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REVIEW

Taking another look at the management of obesity

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Obesity is a common health condition that is increasing worldwide. Obesity is also a multifactorial condition that affects many physiological systems in the human body. Some include the following: central nervous system (CNS) effects, metabolic effects such as type 2 diabetes (T2D), various effects on the cardiovascular system (CVS), haematological effects and infertility in females. Treatment is suggested to be initiated by first making lifestyle changes such as increasing physical activity, decreasing caloric intake of foods, inclusion and accessibility to healthy foods (e.g. fruits, fibre, vegetables) and consuming foods of a lower glycaemic content. In addition to these interventions, pharmacological management strategies can also be considered adjuncts to managing obesity. These medicines (monotherapies/combined products) include amfepramone, cathine (syn D-norpseudoepherine), phendimetrazine, phentermine, orlistat, liraglutide, semaglutide, bupropion and the bupropion-naltrexone combination, and phentermine-topiramate combination. The pharmacist plays an essential role in identifying obese individuals, making suggestions for losing excess weight, suggesting lifestyle modifications, providing information about anti-obesity medicines and dispensing these medicines.

Keywords: causes, consequences, diagnosis, management, obesity, risk factors

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Introduction

The World Health Organization (WHO) defines obesity as an 'abnormal or excessive fat accumulation that may impair health' and further classifying that 'the fundamental cause of obesity and overweight is an energy imbalance between calories consumed and calories expended'.[1]

Obesity is a major public health condition worldwide and accounts for the fifth most common health condition leading to death worldwide. Obesity is also linked to many other health conditions, of which some form part of the cardiovascular, renal and metabolism (CVRM) diseases. Lifestyle changes and medication(s) can effectively manage this health condition. It is important to always take note of the fact that obesity is a lifestyle disease.[2]

Research conducted estimated that the number of 641 million obese adults identified in 2014 was a significant increase when compared to the 105 million identified in 1975.[3] Nwosu et al. (2022)[4] conducted a study where they collectively analysed nationally representative surveys covering nearly two decades to investigate trends in the prevalence of adolescent obesity in South Africa. Their findings showed that by 2016, the prevalence of adolescent obesity was high in South Africa – more than one in five adolescents. These figures are similar to those in Europe; however South African girls appear be at higher risk of overweight and obesity in contrast to Europe, as well as adolescents from high-earning families.

Contributing factors to obesity are the ratio of increased intake of unhealthy foods (e.g. fast foods) to lower levels of physical activity. The lower this ratio, the more likely the individual will have CVRM – diseases also known as cardiometabolic diseases, hypertension, dyslipidaemia and type 2 diabetes (T2D). The following systems are also noteworthy links to obesity: respiratory (obstructive sleep apnoea [OSA]), gastrointestinal (GI) (non-alcoholic fatty liver disease), muscular adverse effects, physiological problems (depression) and social (stigmatisation) effects. It is thus imperative to test for these conditions and effects, screen for comorbidities, and determine their management.[5-8]

Considering the potential consequences of obesity, pharmacists need to identify overweight and obese adults and adolescents. This article focuses on adult obesity.

Causes

Potential factors that influence and/or cause obesity

Obesity is a complex health issue stemming from a combination of factors, including:[2,6,9]

- Individual factors (e.g. genetics, epigenetic environments, learned behaviours)
- Substantial causes (e.g. unhealthy societal/cultural eating habits, food, desserts, etc.)
- Acquired conditions (e.g. those that depend on low rates of physical exercise, chronic overeating despite genetic and epigenetic factors, longer screen time and a sedentary lifestyle)
- Geographic regions (e.g. those that signal social, economic and environmental factors in an 'obesogenic' environment)

Comorbidities

The different forms of obesity, including abdominal obesity, have the potential to lead to an increased risk of several conditions and

diseases, e.g. asthma, cancer, diabetes, hypercholesterolaemia, and cardiovascular diseases (CVDs).[10] Other studies also indicated that obesity can affect multiple organ systems, such as the cardiovascular, endocrine, central nervous and GI systems, and cause coronary heart disease (CHD), atrial fibrillation (AF) and heart failure (HF).[11]

Neurodegenerative diseases

Evidence indicates that there are correlations between adult obesity and the development of Alzheimer's disease and Parkinson's disease. This is due to the correlation factor of T2D.[12] Dementia has also been linked to these factors.

