Appetite Suppressants as Adjuncts in the Treatment of Obesity

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Obesity is a common and challenging problem that often leads to other medical problems, including type II diabetes, hyperlipidemia, hypertension, coronary artery disease, and degenerative joint disease. Weight loss, which is central to the dietary treatments for obesity, is often of limited success. Recent studies have documented the safety and efficacy of certain appetite suppressants for assisting in long-term weight loss and maintenance of weight loss. Since appetite suppressants, alone or in combination, have been documented to be safe and effective adjuncts for treating obesity and complicated obesity, physicians should consider using these agents in the pharmacotherapy for obese patients.

Key words. Obesity; diabetes; hyperlipidemia; anorectic agents; appetite depressants.
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Obesity is a chronic condition that complicates or contributes to multiple medical problems.[1,2] In spite of increasing public awareness of the hazards of obesity, the incidence of significant obesity in America has been increasing over recent decades.[3–5] The treatment of obesity and the metabolic diseases that often complicate obesity is challenging. While much is known about the metabolic changes that occur in these conditions and the nutritional approaches that are helpful in their management, patients face major obstacles in attempting to adhere to recommended dietary changes.[6,7] This, in turn, leads to frustration on the part of not only the physician and the medical care team who repeatedly give the same message but also of the patient who is unable to adhere to the program and does not improve. This cycle increases the physician's tendency to be cynical about the possibilities for success in treating patients with these challenging obesity-related conditions. Adjunctive use of appetite suppressants for each of these conditions can be helpful.[6–13]

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Dietary Management of Obesity

There is well-documented evidence that hypocaloric diets result in weight loss, but adherence is a major problem for patients.[8] Those who have become obese have, by definition, a self-selected diet that is in excess of caloric needs. The challenge of achieving weight loss involves breaking ingrained activity and dietary habits. For most persons, weight loss regimens involve significant and permanent changes in the major discretionary activities of life: eating and recreation. These changes cause major disruption in all aspects of personal and family life and are difficult to achieve and maintain. Moreover, any attempt to lose weight is met with formidable opposition from the physiologic mechanisms designed to maintain weight. The body's weight-maintenance mechanism is truly remarkable. The average adult takes in between 700,000 and 1,000,000 calories per year (2000 to 2700 per day). While this is enough to deposit 200 to 285 lb of additional weight, the average person's weight rarely varies by more than a few pounds, usually no more than the day-to-day variability due to hydration and recent meal effects. Most obese persons are stably obese, with their weight varying by only a few pounds a year despite periods of restricted and unrestricted eating.

Weight appears to gravitate to a "set point" for any given individual.[14] It is unfortunate that we do not un-

Table. Anorectic Agents Used as Adjuncts in Treating Obesity

Type of Agent	Generic Name	Trade Names	Classification	Dosage
Adrenergic	Phenylpropanolamine*	Dexatrim	OTC	75 mg in morning
	Phentermine*	Adipex-P, Ionamin, Fastin	Schedule IV	30 mg in morning
	Mazindol*	Sanorex, Mazanor	Schedule IV	1 mg in morning
Serotonergic	Fenfluramine†	Pondimin	Schedule IV	20 mg tid
	Fluoxetine‡	Prozac	Schedule IV	80 mg in morning

**Side effects include nervousness, jitteriness, decreased sleep, dry mouth, dizziness, palpitations, and other adrenergic symptoms.*
†Side effects include fatigue, dizziness, confusion, agitation.
‡Side effects include agitation, nausea, and gastrointestinal distress, fatigue.
OTC denotes over the counter; tid, three times daily.
NOTE: US classification schedules indicate potential for abuse on a scale of I (highest potential) to V (lowest potential).

derstand more about the determination and maintenance of this set point so that it can be adjusted lower.[14] Some of the theories about the cues and feedback for the set point include body temperature maintenance, fat mobilization maintenance, and actual "pondostat," the central mechanism monitoring fat or weight and maintaining stability. Some researchers have suggested that appetite suppressants may act, in part, to reset this set point downward.[15] If this is the case, long-term and/or cyclic use of appetite suppressants may be warranted.[7–46]

