy across four types of outcome measures—physical status, self-report of FMS symptoms, psychological status, and daily functioning.

After controlling for study design, antidepressants resulted in improvements on physical status measures (e.g., tender point index and myalgic score), and self-reported FMS symptoms (e.g., fatigue, morning stiffness, and pain). All non-pharmacological treatments were associated with significant improvements in all four categories of outcome measures with the exception of physically-based treatment (primarily exercise), which improved three of four outcome measures.

When compared, non-pharmacological treatment appears to be more efficacious in improving self-report of FMS symptoms than pharmacological treatment alone. A similar trend was suggested for functional measures. The optimal intervention for FMS would include non-pharmacological treatments, specifically exercise and cognitive-behavioral therapy, in addition to appropriate medication management as needed for sleep and pain symptoms.

■ COMMENT

Sleep disturbances, fatigue, pain, slowed daily function, and emotional distress trouble many patients with FMS, constantly. Many physicians feel as helpless with these patients as the patients do, not knowing what to try next.

These investigators, nearly all from the Department of Psychology at the University of Missouri, received NIH and NIDDR support to search MEDLINE, CINAHL, PsycINFO, and Dissertation Abstracts and to create a quantitative review of FMS treatment outcomes. Their review is rigorous, carefully performed, and extensively referenced. Unfortunately, no pharmacological treatment alone resulted in improved daily functioning, and antidepressants and muscle relaxants did not improve psychological outcomes.

Significant improvements were observed in the use of antidepressants for FMS symptoms, and muscle relaxants

for FMS symptoms and physical status measures. Many "alternative" measures positively influenced physical status, FMS symptoms, and psychological status. Fewer data were available about the use of NSAIDS alone, but as such, they had no significant impact on any outcome measure. "Alternative" pharmacological treatments reviewed include S-adensyl-L-methionine (SAMe) and 5-hydroxytryptophan; other alternatives included ibuprofen combined with cyclobenzaprine, and then again with alprazolam, and amitryptiline with naproxen. Non-pharmacological treatments include biofeedback, acupuncture, aerobic exercise, education, and hypnotherapy.

Although it may seem paradoxical (or worse, impossible) to recommend exercise to patients who cannot find the energy to get out of bed, cycling, treadmill, walking, and stretching were all found in different studies to have significant effects on physical status and on symptoms, and in one study on psychological effects of illness. In fact, physically based and psychologically based non-pharmacological treatments positively influenced outcomes more than did pharmacological treatments.

The authors are well aware of potential recruitment, retention, and selection biases in their methods. The effect size (ranging from 0.29-0.89 for pharmacological treatments and 0.38-0.71 for non-pharmacological treatments), however, is substantial and appears adequate to draw conclusions. The experience of more than 2,000 patients is analyzed.

Recommendation

Non-pharmacological treatments—specifically cognitive-behavioral therapy and exercise, preferably aerobic—should be prescribed to help manage FMS symptoms and daily function. Medication, including antidepressants and muscle relaxants, should be used for sleep and pain symptoms. NSAIDS should not be used alone. ❖

Progesterone Cream and Menopause

Source: Leonetti HB, et al. Transdermal progesterone cream for vasomotor symptoms and postmenopausal bone loss. *Obstet Gynecol* 1999;94:225-228.

TO DETERMINE THE EFFECTIVENESS OF transdermal progesterone cream for controlling vasomotor symptoms and preventing postmenopausal bone loss, we randomly assigned 102 healthy women within five years of menopause to transdermal progesterone cream or placebo.

Study subjects and investigators were masked until data analysis was completed. An initial evaluation included complete history, physical examination, bone mineral density determination, and serum studies (TSH, FSH, lipid profile, and chemistry profile). The subjects were instructed to apply a quarter teaspoon of cream (containing 20 mg progesterone or placebo) to the skin daily. Each woman received daily multivitamins and 1,200 mg calcium and was seen every four months for review of symptoms. Bone scans and serum chemistries were repeated after one year.