Cardiovascular disease

Obesity worsens several risk factors, particularly hypertension, CVD, AF and HF. These are all exacerbated by obesity as a pre-existing condition.[13] CVDs, such as high systolic and diastolic blood pressure, are major presentations of obesity, with endpoint diseases such as ischaemic heart disease and stroke.[8] Dyslipidaemia (raised low-density lipoprotein cholesterol [LDL], increased triglycerides and low high-density lipoprotein cholesterol [HDL-C]) is one of the most common CV abnormalities in obesity.[7,8]

Prostate diseases

Parikesit et al. found that obesity is a risk factor for different prostate diseases, including benign prostate hyperplasia and prostate cancer.[14]

Respiratory diseases

Respiratory systems/diseases are also affected by obesity. Respiratory problems such as asthma and OSA are more prevalent in obese children compared to their peers with healthy weights.[15]

Autoimmunity

The relationship between obesity and autoimmune disorders has been shown. Autoimmune conditions include rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease, multiple sclerosis, type 1 diabetes and thyroid autoimmunity – especially Hashimoto thyroiditis.[16]

Diabetes

T2D has been shown to be implicated in obese individuals.[17] The twin epidemics of obesity and diabetes have combined to form part of major health crises. Several studies have shown that diabetes is one of the most considered comorbidities of obesity.[18-20] Obesity is also associated with the development of insulin resistance.

Diagnosis

Direct measures

Although Body Mass Index (BMI) is the most frequently indirect method used to measure obesity, there are alternative direct measures that can also be used. These direct measures include measurement of body fat directly by using dual energy x-ray absorptiometry. In recent years, abdominal obesity was defined by using waist circumference while waist-hip ratio was used in earlier years.[21]

Indirect measures (Body Mass Index)

BMI is a simple way to determine different kinds of obesity. Body Mass Index (BMI) is calculated as follows:

$$\text{BMI} = \frac{\text{weight (kg)}}{\text{height (m}^2\text{)}}$$

The BMI is used to classify adults into the following categories:[22]

a. Underweight

b. Overweight

c. Obese

Table I gives a BMI classification of adult weights based on the WHO schema.

Obesity and its collateral damage

The following are potential consequences that may impact the patient, and are important for the holistic management of the patient:

Haematological consequences of obesity

Since obesity is considered a chronic inflammatory condition, it also has theoretical and established downstream effects. This state of low-grade systemic inflammation is characterised by an acute adipose tissue phase response with interleukin (IL), IL-6, IL-1 and IL-8 and tumour necrosis factor (TNF)-α playing the largest role, which results in subsequent elevation of acute-phase proteins such as c-reactive protein (CRP).[23] This implies a subsequent/relative state of leucocytosis and an increased risk for venous thromboembolism (VTE).

This article briefly discusses only a few haematological consequences of obesity. Other haematological conditions

Table I: WHO BMI adult classification[2]

Classification	BMI (kg/m²)	Risk of comorbidities
Underweight (B2.5)	< 18.5	Low, but the risk of other clinical problems increased
Normal weight	18.5–24.9	Average
Overweight	25.0–29.9	Mildly increased
Obese	≥ 30	
Obese I	30.0–34.9	Moderate
Obese II	35.0–39.9	Severe
Obese III	> 40	Very severe

include obesity and platelet count, obesity and thrombosis, obesity and elevated levels of coagulation factors and von Willebrand factors,[24] obesity impairment in fibrinolysis,[25] obesity's role in promoting platelet hyperactivity[26] and obesity's role in promoting endothelial dysfunction.[27]

Obesity and iron deficiency

A study published in 1962 first reported lower serum iron levels in obese adults vs. non-obese adolescents.[28] Although it appears counterintuitive to expect an iron deficiency (ID) in a setting of calorie and nutrient excess, lower concentrations of serum iron have been observed in relation to an increased BMI for decades.[23] The link between obesity and anaemia remains less certain and more studies should be conducted regarding this matter.

Obesity in red blood cell count

It is noteworthy to consider that ID is expected to have an increased rate that can progress to iron deficiency anaemia (IDA).[39] Studies have indicated that obese adults have lower levels of haemoglobin than non-obese adults,[29,30] but some studies have shown no correlation[31] of a protective effect.