Medical Approaches to Weight Control

Approaches to weight control usually involve dietary changes, increased physical activity, and altered eating behavior. Dietary regimens include calorie- and fat-restricted diets. Very low-calorie liquid diets have a high initial success rate among patients following the program, but rapid regain is often a problem because this diet plan does not include learning healthier permanent eating habits.[1,6,7] Adherence is a significant problem for many patients undergoing any dietary modification.[1,6] Exercise regimens alone rarely result in major weight changes but appear to be of significant importance in the maintenance of weight loss.[47] Behavioral programs that modify external cues to eating and overcome other defeating habits are also helpful in maintaining weight loss.[48]

There are many medical adjuncts to these approaches. Appetite suppressants have been demonstrated to be helpful in some patients.[7–46] Other approaches include bulking agents that produce a sensation of "fullness," enzyme inhibitors that alter digestion or absorption, fat substitutes such as olestra, sugar substitutes, and metabolic stimulants.[1] Except for the latter, most of these have had disappointing results in clinical studies. As for metabolic stimulants, the combination of ephedrine and caffeine, as is available in over-the-counter preparations for asthma, has been found to increase fat loss but not total weight loss relative to placebo.[49] Based on the results of animal studies, experimental beta-adrenergic lipolytic agents look promising.[1]

Overall, medical adjuncts for weight loss have been relatively limited. Gastric surgery for weight loss has a much greater success rate: approximately two thirds of patients achieve and maintain over a 2-year period an average 60-lb weight loss.[50] The apparent mechanism in this approach to weight loss is altered eating behavior due to reduced gastric capacity. However, since surgical risks are not insignificant, gastric surgery should be considered only for selected severely obese individuals.[50]

Adjunctive Use of Appetite Suppressants

Much recent work has documented the safety and efficacy of appetite suppressants in weight control.[7–46] Appetite suppressants that have been studied and found to be safe, effective, and of low abuse potential include diethylpropion hydrochloride (75 mg daily), mazindol (1 mg daily), phentermine hydrochloride, fenfluramine hydrochloride (d-fenfluramine and the racemic dl-fenfluramine), fluoxetine hydrochloride (60 to 80 mg daily), and phenylpropanolamine hydrochloride (75 mg daily, available over the counter)[7–46] (Table). There have been numerous publications on the efficacy of prescription appetite suppressants,[7–47] and there have been several comparative reviews of this work.[7–9,11–13, 24–26] Studies have ranged in duration from 6 to 156 weeks. In most recent studies, the appetite suppressants were combined with dietary restriction, with or without behavioral and exercise programs, and treatment lasted for 36 or more weeks. This is in marked contrast to the shorter term use indicated in the *Physicians' Desk Reference*.[51] In all but two studies, the weight loss with appetite suppressants was significantly greater than with placebo.

In the Food and Drug Administration (FDA) review of studies with various agents (4543 patients being ac-

tively treated, 3182 receiving placebo), the average weight loss was about one half pound per week greater than with placebo in these short-term studies.[12,24] Rates of dropout at 4 weeks were 18.5% for placebo and 24.3% for active drug; overall dropout rate was not quite 50%. In the longer term studies of diethylpropion, mazindol, phentermine, and fenfluramine, weight loss often plateaued after 20 to 24 weeks, but there was no regain of weight with continued use of the agent.[7,23,26] In longer term studies, regain of some or all of the weight has been noted on discontinuation of the appetite suppressant.[7] Adjunctive diet and behavioral and exercise programs were associated with greater amounts of weight loss.[7] Alternatively, appetite suppressants assisted with adherence to, and therefore greater efficacy of, weight-control regimens involving changes in diet, exercise, and other behaviors.

In the longer term studies, continued weight loss over a 3- to 6-month period was more likely to occur with appetite suppressants than with placebos.[7,15–23] The results may be different with fluoxetine, as some studies show regain of weight despite continued use of the agent.[7,36,37] A review of multiple studies of the nonprescription agent phenylpropanolamine showed a weight loss of 0.24 kg/week greater with the use of the active agent compared with placebo, a rate similar to that of prescription appetite suppressants.[7,12,24] Thus, there is ample documentation of the modest efficacy of these agents, the high dropout rates, and the tendency to regain the weight when the agent is discontinued.

