

**MANAGEMENT OF  
OBESITY:  
PHARMACOLOGICAL  
TREATMENT**

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## LEARNING OBJECTIVES



This chapter will enable you, the Family Physician:

1. To prescribe pharmacotherapy in the management of the obese patient.
2. To counsel patients on safe life style approaches to weight management and balancing calorie intake and physical activity.
3. To advise patients in the use of over the counter (OTC) preparations.
4. To give dietary advice to patients attempting to lose weight.

## Introduction



Obesity is a complex, multi-factorial condition in which excess body fat may put a person at health risk. Basic treatment of overweight and obese patients requires a comprehensive approach involving diet and nutrition, regular physical activity, behavioral change and pharmacotherapy (where indicated), with an emphasis on long-term weight management rather than short-term extreme weight reduction.

Family physicians have an important role in promoting preventive measures and encouraging positive lifestyle behaviours, as well as identifying and treating obesity-related comorbidities. They are also ideally suited to counsel patients about safe and effective weight loss and weight maintenance programs.

Treatment involves assessment and management:

### Assessment:

This requires the determination of the degree of overweight and a patient's overall risk status. In 1997, the International Obesity Task Force, convened by the World Health Organisation (WHO), recommended a standard classification of adult overweight and obesity based on the following BMI (Body Mass Index =  $\text{Weight} / \text{Height}^2$ ) calculations; a BMI of 25.0 – 29.9 kg per  $\text{m}^2$  is defined as overweight and a BMI of 30.0 kg per  $\text{m}^2$  or more is defined as obesity. The BMI together with waist circumference (which correlates with abdominal fat content) is used to determine the patient's overall risk status.

Treatment is recommended for patient's with a BMI of 25.0-29.9 kg per  $\text{m}^2$  or a high waist circumference and two or more obesity related risk factors (i.e. hypertension, dyslipidemia, coronary heart disease, type 2 Diabetes Mellitus and sleep apnea). Treatment is also recommended for patients with a BMI of 30 or more kg per  $\text{m}^2$  regardless of risk factors. Overweight persons without risk factors should be encouraged to avoid further weight gain. The decision to start drug therapy should carefully weigh the risk of therapy vs. the benefits of potential weight loss. Patient's receiving weight loss drugs should be carefully monitored by the physician to ensure the safety and efficacy of the drug therapy.



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Some of the more common drugs (past and present) will be discussed below:

➤ *Fenfluramine and Dexfenfluramine:*

These drugs primarily increase the release of serotonin in brain synapses although there is a minor effect on re-uptake. They are associated with cardiac valve abnormalities as well as pulmonary hypertension and are therefore now discontinued.

➤ *Fluoxetine:*

Fluoxetine is a selective re-uptake inhibitor of *Serotonin* in neural synapses. In studies, 6 months in duration, weight loss was greater than with placebo but after 6 months, weight regain is frequent and long term weight loss approaches that of placebo.

Fluoxetine has not been approved for the treatment of obesity but there have been studies in obese subjects with and without binge eating disorders in the absence of clinical depression. Fluoxetine (60mg/d) was found effective in decreasing the frequency of bingeing episodes.

➤ *Phentermine:*

This drug modulates noradrenergic neurotransmission, which results in appetite suppression. Its use was more widespread after combination with *fenfluramine*. This combination, also known as "Phen-fen" is no longer available due to the latter's side effects. Phentermine alone has not been reported to cause valvular disease.

➤ *Sibutramine:*

Sibutramine is a re-uptake inhibitor of both serotonin and noradrenaline. These two mechanisms acting synergistically are responsible for its anorectic effect (different from fenfluramine, which increased serotonin release only). However it does not have a major effect on appetite but it increases satiety after eating. Although some literature suggests that Sibutramine may increase the metabolic rate, this has not been proven conclusively in humans. Adverse effects include headache, dry mouth, constipation and insomnia. The effect that is of most concern is that of elevation of blood pressure as well as the pulse rate. Therefore blood pressure should be monitored regularly while the patient is on therapy.

Contraindications include anorexia nervosa, hypersensitivity to drug or ingredients, therapy with monoamine oxidase inhibitors or other serotonergic drugs, coronary heart disease, congestive cardiac failure, stroke, arrhythmia, uncontrolled hypertension, severe hepatic or renal disease, pregnancy and lactation. Caution is advised in individuals younger than 18 years or older than 65 years and in those with a history of seizures and those that use other medications capable of raising blood pressure or with central actions.

Initial weight loss is a good predictor for response. If no weight is lost in the first 4 to 6 weeks of therapy, Sibutramine should be stopped.