Obesity and thrombosis

Evidence that obesity, as a proinflammatory condition, promotes an environment that promotes a prothrombotic state, supporting arterial and venous thrombosis. Studies have also indicated associations between abdominal obesity and VTE.[32-34] Other studies undertaken indicated that the risk for VTE is higher in women compared to men, with women having a higher risk for stroke, compared to men affected by CVD.[35,36]

The role of leptin in obesity

Leptin is a peptide hormone that is part of the product of the obese (*ob*) gene that regulates food intake, body mass, and reproductive function and plays a role in foetal growth, proinflammatory immune responses, angiogenesis and lipolysis. Hyperleptinaemia and resistance to a reduction of body mass are two common characteristics of obesity.[37]

Studies have shown that the concentration of circulating leptin decreases during fasting or energy restriction but increases during refeeding, overfeeding, and surgical stress.[38-41] These effects provide an overview of the various pathways that regulate leptin signalling system to maintain body mass, e.g. an increase of fat cells leads to a leptin level, which in turn binds to the leptin receptors (LEP-R) in the brain signalling the inhabitation of food intake and an increase in energy expenditure.[42]

The leptin receptor

Leptin acts by binding to the LEP-R that exhibits structural similarity to the class I family of cytokine receptors, which include receptors for interleukins (ILs), leukaemia inhibitory factor (LIF), colony-stimulating factor 3 (CSF-3), growth hormone (GH), prolactin and erythropoietin.[43]

Regulation of energy balance

Energy balance is maintained when energy from food intake is equal to energy expenditure.

Leptin regulates appetite and metabolism by inhibiting the synthesis and release of neuropeptide Y (NPY) in the arcuate nucleus (ARC). Subsequently, it was discovered that the LEP-R isoform b (LEP-Rb) in the ventromedial hypothalamic nucleus (VMH), ARC, lateral hypothalamic nuclei (LH), and the dorsomedial hypothalamic nucleus (DMH), which play a crucial role in the regulation of energy balance and body mass, was driven by leptin.[6]

Later studies demonstrated that leptin can inhibit neural pathways activated by appetite stimulants (orexigenic) to reduce energy intake and activate pathways targeted by anorexigenic agents to suppress appetite.[44] Examples of orexigenic neuropeptides include NPY and the agouti-related protein (AgRP). The product of proopiomelanocortin (POMC), alpha-melanocyte-stimulating hormone (a-MSH), is an anorexigenic.[45]

In brief, leptin regulates energy balance by modulating the activity of NPY/AgRP and POMC neurons in the ARC nucleus.[45]

Regulation of leptin's secretion

Leptin is primarily produced in white adipose tissue, although smaller amounts have been detected in other body tissues, including the brown adipose tissue (BAT), placenta, foetal tissue, stomach, muscles, bone marrow, teeth, and brain. Leptin circulates in the blood in both free and protein-bound forms, where the free form of leptin is the biologically active form. The equilibrium between free and bound leptin regulates leptin bioavailability.[46]

Leptin can enter the CNS by receptor-mediated transport. The LEP-R isoform plays a particularly significant role in transporting leptin through the blood–brain barrier (BBB).[47]

A complex array of endocrine, neuroendocrine, and paracrine signals governs leptin synthesis and secretion.[48] The secretion of leptin is proportional to body mass and nutritional status. The serum leptin levels decrease during starvation, associated with an adaptive physiological response to the state of starvation.[48]

Food intake, total body fat, as well as several hormones regulate leptin secretion.[48] Insulin and, to a lesser extent, other pancreatic peptide hormones, including amylin, glucagon, and pancreatic polypeptides, reduce food intake and affect leptin secretion.[49] Insulin is the primary regulator of leptin production; hence prolonged hyperinsulinaemia leads to an increase in the plasma concentration of leptin, while short-term hyperinsulinaemia does not cause such a change.

Expression in obesity

Severe early obesity develops from rare genetic mutations that affect leptin signalling. Such mutations often lead to congenital leptin deficiency or high, but ineffective, leptin and leptin resistance.[50] Hyperleptinaemia and resistance to reducing body mass are two characteristics of typical obesity.[51]

Leptin is overexpressed at the gene level in the adipose tissue of individuals with obesity.[52] Furthermore, strong positive associations exist between plasma leptin levels and body fat percentage.[53] Other studies point towards leptin resistance.

