Review Article

Obesity- Causes and it management by herbal drugs

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Abstract

Obesity is one of the most prominent and wide spread diseases throughout the world, affecting each and age group. Obesity has became as of the most prevalent health concerns among all populations and age groups worldwide, resulting into a significant increase in mortality and morbidity related to coronary heart diseases, diabetes type 2, metabolic syndrome, stroke and cancers . Prevention and treatment to this problem are an important objects for health systems, whose aim are to reduce the obesity and overweight prevalence, and related complications over the world . Both lifestyle and pharmacotherapy interventions have been considered by physicians and other health care professionals as obesity treatment modalities studies. The complex pathogenesis of obesity indicates the need of different intervention strategies to confront this problem with a simple drug therapy which is more acceptable to patients. Disappointing results, after cessation the lifestyle modification or pharmacotherapy indicated the need of other treatment modalities to produce better and long-lasting results, in terms of weight loss. Herbal supplements and diet-based therapies for weight loss are among the most common n complementary and alternative medicine [CAM] modalities [7]. A vast range of these natural products and medicinal plants, including crude extracts and isolated compounds from plants can be used to induce weight loss and prevent diet-induced obesity. Therapeutic strategies include synthetic drugs and surgery, which may entail high costs and serious complications. Plant-based medicinal agents offer an alternative approach. A review of the studies on accessible pharmacognostical sources for the treatment of obesity is provided, which attempts to explain how these medicinal plants act to cause weight loss, and which approach a better, safer and efficient way of reducing weight.

Keywords: Antiobesity, weightloss, herbal antiobesity drugs

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1. Introduction

Antiobesity drugs are those drugs which help in reduction of weight either by altering the appetite or absorption of calories [1]. Obesity is measured by the body mass index (BMI), which is a ratio of height (in meters) to weight (in kilograms). BMI is a criterion used to classify a person as underweight, normal, overweight, or obese. A BMI ≥ 25 kg/m2 is considered overweight, while a BMI ≥ 30 kg/m2 are considered obese. Overweight or obesity is a major risk factor for many chronic diseases, including diabetes mellitus, cardiovascular diseases, and cancer. There are many etiologic

factors for worldwide apread of obesity, which includes genetic, metabolic, behavioral, and environmental variables. The rapid increase in the prevalence of overweight and obesity suggests that behavioral and environmental influences are predominant, rather than biological changes. There are two major causes of obesity: first is an increased intake of foods with excessive amounts of fat, salt, and sugars, but less vitamins, minerals, and other nutrients; and second is a decrease in physical activity due to increasingly sedentary lifestyles, changing modes of transportation, irregular daily routines, and increasing urbanization.

1. Diet

Obesity rates in the India (1990–2015) increased from 14.5% to 30.9% [24]. During the same period, there was an increase in the average amount of food consumed (average increase for women 335 and 168 cal. /day). Most of this extra food energy was due to the increase in carbohydrates rather than fat consumption [2].

2. Sedentary lifestyle

The working patterns of people have been changed considerable. With increasing digitalization the long duration shift demands less physical activity and more mental activity. Around 60% world population gets insufficient exercises due to mechanized transportation and physical work saving technology at home [3]. The WHO indicates people worldwide are taking up less active recreational pursuits. In both children and adults, there is an association between television viewing time and the risk of obesity.

3. Genetics

Obesity is the result of interplay between genetic and environmental factors. Polymorphism occurs in various genes, controlling appetite and genes responsible for metabolism of predispose to obesity when sufficient food energy is present. People with two copies of the FTO gene (fat mass and obesity associated gene) have been found on average to weigh 3–4 kg more and have a 1.67 fold greater risk of obesity compared to those without the risk allele. Some cases of obesity are related to single-gene mutations, e.g. melano-cortin-4 receptor (MC4R) gene,

dopamine receptor D4 (DRD4), peroxisome proliferator-activated receptor γ2 (PPARγ2) or the leptin genes. [8]

4. Medical and psychiatric illness

Medical illnesses that increase obesity risk include several rare genetic syndromes (Cohen syndrome), as well as some congenital or acquired conditions: hypothyroidism, growth hormone deficiency, and eating disorders (binge eating disorder and night eating syndrome). The risk of overweight and obesity is higher in patients with psychiatric disorders than in persons without psychiatric disorders [9].