Thirty of the 43 (69%) in the treatment group and 26 of the 47 (55%) in the placebo group complained initially of vasomotor symptoms. Improvement or resolution of vasomotor symptoms, as determined by review of weekly symptom diaries, was noted in 25 of 30 (83%) treatment subjects and five of 26 (19%) placebo subjects ($P < 0.001$). The number of women who gained bone density of 1.2% or more did not differ ($\alpha = 0.05$, power of 80%). Two women developed rashes (one placebo and one control), and lipid profiles were not significantly changed. Eight of 43 treated subjects reported vaginal spotting lasting 1-2 days. Although we found no protective effect on bone density after one year, we saw a significant improvement in vasomotor symptoms in the treated group.

COMMENT

These Pennsylvania investigators recruited women for a randomized, double-masked, placebo-controlled trial to answer the question: "Does 'natural progesterone' control menopausal symptoms and prevent bone loss?"

Many women are reluctant to take hormone replacement therapy; discovering that Premarin® is drawn from the urine of mares, and that cardiovascular disease is a bigger threat than breast or uterine cancer is not reassuring to most women. Can topical progesterone from diosgenin, extracted from Mexican yams, reportedly identical to the progesterone of the human ovary and placenta, have the beneficial effects of oral medroxyprogesterone acetate without side effects?

These investigators say yes to symptom control, no to bone density. Flushing is common and bothersome to many menopausal women, and this once daily cream seemed effective in controlling it within four months: Most reported maximal relief within a month. The presence of spotting in the treated women suggests a systemic effect. Insignificant declines in bone mineral density, performed using a Hologic Quantitative Digital Machine, were observed.

Weaknesses of this study include the absence of published tabular data at four, eight, and 12 months, including remeasurement of initial baseline values, and the absence of control of other measures known to influence bone density, e.g., weight-bearing exercise and Vitamin D intake.

Recommendation

Transdermal progesterone derived from Mexican yams appears effective in controlling hot flushes, and can be offered to women with the same provisos as oral progesterone. To protect the heart and the bone, however, other tools are needed. Aerobic, weight-bearing exercise and a plant-based, high complex carbohydrate, whole foods diet should be part of every menopausal woman's repertoire. ❖

In Future Issues:

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CHEF Clinic Culinary and Lifestyle Training for Treatment of Obesity and Obesity-Related Conditions: Report of a Pilot Study and a Practice-Based Intervention

By John La Puma, MD and Jennifer Becker

Abstract

Background: Sixty-three percent of men and 55% of women are overweight; 21% of men and 27% of women are clinically obese. Treatment of obesity is notoriously unsuccessful, and pharmacological treatment in particular has been hazardous for patients.

Methods: Two sets of methods: prospective controlled pilot research study, with 60 hours of hands-on culinary, shopping, eating out, mind-body, and fitness programming over 21 weeks; pre-post practice-based clinical program with an average of 19.5 hours of hands-on programming over an average of 10 weeks.

Subjects: Two sets of subjects: 21 Midwestern sedentary obese subjects; 23 Midwestern overweight patients.

Results: Two sets of results: In the pilot, participants' triglyceride levels dropped an average of 56 mg/dL while controls' levels increased 25 mg/dL; participants lost 10% of their body fat while controls gained 6%; participants' average body mass index (BMI) dropped from 34.5 kg/m^2 to 32.2 kg/m^2. Participants reported cooking with fresh vegetables and grains, and cooking and eating both grains and fresh fruits significantly more often than controls. In the clinical study, participants' average BMI dropped from 33.58 kg/m^2 to 31.79 kg/m^2; they lost 11% of their body fat; their average waist measurement decreased from 40 in to 37.8 in; and their average hip measurement decreased from 46.9 in to 45 in. Average blood pressures dropped from 133/80 mm Hg to 127/76 mm Hg; average LDL levels dropped from 148.5 mg/dL to 116 mg/dL; triglycerides dropped from 199 mg/dL to 174.5 mg/dL. Participants increased their average main meal daily cooking time from 24.1 min to 33.2 min, and increased the number of whole fresh vegetables consumed from 1.6 to 3.5 whole vegetables daily.

Conclusion: Teaching new hands-on lifestyle skills to motivated patients can have beneficial, desired effects on BMI, blood pressure, lipid levels, and eating and cooking habits, and result in the consumption of more fresh vegetables.