Resistance in obesity

Leptin resistance is characterised by reduced satiety, over-consumption of nutrients, and increased total body mass. This often leads to obesity, which reduces the effectiveness of using exogenous leptin as a therapeutic agent.[54] Leptin resistance occurs due to the leptin's inability to reach the target cells, reduced LEP-R expression, or disturbed LEP-R signalling.[55]

Obesity and female infertility

Obesity affects women of reproductive age with some of the following presentations: menstrual irregularities, endometrial pathology and infertility. Obese women also have increased pregnancy complication rates, e.g. hypertensive disorders, gestational diabetes, preterm birth, and caesarean delivery rates.[56]

Clinical effects

Obesity has a negative effect on female reproduction function, primarily through functional abnormalities of the hypothalamic-pituitary-ovarian (HPO) axis. Higher than normal levels of insulin have been associated with increased ovarian androgen production. The increased circulation of androgens is aromatased to oestrogen, ultimately leading to negative feedback on the HPO axis, thus affecting gonadotrophin production,[57] which, in turn, manifests as menstrual irregularities and ovulatory dysfunction.

The increase in insulin leads to the implicated manifestation of polycystic ovarian syndrome (PCOS), which is characterised by oligomenorrhoea and hyperandrogenism.[58] In PCOS, the deposition of visceral fat leads to insulin resistance and hyperinsulinaemia (due to increased androgen levels), which further leads to the stimulation of adrenal and androgen production in the perpetual cycle.[58]

It is noteworthy to mention that obese women remain sub-fertile even in the absence of ovulatory dysfunction. Obese women also seem to struggle with getting pregnant through assisted reproductive technology (ART), which provides more evidence than just having an ovulatory disorder. Obese women also have smaller oocytes that are less likely to be fertilised.[59]

Other studies conducted reported a negative impact on live birth rates (LBRs), which corresponds with increased BMI.[60-62]

Management

The management of obesity needs to be individualised, taking a holistic view of the individual concerned. One should start with lifestyle changes and modifications: increase of physical exercise and lower caloric intake, and only after that, opt for pharmacological interventions.

Nonpharmacological management

Obesity is traditionally seen as an imbalance between caloric food intake and energy output. However, the current standpoint involves a complex interplay of biological and psychosocial factors. It is noteworthy to mention that current research has shown that a weight loss between 5% and 10% is enough to induce clinically relevant improvements in health risk factors such as hyperglycaemia and other biomarkers related to the augmented risk of CVD.[63]

To achieve successful weight loss maintenance over time, the WHO, European Union (EU)[64] and the US Academy of Nutrition and Dietetics[65] recommend lifestyle changes, including a diet that reduces excessive energy intake and improves dietary quality. However, successful treatment of obesity may, in several cases, require adjuvant pharmacotherapy.

A critical factor for success in managing obesity includes, among others, motivation, i.e. the use of motivational interviewing techniques. This includes the following four primary skills, which can be remembered by the acronym **AIAL**:

- **A**sking
- **I**nforming
- **A**dvising
- **L**istening

Other interventions should include the creation of a healthier environment by providing easy access to food, increased pleasurable physical activities (avoiding sedentary activities), social support systems and compliance and positive thinking with goals set on self-motivation, reinforcements, rewards and peer monitoring.[5,66]

Pharmacotherapy should be considered for hypertension > 99th percentile, LDL-C > 4.9 mmol/l and diabetes not responding to lifestyle changes.[67] Current recommended dietary approaches to obtain weight loss are classified into two main groups:[68]

1. **Energy restriction-based diets,** e.g. low-fat, low-carbohydrate and the Mediterranean diet.
2. **Restriction of specific foods** (the Paleo concept) or intermittent calorie restriction (the intermittent fasting concept).[5]

Pharmacological management

As stated above, interventions for weight loss are initially started with lifestyle modifications. Pharmacological treatments are added as adjunct benefits.

Prescribing guidelines for the obese patient[69]

Dosage regimens for obese individuals need to be adjusted and can be done in various ways.

Different weights can be considered to calculate the medication dosing for the obese patient. Dose prediction is more mechanically based by separating fat-free mass (FFM) from fat mass.