In contrast to the descriptions of FDA-approved drugs for short-term use, the work of Weintraub and associates[15–23] provides excellent demonstration and documentation of the safety and efficacy of appetite suppressants used over the long term in treating obesity. They used a combination of phentermine, 30 mg a day, and fenfluramine, 60 mg a day in divided doses, for up to 2 years, and followed up for 4 years. This combination of medium- to low-dose agents seems to act differently and is well tolerated.[15,16] Side effects may be minimized by using medium doses of different drugs rather than high doses of either drug alone. Phentermine is an adrenergic agent, the chief side effects of which are tremulousness, jitteriness, anxiety, dry mouth, and mild insomnia. Fenfluramine's predominant action may be on serotonergic systems. Either can be effective at the doses used, but the combination appears to be more effective.[15–23] The research on this combination demonstrated not only successful weight loss, but also successful maintenance of the reduced weight and reduction of hyperlipidemia and glucose intolerance. The combination usually does not exacerbate hypertension.[7,16] Thus, there is good documentation of the safety and efficacy of some appetite suppressants for obesity.[7–23]

The Potential for Abuse

Many appetite suppressants were developed from modification of amphetamine-like agents. As such, they have a reputation as being drugs of abuse in spite of little evidence of addicting properties.[7–46] In animal studies, phenylpropanolamine, fluoxetine, phentermine, and fenfluramine have shown little potential for addiction.[52] In clinical studies, euphoria, reinforcement, and addicting potential have not been demonstrated.[7,8] It is important to note that diethylpropion, phentermine, and fenfluramine, which are classed as schedule IV agents by the FDA, have not become significant "street drugs" of abuse.[7,8] These agents, however, are often less discriminately prescribed by physicians for patients of near-normal weight who want to be fashion-model thin. Over-the-counter phenylpropanolamine has also been overused by many young women in an effort to be fashionably thin.[53] Some regulatory and licensing agencies have restricted the use of this medication despite a lack of evidence of addiction or abuse by patients.[10] The FDA recommends only short-term limited use, in spite of evidence demonstrating safe and effective longer term use. In addition, there is general societal disdain for the use of such agents when "willpower" should be sufficient.[6,7,10,13] Thus, there are many biases and pressures that keep physicians from using such agents in their practices even though evidence has accumulated that does not support these prejudices.

Side Effects

Common side effects with the "adrenergic" appetite suppressants include dry mouth, sleep disturbances, dizziness, gastrointestinal complaints (eg, abdominal pain, diarrhea, constipation, nausea, and metalic taste), fatigue, and nervousness.[7,9,11,12] In Weintraub's study,[16] these side effects diminished considerably after 4 weeks. Although elevated blood pressure was not a problem in the same study, it has been known to occur with appetite suppressants, including phenylpropanolamine.[53–56] Severe hypertension, pulmonary hypertension, severe headaches, atrioventricular conduction blocks, and bowel infarction also have been reported with phenylpropanolamine, but such adverse events appear to be rare considering the widespread use of this agent, which is also an ingredient in many over-the-counter diet and cold preparations.[53–56] Fenfluramine tends to have a different profile of side effects, including more marked fatigue, drowsiness, depressive feelings, and other central nervous system complaints, but less marked nervousness and agitation.[7,16] Neither euphoria nor withdrawal effects were noted with these agents. At appetite-suppressive doses of 60 to 80 mg, fluoxetine can have gastrointestinal and

central nervous system side effects, with nausea and agitation being prominent.[37]

Complicated Obesity

Obesity is a risk factor for multiple chronic medical conditions. Type II diabetes and hyperlipidemias are very common in obese persons. Biliary tract disease, degenerative joint disease of the lower extremities, hypertension, coronary artery disease, and many other disorders are associated with or worsened by obesity.[1,2,57] Control of all these conditions, with the exception of biliary tract disease, is improved by weight loss,[1,2,57] although it should be noted that rapid weight loss achieved by any approach can increase the likelihood of gallstones and associated problems.[1]