➤ *Orlistat:*

In 1999, the drug Orlistat was approved by the Food and Drug Administration (FDA) as an obesity treatment. Orlistat is a lipase inhibitor that blocks the absorption of dietary fat by inhibiting gastrointestinal lipases. Fat absorption is reduced by about one third by this method. There is no documented effect on intestinal hydrolases (amylase, trypsin, chymotrypsin etc) and hence no effect on the absorption of carbohydrates, protein and phospholipids. It is minimally absorbed from the gastrointestinal tract, and excretion is almost completely in the faeces.

Clinical trials in the United States and Europe showed that Orlistat at 120mg 3 times daily was associated with an 8.8% to 10.2% weight loss after 1 year. There were also significant decreases in total cholesterol, low-density lipoprotein cholesterol, fasting blood glucose, insulin levels and

blood pressure. Orlistat has also been studied for weight maintenance. A dosage of 120mg 3 times daily was associated with less weight regain than Orlistat 60mg 3 times daily.

**Adverse effects** while on Orlistat included oily fecal spotting, flatus with discharge, faecal urgency and fatty or oily stools. Adverse effects were mild, encountered early in therapy and generally resolved. Decreases in fat soluble vitamins were observed but no deficiencies were reported. Patients taking Orlistat should be advised to take a daily multivitamin 2 hours before or after Orlistat dosing.

Contraindications include chronic mal-absorption, cholestasis, known hypersensitivity, pregnancy and lactation. Caution is advised when it is used in combination with cyclosporine.

In conclusion, many studies have reported that when drug treatment is stopped, weight regain usually follows. Maximum weight loss occurs in the first 6 months of treatment. There is little justification for short-term drug use and once drug treatment is initiated, it should be continued long-term. Patients should be carefully selected for pharmacotherapy and should be fully instructed in the use of such agents. They should understand that life style changes in the areas of diet, exercise and behavioral modification are critical for success, and improvement in long-term health is the most important goal of treatment. Although long term treatment of obesity is advocated one must bear in mind that little information is available on the safety and effectiveness of these medications when used for more than two years.

Research is ongoing, evaluating agents such as leptin, B agonists, uncoupling proteins, and others in a search for new pharmacologic agents to treat obesity.

#### ***Over the counter (OTC) preparations:***

The efficacy of these preparations is doubtful and they are therefore best avoided. Amphetamine-type agents e.g. norpseudoephedrine, phentermine and diethylpropion may cause anxiety, agitation and insomnia. Caffeine is in many non-prescription weight loss medications. Ephedrine and ephedra are also widely available in OTC weight loss preparations and are sometimes combined with caffeine. This combination may increase the risk of adverse effects (including death) which have also been linked to the use of ephedra e.g. Redupon – which is a combination of caffeine 50mg, ephedrine HCL 17.5 mg and phenolphthalein 30mg. Another similar preparation is Dietaid Diffucaps.

There are several d-Norpseudoephedrine HCL 50mg capsules on the market e.g. Appetrol, Dietene, EetLess, Slim 'n Trim, Nobese No. 1 and Thinz capsules.

In addition there are phenylpropanolamine HCL 75mg preparations available e.g. Acutrim, Restaslim.

#### ***“Natural” Medications:***

Vita-force Juniwa is a “herbal” diuretic containing Juniper oil that helps regulate water levels, preventing excessive fluid retention.

Vitaforce Lean Body Factor 1 capsules containing Citrimax, Chrome Mate and L-Carnitine that are said to be used for advanced weight reduction.

Vitaforce Lean Body Factor 2 capsules that are said to be for weight maintenance once you have lost weight.

There is no scientific evidence that proves that the above preparations are effective in causing weight loss.

***Weight Loss gimmicks:***

- Herbal “Phen/fen” – the combination of St. John’s Wort and ephedrine has been promoted as a safe alternative to “phen/fen” has been withdrawn. Ephedrine can result in heart attacks, hypertension and shakes.
- Megaslim capsules – capsules containing “high potency” L-Carnitine with magnesium and pyruvate.
- Grapefruit/Cider capsules – are said to have a fat-burning effect. Needless to say that these claims are not substantiated by scientific evidence.
- Pyruvate – Pyruvate is a 3-carbon intermediary in the metabolism of glucose and has been promoted as a “metabolic stimulant”. There is as yet no proof that supplementing your diet with pyruvate will result in weight loss.
- Chromium picolinate - Chromium is promoted as an agent which will increase metabolism and suppress appetite, thus leading to weight loss but this has not been proven.
- The “ear patch” – A patch which if put behind the ear will cause a decrease in appetite and hence weight loss. This is not true.
- “Slimming” soap – No soap will “wash away” the extra fat.
- Diet magnets – as before, it remains to be proven that magnets will promote weight loss.
- Apple cider vinegar – Vinegar is a good condiment but does not assist in weight loss (nor does it remove toxins, speed up metabolism or decrease appetite).
- Exercise pills in a bottle – Some of these pills contain ephedrine with its accompanying side effects as mentioned before.