IN 1986, FORMER SURGEON GENERAL C. EVERETT KOOP SAID, "WHEN I LEFT OFFICE, 26% OF AMERIcans were more than 20% overweight. It has now shot up to 33%. That would be my new smoking."[1]

Successful long-term treatment of obesity is rare. Targeting individual behavior is now thought to be so ineffective that experts advocate environmental change as primary prevention.[2] Although good research in this area is lacking, only 5% of people who have lost 30 lbs or more keep it off for five or more years.[3]

Few clinical programs offer skills training for habit change. CHEF Clinic (Cooking, Healthy Eating and Fitness) aimed to assess the effect of hands-on cooking, shopping, eating out, fitness, and mind-body skills training on sedentary, obese, middle-class, otherwise healthy Midwestern participants in a research pilot. CHEF Clinic also aimed to assess a condensed, practice-based clinical Mini Program. Here, we report preliminary results, propose clinical strategies, and identify future research objectives.

Methods

CHEF Clinic Research Pilot

Hypothesis: Obese patients who create new foods and flavors, accept personal fitness coaching and available mind-body techniques, and retain a change in their eating habits and patterns can avoid obesity-related disease.

Assessment: At both pre- and post-intervention, participants completed validated, pre-tested cooking, eating, quality-of-life, satisfaction, diet-readiness, and well-being questionnaires,[4] and three-day food records. BMI, waist-hip ratio, body fat percentage, complete fasting plasma lipid profile, fasting serum glucose, and resting blood pressures were also measured. Qualitative evaluations, including structured focus groups, were completed post-intervention.

Study Methods: Participants were referred from other physicians and also recruited directly. Potential participants on any regular medication or with any cardiac, renal, hepatic, or pulmonary medical problems were excluded. Eligible persons ages 35-65 years, with BMI > 27 kg/m^2 < 40 kg/m^2 were screened with a diet-readiness instrument for clinical eating disorders; and if still eligible, underwent screening laboratory exams; and if still eligible, underwent modified Bruce treadmill exams. Ineligible patients were referred back to their primary physicians with the above findings.

Curricular Content: Participants were offered 60 hours of programming over 21 weeks, taught by a physican chef, an exercise physiologist, a registered dietitian, and a holistic health registered nurse. Specific culinary, fitness, and behavioral tools were provided. Cooking and shopping classes adapted professional culinary techniques and shopping skills for home use. Plant-based recipes focused on seasonal, high-flavor, low-fat whole foods. No food was considered off limits. Eating out classes were held in local restaurants, and participants were taught how to make good choices. Mind-body skills included breathing techniques, guided visual imagery, music therapy, and group-building activities. Patients were discouraged from weighing themselves or counting calories. Fitness classes were held both individually with a progress assessment, and as a group.

Data Analysis: Statistical analysis was accomplished using SPSS™ and Food Processor™ software; statistical comparisons of group means used Wilcoxon's signed rank test; the chi squared statistic was used to test differences in categorical variables.

Informed Consent: Written and verbal consent to participate in the study was obtained from all participants. The study was approved by the Alexian Brothers Medical Center Institutional Review Board. Confidentiality of data collection was assured.

Financing: Unrestricted grant: Alexian Brothers Medical Center.

Table 1

CHEF Clinic SAMPLE Clinical Strategies for Weight Loss

Surround. If it's not in the house, it can't be eaten.

Adapt. Adapt professional culinary techniques.

Model. Modeling good behavior carries credibility.

Plan. People do not fail. Plans do.

Log. Successful patients count and record something other than pounds.

Enjoy. Create options that people like.

Table 2

Research to Practice in Obesity

Top Five Suggestions

1. Include spouses, partners, and significant others in the initial basic data gathering.
2. Offer the program directly to participants and do not depend on referrals for enrollment.
3. Do not expect obesity to be on any managed care organization's radar screen any time soon.
4. Make it fun! And easy!
5. Emphasize planning skills: Self-confidence and personal choice are within most people's grasp.

CHEF Clinic Mini Program

Hypothesis: Patients who learn specific culinary and eating out skills, and accept personal fitness coaching and mind-body skill practice in a group setting will achieve a desired medical goal (such as weight loss or blood pressure control) and a non-medical goal (such as controlling urges to eat or a desire to eat that is not hunger).