5. Social determinants

Genetic influences are important to understand obesity. They cannot explain the current dramatic increase in obesity. Though, excess energy consumption than energy expenditure leads to obesity on individual basis. The cause of the shifts in these two factors on societal scale is much debated [35]. In developing countries women of a high social class were less likely to be obese. No significant differences were seen among men of different social classes. In the developing world, population of high social classes had greater rates of obesity. Smoking has a significant effect on an individual's weight. Those who quit smoking will gain an average of 4.4 kg (men) and 5.0 kg (women) over ten years. However, changing rates of smoking have little effect on the overall rates of obesity [10].

6. Infectious agents

The study of infectious agent's effect on metabolism is still in its early stages. The gut flora in obese and lean individuals can affect the metabolic potential. This apparent alteration is believed to confer a greater capacity to gain energy contributing to obesity. An association between viruses and obesity has been found in humans and several different animal species [11].

7. Path physiology

Leptin and ghrelin are internal mediators that affect feeding and appetite. Ghrelin is produced by the stomach modulating short-term appetitive control (i.e., to eat when the stomach

is empty and to stop when the stomach is stretched). Leptin is produced by white adipose tissue to signal fat storage reserves in the body and mediates long-term appetitive controls (i.e., to eat more when fat storages are low and less when fat storages are high). It plays a critical role in the regulation of body weight and energy balance by inhibiting food intake and stimulating energy expenditure [11]. Although, administration of leptin may be effective in a small subset of obese individuals who are leptin deficient. Most obese individuals are thought to be leptin resistant and have been found to have high levels of leptin. This resistance is thought to explain in part why administration of leptin has not been shown to be effective in suppressing appetite in most obese people. Although leptin and ghrelin are produced peripherally, they control appetite through their actions on the central nervous system. Thus, a deficiency in leptin signaling either via leptin deficiency or leptin resistance leads to overfeeding and may account for some genetic and acquired forms of obesity [11].

8. Pathologies associated with obesity and its effects on health

In addition to, mechanical effects on the body (i.e., exacerbating osteoarthritis and back pain due to extra weight) because of the extra weight placed on the skeleton, obesity is associated with a higher incidence of several pathologies.

8.1. Diabetes mellitus

Accumulated data demonstrate the association between obesity and noninsulin-dependent diabetes mellitus, which is the most common primary form of diabetes and impaired glucose tolerance. In obese individuals, adipose tissue releases high amounts of non-esterified fatty acids, glycerol, pro-inflammatory cytokines, and hormones. They are linked with the development of insulin resistance, which generate compensatory hyperinsulinemia with overstimulation of pancreatic cells and reduction of insulin receptors [12].

8.2. Hypertension

Epidemiological studies have demonstrated that 65–75% of the risk of hypertension is accounted for by obesity [44]. Endocrinological studies of the adipose tissue revealed links between obesity and hypertension, likely consequent to the fact that the adipose tissue secretes bioactive molecules and immunomodulators [15].

8.3. Dislipidemia

Obesity is the most common cause of dislipidemia. Lipid over-supply in a state of obesity, hyperinsulinemia, and/or insulin resistance results in increased non-esterifies fatty acid availability and, in turn, higher TG stores in non-adipose tissues, e.g. the muscle, liver, and pancreas [15, 16]. Fatty acid-induced disorders are referred to as lip toxicity. Thus, elevated TG level is often accompanied by a slight increase in total cholesterol and a marked drop in high-density lipoprotein (HDL) cholesterol. Moreover, low-density lipoproteins (LDL) rich in TG, partially metabolized by hepatic lipase, are converted into small LDL, with higher atherogenic potential [18].

8.4. Cardiac alterations

Obesity increases the risk of heart failure, sudden cardiac death, angina or chest pain, and abnormal heart rhythm. Increased electrical alterations in obesity lead to frequent ventricular dysrhythmias even in the absence of heart dysfunction. The annual sudden cardiac death rate was nearly 40 times higher in obese people than in non obese population [18].

8.5. The metabolic syndrome

Obesity is the major component of the metabolic syndrome (multiple metabolic disorders). This syndrome is characterized by the co-occurrence of multiple metabolic disorders, namely overall and abdominal obesity, insulin resistance, hypertension, hyperglycemia, impaired glucose tolerance, and the combination of low HDL cholesterol and elevated TG level [19].