Obesity and Diabetes

Over 90% of adult patients with type II diabetes are obese, and weight loss, even modest amounts of 10 to 20 lb, may result in control of the diabetes.[39–44] It is likely that greater amounts of weight loss would result in control of diabetes in a larger precentage of obese patients with type II diabetes. While a focus on diet and weight control is the first step in treating persons with type II diabetes, appetite suppressants have not been commonly recognized as adjuncts to this process. There have been a few studies[40–43] of the use of appetite suppressants in the management of obese patients with type II diabetes that showed modest efficacy with low risk. These studies have influenced physician use of appetite suppressants as an adjunct to support dietary adherence in such patients.

Management of Hyperlipidemia

Hypertriglyceridemia and hypercholesterolemia are two other important cardiovascular risk factors. Hypertriglyceridemia, which is commonly associated with poorly controlled diabetes and obesity, improves when these conditions improve. Therefore, appetite suppressants would seem to be a logical adjunct for selected patients with these associated problems. Recent studies[22,46] have shown that the dietary management of high cholesterol levels is most effective when an obese person loses weight. In selected patients with obesity and hyperlipidemia, appetite suppressants may be effective adjuncts to traditional therapy.

Appropriate Use of Appetite Suppressants

The cure rate for obese patients presenting to a physician is miserable. As noted earlier, there are many mechanisms for maintaining weight, and constant vigilance during this process is required. Obesity is strongly associated with increased cardiovascular risk factors, including diabetes, hypertension, and hyperlipidemia.[1,57] While there are some risks associated with the use of appetite suppressants, they are less life-threatening than are the complications of obesity.[7–16] Thus, it is reasonable and logical to selectively use appetite suppressants in the treatment of obese patients with complications and those at risk of these complications.

Adjunctive use of appetite suppressants for obesity in smokers may also support patients' efforts to stop smoking, in that it may counteract fear of weight gain and appetite stimulation that generally accompany smoking cessation.

It is usually inappropriate to use appetite suppressants in minimally obese patients. Certainly, it would not be appropriate to prescribe these agents to help a patient achieve, at higher risk, a state of unnatural thinness, even though it is cosmetically popular. However, reluctance to use them in certain situations should not preclude appropriate, medically indicated use of appetite suppressants. It should also be noted, however, that these products are by no means 100% effective. Many patients do not tolerate them well, and for many, they do not result in significant weight loss.

Patient Selection

Patient selection is central to the effective and safe use of appetite suppressants. These agents should be avoided in children, elderly people, pregnant women, and in patients with uncontrolled hypertension, mild degrees of obesity, and intolerance to adrenergic agents. Except for fluoxetine, they should also be avoided in patients with unresolved anxiety or depressive disorders. Well-motivated patients whose major barrier to success in weight loss has been dominating hunger can be ideal candidates for such therapy. Overall, no more than one half of all obese individuals are potential candidates for these agents. Of those who use appetite suppressants to control obesity, only about one half will do so successfully; the remainder will drop out because of side effects or personal objections to the therapy or because they have received no apparent benefit from the medications.[12,24] Thus, although these agents are not appropriate for all obese patients, they can be a helpful adjunct for a select minority.

Guidelines for Prescribing Appetite Suppressants

The following information should be taken into consideration in the decision whether to prescribe appetite suppressants in the treatment of obesity:

- Appetite suppressants can be viable adjunctive pharmacotherapy for obesity complicated by diabetes, hyperlipidemia, or hypertension.
- Appetite suppressants should always be offered in conjunction with dietary instruction, an exercise program, and a lifelong plan for behavior modification aimed at maintaining weight loss. They should never be presented as "making it easy" or as a short-term, one-time "miracle cure."
- Appetite suppressants are usually best started as an adjunct to a failing attempt at caloric restriction in which hunger is an increasing problem, ie, an aid to enhance adherence to a dietary program.
- This type of pharmacotherapy should be offered to patients rather than required of them. It is important to explain the side effects and amphetamine-like classification of the drugs. Some patients have personal objections to medications that may be perceived as "controlled substances" or "street drugs."
- While taking appetite suppressants, patients should be seen at least every 6 weeks, preferably every 4 weeks, to enhance active adherence and motivation.
- Medication is likely to be needed for months to achieve weight loss goals. During the weight-maintenance phase, patients may need to take appetite suppressants intermittently. Patients should check their weight at least weekly, and for each 5-lb weight regain, they should intensify their dieting efforts and use adjunctive appetite suppressants for 1 to 2 months. Short-term use of these medications may be helpful during holidays and other "calorically challenging" times.
- The pharmacologic agents of choice are *phenylpropanolamine* (75 mg daily in the morning; nonprescription) or *phentermine* (30 mg daily in the morning) or *fenfluramine* (20 mg three times daily) or a *combination of phentermine* (30 mg daily) *and fenfluramine* (20 mg three times daily). Other low-risk choices include *diethylpropion* (75 mg daily) or *mazindol* (1 mg daily) or *fluoxetine* (60 to 80 mg daily).

By the time many patients consult a physician, they will have already tried phenylpropanolamine because it is the least expensive agent and it is available over the counter. Among prescription agents, phentermine is generally the best tolerated and least expensive of the adrenergic agents, which include mazindol and diethylpropion. If phentermine is not tolerated because of anxiety or tremulousness or similar adrenergic symptoms, it is unlikely that any other adrenergic agents would be better tolerated. Amphetamines are more likely to cause problems including mania, paranoia, and addiction. Overall, the risks associated with amphetamine use make these agents poor choices for the treatment of obesity.

When a patient reaches a 20- to 30-lb weight loss goal, it is useful to try a maintenance phase. Because maintenance is generally recognized as more difficult than loss, intermittent "practice" at this phase, which also offers a "vacation" from intensive efforts at weight loss, can be constructive. After successful maintenance with or without intermittent drug use, another phase of active weight loss should be tried until the weight goal is achieved. The goal should not be based strictly on weight tables, but rather should be a *maintainable* weight with reduction of associated risk factors. This is usually higher than both the esthetically desired weight and that listed on standard weight tables. The key word to remember is *maintainable*. Using a drug to enhance a "yo-yo" process may be more harmful than helpful.

Conclusions

Many well-trained physicians are uncomfortable with the use of appetite suppressants. Since there are many medical conditions for which obesity plays a significant causative role and weight loss is potentially curative, focusing on the treatment of these conditions with a goal of enhancing weight loss is a well-accepted therapeutic approach. In selected patients, use of appetite suppressants as an adjunct to this process can enhance success.[7-46] New research supports long-term use of these agents in selected patients as both safe and effective. Obesity is an important and therapeutically challenging condition for which further research on treatment is warranted.

References

1. Bray GA. Obesity: basic considerations and clinical approaches. Dis Mon 1989; 18:449–540.
2. Van Italie TB. Health implications of overweight and obesity in the United States. Ann Intern Med 1985; 103:983–8.
3. Kuczmarski RJ. Prevalence of overweight and weight gain in the United States. Am J Clin Nutr 1992; 55:(suppl 1)495S–502S.
4. Kucsmarski RJ, Flegal KM, Campbell SM, et al. Increasing prevalence of overweight among US adults. The NHNES 1960–91. JAMA 1994; 272:205–11.
5. Serdula MK, Mokdad AH, Pamuk ER, Williamson DF, Byers T. Effects of question order on estimates of the prevalence of attempted weight loss. Am J Epidemiol 1995; 142:64–7.
6. Goodrick GK, Foreyt JP. Why treatments for obesity don't last. J Am Diet Assoc 1991; 91:1243–7.