Assessment: As above, without post-intervention three-day dietary food records or mandatory post-intervention laboratory examination.

Inclusion Criteria: BMI > 25 kg/m^2. Between two and four visits were conducted with a board certified general internist to determine eating patterns and habits and to assess goals and reasons for eating other than hunger. Each patient also had at least one visit with an exercise physiologist/physician assistant who wrote an exercise prescription. Entry to the program was conditional on completion of these visits.

Enrollment: Participants were referred by physicians and contacted the clinic directly. Eligible persons were screened with a diet-readiness instrument, underwent screening laboratory exams, and if clinically indicated, underwent modified Bruce treadmill exams. Persons on blood pressure and lipid medications continued to take them.

Curricular Content: As above, except that participants were offered 18-21 hours (mean 19.5 hours) of programming over seven or 13 weeks (mean 10 weeks).

Data Analysis: Statistical analysis was accomplished using Excel™.

Informed Consent: Verbal consent to participate in the study was obtained from all participants. Confidentiality of data collection was assured.

Financing: CHEF Clinic (Cooking, Healthy Eating and Fitness).

Results

Research Pilot: Twenty-one participants were enrolled in the pilot study (11 participants [average age 43.6 years], 10 controls). All participants attended more than 95% of classes offered. Eight (5 women, 3 men) of the 11 participants completed the 21-week program.

Physiological Health Effects: Participants' triglyceride levels dropped an average of 56 mg/dL while controls' triglyceride levels increased 25 mg/dL; participants lost 10% of their body fat, compared to a 6% increase in body fat in the control group ($P < 0.05$ and $P < 0.03$, respectively).

Measures of Weight and Fitness: Five of eight participants lost weight, with the group losing an average of nearly 11.5 lbs

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overall; these results compare with weight loss of only 2.8 lbs among controls ($P = 0.07$). Among those who lost weight, the loss averaged 24.4 lbs; BMIs fell from 34.1 kg/m^2 to 30.0 kg/m^2 ($P < 0.05$). Participants showed significant reductions in waist size ($P < 0.02$) and waist-hip ratios ($P < 0.03$) compared with controls. Participants also reduced their mean BMI from 34.5 kg/m^2 to 32.2 kg/m^2, while controls showed a reduction of only 0.8 kg/m^2 ($P = 0.07$).

Attitudinal Measures of Palate Change and Changes in Cooking and Eating Habits: At post-test, participants reported cooking with fresh vegetables and grains significantly more often than controls ($P < 0.03$ and $P < 0.01$, respectively), and within the participant group, subjects cooked and ate more grains and fresh fruits ($P < 0.03$ in both). Similarly, participants reported a reduction in use of pre-packaged dinners ($P < 0.02$) and a concomitant increase in number of dinners cooked ($P < 0.05$) from the pre-test to the post-test. Participants also reported fewer hours of eating while watching TV compared with controls at post-test ($P = 0.06$).

Behavioral Measures of Eating and Exercise: Participants significantly decreased their use of fat and saturated fat over time (both $P < 0.02$). Participants also were significantly more likely to exercise than were controls at post-test ($P < 0.001$), and increased the duration of exercise over time ($P < 0.0002$). These results were largely maintained at six months.

Mini Program: Twenty (15 women, 5 men, non-Hispanic whites, average age 51.7 years) of the 23 participants completed the program. No follow-up data were available from the three dropouts; all three attended all but one of the scheduled sessions. Initial BMIs ranged widely: 25-29.9 kg/m^2 = 7 (4 female, 3 male); 30-34.9 kg/m^2 = 8 (6 female, 2 male); 35-39.9 kg/m^2 = 0; 40+ kg/m^2 = 5 (5 female); mean 33.58 kg/m^2.