**Diets**

The task of a dieter is not simply losing weight. It is to develop practical, long-term eating habits that will keep weight down for years.

Radical diets, although sometimes successful in the short run, have serious disadvantages.

*Crash Diets:*

- Difficult to maintain and once the person is off the diet, the weight is gained back
- Nutritionally unbalanced and therefore dangerous. Diets that emphasize one category of foods to the exclusion of others can cause serious metabolic imbalances.
- Extreme diets do not change bad eating habits but instead temporarily substitute one unsound dietary pattern for another.

*Very low calorie diets:*

These diets are dangerous and ineffective because they cause the body to become more efficient at energy conservation i.e. the resting metabolic rate drops. As a result many dieters find that periods of severe calorie restrictions make it harder to keep weight off.

*High protein diets:*

High protein diets have recently been proposed as a “new” strategy for successful weight loss. Although these diets may not be harmful for most healthy people for a short period of time, there are no long-term scientific studies to support their overall efficacy and safety. There is no evidence that high-protein diets without concomitant decrease in calorie intake result in sustained weight loss or improved health.

The solution to these problems is two fold:

- Choose a feasible weight loss program that helps develop good eating habits that do not make you feel deprived.
- Use exercise to help burn calories and develop muscle that will raise your resting metabolic rate (even at rest, muscle burns more calories per minute than does body fat)

A reliable support group is the “weight watchers” group. They do not advocate any gimmick diets but aim to moderately restrict calories and increase physical activity to promote weight loss.

**Eating disorders**

In the management of eating disorders, psychotherapy remains the essential cornerstone of treatment.

Patients presenting with both obesity and binge eating disorders (BED) face multiple challenges; namely normalizing their eating, improving their physical health and working to enhance their own acceptance of their body image.

Several psychological and pharmacological treatment approaches have been used in these patients. Most suppress binge eating in the short term but sustained weight loss remains largely an unrealized goal. In either approach it is clear that adopting a long-term focus and promoting enhanced self-acceptance will have more tangible results.

➤ *Bulimia Nervosa (BN):*

The drug most studied is fluoxetine, which is shown to be superior to placebo but less effective than cognitive behavioral therapy (CBT) alone. Combination of fluoxetine and CBT may provide optimal treatment. The dose of fluoxetine found to be effective is 40-60 mg daily. Sibutramine has not been tested in BN yet.

➤ *Anorexia Nervosa (AN):*

Information available thus far suggest a lack of efficacy of SSRI's in AN. They may be of value in combination with CBT in patients following weight recovery.

CBT continues to be one of the recommended evidence-based interventions in the treatment of eating disorders, for both AN and BN.

➤ *Nutritional supplements and/or pharmacotherapy in AN:*

Most patients with advanced cancer, anorexia and/or weight loss do not appear to benefit from nutritional supplementation. Work in this field is still in the experimental stages. Some of the interventions which have been studied are listed below:

- ◆ Progestational agents
- ◆ Corticosteroids
- ◆ Thalidomide (Thalomid)
- ◆ Eicosapentaenoic acid
- ◆ Adenosine triphosphate
- ◆ Non-steroidal anti-inflammatory agents

These interventions promise to replenish lean tissue but require further investigation before they can be recommended as standard clinical practice.

### QUESTIONS:



1. Briefly describe the role of the Family Physician in the management of the obese patient.
2. Define BMI (Body Mass Index) and indicate how it is used to classify adult over weight and obesity.
3. Management of obese patients requires a comprehensive approach. List all the factors, which must be taken into consideration when managing a patient with obesity.
4. What are the indications of pharmacotherapy in the management of the obese patient?
5. Give the classification of drugs used in the treatment of obesity with examples in each group.
6. Discuss the mode of action and side effects of sibutramine (Reductil) and orlistat (Xenical)
7. List some of the counter over the counter (OTC) preparations what are the risks involved in using these preparations?
8. There are numerous popular weight-loss gimmicks on the market. Mention some of them. What advice would you give to your patient regarding the use of these gimmicks?
9. When advising your patient regarding his/her diet, what will be the broad principle of your dietary advice?
10. Is there any role for pharmacotherapy in the management of the eating disorders? If so, discuss this further.

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