7. Goldstein DJ, Potvin JH. Long-term weight loss: the effect of pharmacologic agents. Am J Clin Nutr 1994; 60:647–57.
8. Wilson MA. Southwestern Internal Medicine Conference: treatment of obesity. Am J Med Sci 1990; 299:62–8.
9. Atkinson RL, Hubbard VS. Report on the NIH workshop on pharmacologic treatment of obesity. Am J Clin Nutr 1994; 60:153–6.
10. Bray GA. Barriers to the treatment of obesity. Ann Intern Med 1991; 115:152–3.
11. Weintraub M, Bray GA. Drug treatment of obesity. Med Clin North Am 1989; 73:237–49.
12. Bray GA. Drug treatment of obesity. Am J Clin Nutr 1992; 55: 538S–544S.
13. Bray GA. Use and abuse of appetite-suppressant drugs in the treatment of obesity. Ann Intern Med 1993; 119:707–13.
14. Stunkard A. Anoretic agents lower a body weight set point. Life Sci 1982; 30:2043–55.
15. Weintraub M. Long-term weight control: the NHLBI funded multimodel intervention study. Clin Pharmacol Ther 1992; 51:581–5.
16. Weintraub M, Sundaresan PR, Madan M, et al. Long-term weight control study I (weeks 1 to 34). Clin Pharmacol Ther 1992; 51: 586–94.
17. Weintraub M, Sundaresan PR, Schuster B, et al. Long-term weight control study II (weeks 34 to 104). Clin Pharmacol Ther 1992; 51:595–601.
18. Weintraub M, Sundaresan PR, Schuster B, Moscucci M, Stein EC. Long-term weight control study III (weeks 104 to 156). Clin Pharmacol Ther 1992; 51:602–7.
19. Weintraub M, Sundaresan PR, Schuster B, et al. Long-term weight control study IV (weeks 156 to 190). Clin Pharmacol Ther 1992; 51:608–14.
20. Weintraub M, Sundaresan PR, Schuster B, Averbuch M, Stein EC, Byrne L. Long-term weight control study V (weeks 190 to 210). Clin Pharmacol Ther 1992; 51:615–8.
21. Weintraub M, Sundaresan PR, Cox C. Long-term weight control study VI. Clin Pharmacol Ther 1992; 51:619–33.
22. Weintraub M, Sundaresan PR, Schuster B. Long-term weight control study VII (weeks 0 to 210): serum lipid changes. Clin Pharmacol Ther 1992; 51:634–41.
23. Weintraub M. Long-term weight control study: conclusions. Clin Pharmacol Ther 1992; 51:642–6
24. Scoville BA. Review of amphetamine-like drugs by the Food and Drug Administration: clinical data and value judgments. In: Bray GA, ed. Obesity in perspective, Bethesda, Md: National Institutes of Health, 1975:441–3. DHEW publication No.(NIH) 75-708.
25. Weintraub M. Phenylpropanolamine as a anorexiant agent in weight control: a review of published and unpublished studies. In: Morgan JP, Kagan DV, Brody JS, eds. Phenylpropanolamine. New York, NY: Praeger Scientific, 1985:53–79.
26. Silverstone JT, Solomon T. The long-term management of obesity in general practice. Br J Clin Pract 1965; 19:395–8.
27. McKay RHG. Long-term use of diethylpropion in obesity. Curr Med Res Opin 1973; 1:489–93.
28. Enzi G, Baritussio A, Marchiori E, Crepaldi G. Short-term and long-term clinical evaluation of a non-amphetaminic anorexiant (mazindol) in the treatment of obesity. J Int Med Res 1976; 4:305–17.
29. Judson KD. The anoretic and hypotensive effect of fenfluramine in obesity. J R Coll Gen Pract 1977; 27:497–501.
30. Stunkard AJ, Craighead LW, O'Brien RM. Controlled trial of behavior therapy, pharmacotherapy, and their combination in the treatment of obesity. Lancet 1980; 2:1045–7.
31. Craighead LW, Stunkard AJ, O'Brien RM. Behavior therapy and pharmacotherapy for obesity. Arch Gen Psychiatry 1981; 38:763–8.
32. Douglas JG, Gough J, Preston PG, et al. Long-term treatment with fenfluramine in obese subject. Int J Clin Pharmacol Res 1985; 4:247–53.