Physiological Health Effects: Eight of the 20 participants were on medication for hyperlipidemia. Total cholesterol levels dropped an average of 45 mg/dL from 241.4 mg/dL +/-40.5 to 196 mg/dL +/-16.7; HDLs rose from 51.3 mg/dL +/-18.9 to 54.5 mg/dL +/-15.6; LDLs dropped from 148.5 mg/dL +/-35.6 to 113.6 mg/dL +/-75.9; triglycerides dropped from 199 mg/dL +/-86.5 to 174.5 mg/dL +/-127.5. Average blood pressure fell from 133/80 mm Hg to 127/76 mm Hg. Two patients were able to avoid blood pressure medication altogether (150/84 mm Hg to 126/78 mm Hg; 170/108 mm Hg to 124/80 mm Hg). Body fat percentage dropped 11% overall, averaging 35.0% (range 16-53%) initially, dropping to 31.2% (range 15-44%).

Measures of Weight and Fitness: Nineteen of 20 CHEF Clinic participants lost weight, with the group losing an average of 12.2 +/-6.2 pounds, from an average of 206.4 lbs (range 142-332 lbs) to 194.2 lbs (range 141-292 lbs); one person gained 2 lbs, from 145 lbs to 147 lbs, and reduced her body fat from 42% to 26%. Mean BMIs fell from 33.58 kg/m^2 to 31.79 kg/m^2 ($P < 0.05$). CHEF Clinic participants also showed significant reductions in waist size (from 40 in to 37.8 in), hip size (from 46.9 in to 45 in), and waist-hip ratios (from 0.86 to 0.84).

Attitudinal Measures of Palate Change and Changes in Cooking and Eating Habits: At post-test, participants reported doubling the number of fresh vegetables eaten, consuming 3.5 +/-1.6 fresh whole vegetables daily (range 1.5-7.5), vs. 1.6 +/-1.0 (range 0-3) initially. Time spent cooking daily also rose from an average of 24.1 min +/-17 (range 0-60 min) to 33.2 min +/-17 (range 10-75 min). Most commonly snacked on foods changed from fruit, cookies, chips, candy, crackers, and ice cream to fruit, vegetables, yogurt, pretzels, and popcorn.

Behavioral Measures of Eating and Exercise: Participants averaged 48.6 min of largely aerobic exercise 4.6 times weekly at the conclusion of the program.

Comment

Our results show the short-term success of a skills-based lifestyle modification program in a controlled prospective research pilot and in a practice-based clinical study. In the research pilot and in practice, outcomes of reduced weight and waist and hip measurements, and significant increases in the number of whole fresh vegetables consumed were noted.

Table 3

CHEF Clinic Recommended Kitchen Essentials

Pantry

- Canned or dried beans: pinto, black, cannellini, kidney, garbanzo
- Whole wheat pasta, couscous, and bread
- Brown rice
- White, yellow, and red onions
- Garlic
- Canned tomatoes
- Reduced-sodium, reduced-fat stocks or broths
- Dried spices and herbs: bay, oregano, dill, black peppercorns, cumin seeds, aniseed, rosemary, coriander, curry, cinnamon
- Nuts: walnuts, Brazil nuts, almonds
- Dried fruit: figs, apricots, cherries, raisins
- Vinegars: balsamic, Chinese black, herb, fruit-flavored, wine
- Extra virgin olive oil
- Sea salt

Refrigerator

- Light silken tofu
- Skim milk
- Soy milk and soybeans
- Feta cheese
- Parmigiano-Reggiano
- Nonfat sour cream
- Nonfat plain yogurt
- Salsa
- Seasonal fruits
- Seasonal vegetables
- Fresh herbs: cilantro, parsley, mint, thyme, basil
- Pizza shells
- Mustards: spicy brown, dijon, whole grain, other gourmet flavors

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Marked reductions in serum lipid levels were observed, and several patients were able to avoid blood pressure and lipid medication altogether.

Comprehensive weight management programs often focus on behavioral and educational strategies. Teaching practical cooking, shopping, and eating skills within such programs—and practicing those skills with specialists—has not been reported.

Sitting with a patient in an exam room with Family Café's menu, for example, is one thing. Sitting with that patient in a restaurant and watching her pour 4 oz of dressing (without tasting it) on her salad because it's "low fat" is another. Telling a patient how to select and roast a butternut squash is one thing; actually choosing and preparing it is another. Telling a patient not to eat because she's stressed is one thing; sticking a post-it on the fridge that says "It's not in here" or "Are you really hungry?" is another.