The following equations are used:

1. **Total body weight (TBW)** is simply the reading obtained from the scale.
2. **Fat-free mass (FFM)** is similar to lean body weight **(LBW)** but excludes fat in cell membranes. The clinical difference between FFM and LBW is insignificant.

FFM measurements have been used to construct a predictive formula using TBW, length and gender.

$$\textbf{FFM (males)} = \frac{42.92 \times \text{height}\ (m^2) \times \text{TBW (kg)}}{30.93 \times \text{height}\ (m^2) + \text{TBW (kg)}}$$

$$\textbf{FFM (females)} = \frac{37.99 \times \text{height}\ (m^2) \times \text{TBW (kg)}}{35.93 \times \text{height}\ (m^2) + \text{TBW (kg)}}$$

Fat mass (FM) = TBW minus (-) FFM

Obesity is a health concern that is associated with many complex physiological changes that influence the pharmacokinetics of medicines. The extent of this variability depends on patient characteristics (e.g. the degree of obesity, underlying organ dysfunction) as well as the physicochemical properties of the medicine.[69]

The following pharmacokinetics are noteworthy:[69]

The volume of distribution (*Vd*) determines the loading dose.

Clearance (*CL*) is the primary determinant of the maintenance dose.

Both *Vd* and the *CL* influence the ***half-life*** and, therefore, the time to reach steady state.

Distribution: Obese individuals have a higher content of body fat which implies that the *Vd* of highly lipophilic medicines may be increased (e.g. diazepam), while in contrast, the *Vd* of hydrophilic medicines may relate better to FFM, although fat mass still contributes (e.g. gentamycin).

Hepatic *CL*: Clearance of some drugs relates better to TBW in the obese (e.g. propofol) whereas for others, FFM appears better (e.g. remifentanil).

Pathophysiological changes associated with obesity, e.g. non-alcoholic fatty liver disease/liver fat, may impair hepatic blood flow, thus impairing **drug metabolism**.

Renal *CL*: In non-obese individuals, both FFM and FM contribute to the predication of glomerular filtration rate (GFR). For every kg of FFM, there is a 21% contribution/kg of FM to the effective body size determining the GFR. This FFM and FM can be used to predict renal function relative to GFR in a 70 kg TBW non-obese individual.[69]

Renal function is determined by the below equation:[69]

$$\textbf{Renal function} = \frac{\text{FFM} \times 0.21 \times (\text{TBW} - \text{FFM})}{70}$$

Anti-obesity preparations

Anti-obesity preparations can be divided into two groups, namely:[70]

1. **Centrally-acting** anti-obesity products, e.g. amfepramone, phentermine and phendimetrazine, cathine (syn D-norpseudoephedrine).
2. **Peripherally-acting** anti-obesity products, e.g. orlistat.

Table II summarises the two groups of anti-obesity products available in South Africa.

Table II: A summary of centrally- and peripherally-acting anti-obesity products[69,70]

	Dose	Dosage forms	Schedule	Trade names
Centrally-acting				
Amfepramone*	75 mg daily, mid-morning; maximum duration eight weeks	Slow-release tablets, 75 mg	6	Tenuate Dospan®
Cathine (syn D-norpseudoepherine)†	1–2 tablets with breakfast followed by 1 tablet after lunch	Tablets, 20 mg	6	Relislim®
Phendimetrazine*	Adult dose: 105 mg before breakfast Adult dose: 35–70 mg an hour before breakfast and lunch	Long-acting tablets, 105 mg Tablets, 35 mg	6	Obex-LA® Obesan X®
Phentermine*	Adults and children > 12 years dose: 10–30 mg capsules, taken at 07h00am; patients require medical review after a defined course of treatment, which ideally should not exceed three months; can be initiated when BMI < 30 kg/m² in an individual with other risk factors	Capsules, 15 mg, 30 mg	5	Duromine®
Peripherally-acting				
Orlistat‡	Adult dose: 120 mg during or up to 1 hour after each main meal; if a meal is missed/contains no fat, the dose should be omitted; doses above 120 mg 3 x per day do not provide additional benefits; discontinue after 12 weeks only if the patient was unable to lose at least 5% of weight as measured at the start of the treatment	Capsules, 120 mg	3	Xenical®

*Sympathomimetics with CNS stimulant effects; has significant abuse potential. †Sympathomimetic with CNS stimulant effects similar to phenylethylamines; used as an adjunct to lifestyle modification; has significant abuse potential.
‡Management of obesity in conjunction with a hypocaloric diet in individuals with a BMI ≥ 30 kg/m² or BMI ≥ 27 kg/m² with comorbidities, only if 2.5 kg has been lost on diet alone over a four-week period.