33. Finer N, Craddock D, Lavielle R, Keen H. Prolonged weight loss with dexfenfluramine treatment in obese patients. Diabetes Metab 1987; 13:598–602.
34. Finer N, Craddock D, Lavielle R, Keen H. Dextrofenfluramine in the treatment of refractory obesity. Curr Ther Res 1985; 38:847–54.
35. Steel JM, Munro JF, Duncan LJP. A comparative trial of different regimens of fenfluramine and phentermine in obesity. Practitioner 1973; 211:232–6.
36. Goldstein DJ, Rampey AH, Dornseif BE, Levine LR, Potvin JH, Fludzinski LA. Fluoxetine: a randomized clinical trial in the maintenance of weight loss. Obes Res 1993;1:92–8.
37. Fluoxetine and other drugs for treatment of obesity. Med Lett 1994; 36:107–8.
38. Turner P. Dexfenfluramine: its place in weight control. Drugs 1990; 39:53–62.
39. Tauber-Lassen E, Damsbo P, Henriksen JE, Palmvig B, Beck-Nielsen H. Improvement of glycemic control and weight loss in type 2 (NIDDM) diabetics after one year of dexfenfluramine treatment. Diabetologica 1990; 33:A124.
40. Chiasson J-L, Lau DCW, Leiter LA, Tildesley HD, Birmingham CL, Ekoe JM. Fluoxetine has potential in obese NIDDM—multicenter Canadian trial. Diabetes 1989; 38:154A.
41. Willey KA, Molyneaux LM, Overland JE, Yue DK. The effects of dexfenfluramine on blood glucose control in patients with type 2 diabetes. Diabetic Med 1992; 9:341–3.
42. Stewart GO, Steing GR. Dexfenfluramine in type II diabetes: effects on weight and diabetes control. Med J Aust 1993; 158:167–9.
43. Gray DS, Fujioka K, Devine W, Bray GA. Fluoxetine treatment of the obese diabetic. Int J Obes 1992; 16:193–8.
44. Meinders AE, Pijl H. Very low calorie diets and recently developed anti-obesity drugs for treating overweight non-insulin dependent diabetics. Int J Obes 1992; 16:535–46.
45. Watts NB, Spanheimer RG, DiGirolomo M, Rebhard SS, et al. Prediction of glucose response to weight loss in patients with non-insulin-dependent diabetes mellitus. Arch Intern Med 1990; 150: 803–6.
46. Goff DC, Scheklle RB, Moye LA, Katan MB, Gotto AM, Stamler J. Does body fatness modify the effect of dietary cholesterol on serum cholesterol: results from the Chicago Western Electric Study. Am J Epidemiol 1993; 137:171–7.
47. Calles-Escandon J, Horton ES. The thermogenic role of exercise in the treatment of morbid obesity: a critical evaluation. Am J Clin Nutr 1991; 55:533S–537S.
48. Wing RR. Behavioral treatment of severe obesity. Am J Clin Nutr 1992; 55:545S–551S.
49. Astrup A, Buemann B, Christensen J, Toubro S, Thorbek G, Victor OJ, Quaade F. The effect of ephedrine/caffeine mixture on energy expenditure and body composition in obese women. Metabolism 1992; 41:686–8.
50. Kral JG. Overview of surgical techniques for treating obesity. Am J Clin Nutr 1992; 55:552S–555S.
51. Physicians' desk reference. Montvale, NJ: Medical Economics, 1995.
52. Griffiths RR, Brady JV, Bradford LD. Predicting the abuse liability of drugs with animal drug self-administration procedures: psychomotor stimulants and hallucinogens. Adv Biol Pharmacol 1979; 2:163–208.
53. Phenylpropanolamine for weight reduction. Med Lett 1984; 26: 55–6.
54. Bale JF, Fountain T, Shaddy R. Phenylpropanolamine-associated CNS complications in children and adults. Am J Dis Child 1984; 138:683–5.
55. Blackburn GL, Morgan JP, Lavin PT, Noble R, Funderburk FR, Istfan N. Determinants of the pressor effect of phenylpropanolamine in healthy subjects. JAMA 1989; 26:3267–73.
56. Woo OF, Benowitz NL, Bialy FW, Wengert JW. Atrioventricular conduction block caused by phenylpropanolamine. JAMA 1985; 253:2646–7.
57. Grundy SM, Barnett JP. Metabolic and health complications of obesity. Dis Mon 1990; 36:611–731.