Our participants formed important bonds with other participants. Differentiating feelings of anxiety, frustration, loneliness, and boredom from hunger was an initial and necessary step for many. Learning to ask others for help—even for those people inclined to keep private things to themselves—was important for many people to build self-confidence.

Specific strategies were identified as helpful in transitioning from research to practice. (*See Tables 1-3 and "Recommended Top High-Flavor, Healthful Cookbooks.*)

More than half of Americans are considered overweight; the most recent NHANES study found that 63% of men and 55% of women had a BMI of 25 kg/m^2 or greater.[5] The prevalence of self-reported obesity (defined as a BMI > 30 kg/m^2) has increased in the 1990s in every state, across all age groups and educational levels, and in both genders.[6]

Despite its substantial negative physical, emotional, medical, and economic effects,[7] few physicians think of obesity as a rapidly spreading chronic disease in need of treatment, and fewer still can advise about diet or exercise. Physicians find that they have too little time, too little knowledge, too few good materials, and little or no reimbursement for counseling about weight management.[8] Barely two of five overweight people are medically advised to lose weight, but those who do are nearly three times as likely to report making an effort as those who never receive advice.[9]

The strengths of the current data include their prospective nature; excellent community support and sponsorship; keen public interest in the study; its potential application within medical practice; its credible, professional, licensed staff; and its creative, fun, do-something approach to problems. All participants in the pre-study were eligible for the post-study. The changes appear to be substantial, unique, and directly the result of the intervention.

Weaknesses include a personal and professional tendency to focus on weight as a primary outcome instead of fitness. The relative efficacy of each of the component interventions cannot be ascertained. Participants were not randomized, and were motivated to change and to learn from each other. The clinical program is ambitious and comprehensive, requiring attention to detail, excellent organizational and coordinating skills, and careful follow-up.

Recommended Top High-Flavor, Healthful Cookbooks

- Bittman M. *How to Cook Everything: Simple Recipes for Great Food*. Foster City, CA: IDG Books Worldwide; 1998.
- Madison D. *Vegetarian Cooking for Everyone*. New York: Broadway Books; 1997.
- Raichlen S. *Steven Raichlen's High-Flavor, Low-Fat Vegetarian Cooking*. New York: Viking Press; 1995.
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Future research questions include testing a food-centered skills-based program to identify which components confer greatest benefit, and effective ways to teach and train others in this work. Similarly integrated approaches, such as that of the Ornish program, have now been funded on a trial basis by Medicare.

Conclusion

A multidisciplinary, skills-based, food-centered educational program offers a credible, novel departure from previous treatments for obesity, and effective treatment for elevated blood pressure and lipid levels. Practical strategies for helping patients eat in a more healthful way can be offered and implemented within a medical practice using a systematic, food-centered approach. ❖

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ALTERNATIVE MEDICINE ALERT™

A Clinician's Guide to Alternative Therapies

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Clinician Fact Sheet: Review of Herbal Supplements

Ginkgo (*Ginkgo biloba* L. Family: Ginkgoaceae)

1998 Retail Sales: $150,859,328[1] **Part Used:** Leaf extract

Intended Indications

Allergic rhinitis, Alzheimer's disease, antioxidant, anxiety/stress, asthma, dementia, increases mental alertness, peripheral vascular disease, Raynaud's disease, senility, tinnitus, vertigo

Formulation and Dosage

- For memory or circulation: 120 mg/d in 2-3 divided doses
- For Alzheimer's, depression, or tinnitus: up to 240 mg/d in 2-3 divided doses
- Standardized leaf extract containing 24% flavone glycosides and 6% terpene lactones

Adverse Effects

Occasional GI upset, headache, dizziness, palpitations

Interactions

- Ginkgo may inhibit platelet aggregation so bleeding and prothrombin times should be closely monitored in patients on antiplatelet drugs and warfarin
- A theoretical interaction exists with other antiplatelet herbs; therefore, added vigilance is recommended if used in conjunction with ginger, garlic, or feverfew
- Patients taking antidepressants should be carefully monitored given ginkgo's reversible monoamine oxidase inhibitory capacity
- Ginkgo may reverse SSRI-induced sexual dysfunction
- Ginkgo can increase blood pressure when used concomitantly with thiazide diuretics