Table III: A brief summary and an example of a centrally-acting anti-obesity product: phentermine (Duromine®). Indications, dosage form, dose and method of administration, adverse effects, and some pharmacokinetic properties[71]

Indications	• Used as a short-term adjunct in a medically monitored comprehensive regimen of weight reduction (e.g., promotion of exercise, diet [caloric/kilojoule restriction] and behavioural modification in obese patients [BMI† of 30 ≥ kg/m²] who has not achieved a positive clinical response to an appropriate weight-reducing regimen alone) • Can be also be initiated with patients with a lower BMI with other risk factors • Secondary organic causes of obesity should be excluded by diagnosis before prescribing this agent
Dosage form	• Capsules that contain 15 mg of phentermine (opaque green cap with opaque light grey body with marking DUROMINE 15/DUROMINE 15 printed in black ink on both the body and the cap • Capsules that contain 30 mg of phentermine (opaque light grey body with marking of DUROMINE 30/DUROMINE 30 printed in white ink on the body and cap • Capsules are packed into blister formats/strips with 15 capsules spaced per blister form/strip. Two strips are included per commercially available pack
Dose and method of administration	• Doses are taken orally as indicated • Avoid evening dosing as this may cause insomnia • Use only as directed under supervision of a medical practitioner • Do not exceed daily dose • Do not take concomitantly with other appetite suppressants • Patients require medical review after a defined course of treatment, which ideally should not exceed three months
Pharmacokinetic properties	• Absorption: readily absorbed from the GIT (almost complete) • Metabolism (via liver); excretion (urine); half-life: 25 hours

†Note that for more detailed information look at the phentermine (Duromine®) pamphlet. Not all information is tabulated here.

Table III, below, provides a brief summary of an example of a centrally-acting anti-obesity drug, phetermine; its indications, dosage form, dose and method of administration, adverse effects and some pharmacokinetic properties.

Recent advancements with the use of a glucagon-like peptide-1 agonist[70]

Recently the following GLP-1 agonist, liraglutide (Saxenda®), has been used to assist with weight loss in individuals with concurrent T2D.

Table IV, provides some tips of advice that a pharmacist can communicate with patients taking phentermine.

Other pharmacological product combinations

Liraglutide and semaglutide

Liraglutide is a GLP-1 agonist initially approved in 2010 for treating T2D at doses of 1.8 mg subcutaneously (SC) daily. Presumably via effects on the CNS, it has been observed that liraglutide decreases appetite and enhances satiety.[72] Early studies indicated that liraglutide mimics the effects of natural GLP-1 via its interaction with the arcuate nucleus in the hypothalamus,[73] and led to the development of its use in the treatment of obesity. One trial study of 20 weeks demonstrated that liraglutide treatment led to a dose-dependent weight loss of up to 4.4 kg vs. 3 kg for the placebo.[74] It was also observed that prediabetic individuals showed greater weight loss compared to the placebo[75] group. Liraglutide is currently indicated for the treatment of T2D and not as an anti-obesity product.

A drawback of liraglutide is its daily SC injections. Semaglutide, another GLP-1 agonist, can be administered by weekly injections, which makes this more favourable for the patient.[76] In a recent 68-week placebo-controlled trial with obese individuals, it was found that semaglutide treatment (2.8 mg weekly) led to a weight loss of 14.9% compared to 2.4% with the placebo.[77] Another study with a similar design and follow-up period found a weight loss of 16% with semaglutide and 5.7% with the placebo.[78]

Table IV: Some tips of advice that pharmacists can communicate with patients taking phentermine[71]