Contraindications

- Discontinue ginkgo use 7-10 days prior to surgery
- Safety not determined in pregnancy and lactation

St. John's wort (*Hypericum perforatum* L. Family: Hypericaceae)

1998 Retail Sales: $140,358,560[1] **Part Used:** Leaves, flowering tops

Intended Indications

Antibacterial, antifungal, anxiety, mild-to-moderate depression

Formulation and Dosage

- 300 mg tid standardized to 0.3% hypericin extract (extracts standardized to hyperforin may soon appear on shelves as well)

Adverse Effects

Possibly increases photosensitivity in patients with fair complexions, occasional GI upset, dry mouth, dizziness, confusion

Interactions

- Concomitant use of MAO inhibitors, SSR inhibitors, and other antidepressant drugs should be avoided as well as photosensitizing agents
- One recent pharmacologic study showed that 14-day administration of St. John's wort decreased the bioavailability of digoxin by 25-30%[2]

Contraindications
- None documented
- Safety not determined in pregnancy and lactation

Recent Research

A recent study examined the reasons patients self-medicate with St. John's wort instead of seeking traditional health care.[3] Extensive interviews were conducted with 22 women using St. John's wort. Upon review of the transcripts, several decision-making themes became evident. Study participants had a history of alternative medicine use and a desire for personal control of their health care. All St. John's wort users reported depressed mood and occasional irritability, cognitive difficulty, social isolation, and hormonal mood changes. Subjects reported self-diagnosis of minor depression, perceived high risk of prescription drugs, and a belief in the safety of herbal remedies. Additionally, participants noted barriers to and lack of knowledge of conventional health care providers and awareness of the ease of use and popularity of St. John's wort. Six of 22 (27%) participants had informed their primary care providers of their St. John's wort use. Users reported moderate effectiveness and few side effects.

Ginseng (*Panax ginseng* Family: Araliaceae)

1998 Retail Sales: $95,871,544[1]

Part Used: Roots

Intended Indications

Adaptogen, antioxidant, enhances immune function, fatigue, hypocholesterolemia, impotence, infertility, stress

Formulation and Dosage
- 100-200 mg/d standardized extract of 4-7% ginsenosides
- Continuous use not to exceed three months
- Preparations vary widely

Adverse Effects

Breast tenderness in women, nervousness and excitation that decreases with continued use of decreased dose, generally low toxicity from moderate doses of high-quality standardized product, postmenopausal bleeding

Interactions
- Since ginseng has been shown to decrease platelet adhesiveness in animal models, bleeding and prothrombin times should be monitored in patients taking anticoagulant and antiplatelet aggregating medications
- Variable effects on international normalizing ratio
- May interfere with digoxin activity or monitoring
- Because ginseng exhibits a hypoglycemic effect, blood glucose levels of diabetics should be monitored carefully
- Not indicated with caffeine or other stimulants
- Caution recommended for hypertensives

Contraindications
- None documented
- Safety not determined in pregnancy and lactation

Garlic (*Allium sativum* L. Family: Liliaceae)

1998 Retail Sales: $84,054,520[1]

Part Used: Bulb (clove), occasionally leaves

Intended Indications

Antibacterial, antimicrobial for mild respiratory and digestive tract infections, antiseptic, antispasmodic, atherosclerosis, lower blood pressure, lower serum cholesterol

Formulation and Dosage
- Total allicin potential of 3.6-5.4 mg/d or 10 mg/d alliin
- 4 g fresh garlic/d (multiple cloves)

Adverse Effects

Occasional GI upset, changes in gut flora, allergic skin reactions, odor may pervade breath and skin

Interactions
- Since garlic reduces platelet aggregation and increases fibrinolytic activity, bleeding and prothrombin times should be monitored in patients on antiplatelet drugs and warfarin
- A theoretical interaction exists with other antiplatelet herbs; therefore, added vigilance is recommended if used in conjunction with ginger, ginkgo, or feverfew
- May potentiate antihypertensives

Contraindications
- Discontinue garlic use 7-10 days prior to surgery
- Safety not determined in pregnancy and lactation

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