Ask the patient if he/she is taking any **other medications** (e.g., MAO† inhibitors [do not take within 14 days following their administration], insulin/oral hypoglycaemic agents [responses may vary due to alterations in dietary regimes], psychotropic medicines [including sedatives and agents with sympathomimetic activity], sympathomimetic agents [antagonises adrenergic neuron blocking agents], SSRI‡ [may be associated with CVD§]; thyroid hormones [increase CNS‖ stimulation]
Ask the patient if he/she has **preexisting medical conditions** (e.g., cardiac diseases, hyperthyroidism, agitated states/history of psychiatric conditions including anorexia nervosa and depression, glaucoma, history of drug/alcohol abuse/dependence, poorly controlled epilepsy, mild hypertension/kidney impairment, diabetes)
Ask the patient if she is **pregnant** or **lactating** (safety has not been stablished)
Ask patients if he/she has **hereditary problems of galactose** intolerance (lactose monohydrate contained in phentermine, may have an effect on the glycaemic control of diabetic patients)
Inform the patients that he/she should **gradually loose** and **control weight**
Inform the patient that phentermine may **impair** the ability to perform activities such as mental alertness (e.g., driving/operating machinery)
Avoid use in the elderly and children; concomitant alcohol use (increased CNS side effects)

†Note that for more detailed information look at the phentermine (Duromine®) pamphlet, †MAO inhibitors = Monoamine Oxidase Inhibitors; ‡Selective Serotonin Reuptake Inhibitors; §CVD = Cardiovascular Disease; ‖CNS = Central Nervous System

Table V: A brief summary of liraglutide's indications, dosage form, dosing regimen and schedule[70]

Indications	Adjunct to diet and exercise for medically supervised chronic weight management in adults with a BMI ≥ 30 kg/m² (obese) or a BMI ≥ 27 kg/m² to ≤ 30 kg/m² (overweight) in the presence of at least one weight-related comorbidity such as dysglycaemia (an abnormality in blood glucose stability)/ hypertension/dyslipidaemia/OSA
Dosage form	Solution for injection 6 mg/ml, 5 x pens
Dosage regimen	• For SC use only • Administer one daily dose at any time of the day independent of meals but preferably at the same time of the day • Starting dose: 0.6 mg once a day; increase the dose to 3 mg once daily in 0.6 mg increments with at least one-week intervals to improve GI tolerability • If dose is escalated to the next step and is not tolerated for two consecutive weeks, consider discontinuation • A daily dose of higher than 3 mg is not recommended • Discontinue use after 12 weeks on 3 mg/ml if weight loss of at least 5% of initial body weight is not achieved • Re-evaluate treatment annually
Schedule	4

OSA – obstructive sleep apnoea, SC – subcutaneous, GI – gastrointestinal

Bupropion and the bupropion-naltrexone combination

Bupropion is a norepinephrine and dopamine reuptake inhibitor used to treat depression.[79] Via POMC activation, it appears to decrease appetite via hypothalamic functions. This leads to the effects on food intake.[68] Bupropion has been shown to clinically assist with weight loss in obese individuals.[80] Upon combination with the opioid antagonist, naltrexone, it has been shown to alleviate addictive over-eating.[81]

Naltrexone inhibits the appetite-enhancing effects of beta-endorphin caused by cannabinoid-1 receptor activation, and it has been shown to decrease food cravings in obese and binge-eating individuals.[82]

The combined use of bupropion and naltrexone has a synergistic effect on appetite suppression.[83] The combination of bupropion with a low dose of naltrexone resulted in more pronounced weight loss when compared to bupropion monotherapy in a 24-week trial.[84] In a phase-3 study, bupropion (360 mg/day) combined with naltrexone (32 mg/day) resulted in a weight loss of about 6%, compared with about 1% for the placebo.[84]

Phentermine-topiramate combination

The combination of low-dose phentermine (15 mg/day) with low-dose topiramate (100 mg/day) has been investigated for the treatment of obesity, with most of the studies being done in the United States of America (USA). The studies indicated that this combination led to reduced energy intake and substantial weight loss when compared to the placebo.[80] Some adverse effects have been reported when using this combination[68] and although not available in South Africa, will be considered an off label prescription when the combination is prescribed.

Conclusion

Obesity is a common condition that affects many different systems in the body. Some include CVS effects, endocrine disorders, haematological disorders, infertility, and T2D. Lifestyle modification interventions should be the starting point in managing obesity, whereafter pharmacological interventions might be needed. The pharmacist plays an important role in the identification of obese individuals (BMI calculations), making suggestions for lifestyle modifications (e.g. increase physical activity that overshadows increased caloric intake), providing individuals with information about the rationale behind the combination of nonpharmacological and pharmacological management and the dispensing of anti-obesity products.

Conflict of interest

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