8.6. Lung diseases

Obesity is associated with an increased risk of chronic respiratory disorders (e.g. asthma, hypoventilation syndrome, and sleep apnea). Accordingly, weight loss often leads to symptomatic improvement [19].

8.7. Cancer

The link between diet, obesity, and cancer is not completely understood, but the rising world-wide trend in obesity and cancer might be at least in part causal. The putative cause of these obesity-related cancers has been primarily ascribed to excess estrogen production by the adipose tissue, inflammation due to adipocytokines secreted by adipocytes, infiltrating macrophages or associated stromal cells that might also play an important role [20].

8.8. Neurological disorders

Psychological damage caused by overweight and obesity ranges from lowered self-esteem to frank clinical depression. Indeed, rates of anxiety and depression are three to four times higher among obese individuals. Obesity significantly increases the risk of Alzheimer's disease. A strong correlation exists between BMI and high levels of amyloid, i.e. the protein that accumulates in the Alzheimer's brain, destroying nerve cells and producing cognitive and behavioral problems [20].

8.9. Treatment of obesity

Diet, exercise, pharmacotherapy, behavioral therapy, and lifestyle modification each can produce a modest weight loss in the severely obese. Pharmacotherapy, in addition to diet and exercise, has been demonstrated to facilitate a weight loss of 2–10% per year. Long-term maintenance of significant weight loss, continues to be the most challenging problem in the medically based treatment for obesity.

9. Prevention of obesity

As a result of the recent exponential increase in obesity, the Indian Heart Association has released several guidelines for identification and early intervention for both adult and adolescent weight gain. Losing weight can reverse the harmful health effects attributed to excess weight, and may improve or prevent obesity-related diabetes mellitus, dyslipidemia, hypertension, and diastolic cardiac dysfunction [20].

9.1. Dietary intervention

Arrays of diets have been proposed for weight loss in obese patients. Commercial weight loss programs have become increasingly popular for targeted weight loss. However, long-term success is variable, and directly related to patient compliance with these programs. The proposed weight loss programs involved an in person center-based program, a telephone-based weight loss counseling program, and a control group of "usual care". The usual care group received individualized weight loss counseling sessions and monthly contacts; however they did not receive free prepackaged meals. The patients participating in the center and telephone-based groups were provided with prepackaged food items and a planned menu. They were encouraged also to make behavioral changes regarding physical activity [20].

9.2. Diet control

The daily requirements of persons with moderate physical activity vary with age and sex, (3200–2550 kcal for males in temperate climate and 2300–1800 kcal for females). 800–1000 kcal/day ranges are frequently used in weight reduction programs. Fasting or semi-starvation is sometimes proposed as a mean of weight reduction in obesity. Maintaining a well-balanced diet (rich in fibers and low in fats and containing multiple vitamins) will provide the body with nutrients required to function properly. Nutrition education is important for weight management (e.g., low-fat food may still cause weight gain, since both protein and carbohydrates can be metabolically converted to fat). Low calorie diets (<1200 kcal/day) and very low calorie diets (<800 kcal/day) may be associated with diverse effects such as increased uric acid level, increased risk of gall stone formation, loss of lean body mass, electrolyte disturbances and mild liver dysfunction. The number of calories needed to maintain a certain body weight can be estimated by multiplying a person's REE times an appropriate Activity Factor (AF) where REE is the Resting Energy Expenditure and the AF is the Activity Factor (AF) for different levels of activity.

9.3 Surgical treatment for obesity

Bariatric or Weight Loss Surgery (WLS) was previously categorized as malabsorptive, restrictive, or a combination of both. However with a greater understanding of the extensive neural-hormonal effects of WLS on satiety,

hunger and metabolism, the above mentioned broad categories are no longer appropriate. In fact, today Bariatric or WLS is perhaps better referred to as Metabolic Surgery. The most common metabolic surgical procedures include Roux-en-Y gastric bypass, adjustable gastric band, sleeve gastrectomy, and biliopancreatic diversion. The National Institute of Health consensus has suggested the following guidelines for surgery in obese patients:

A-Patients with BMI more than 40.

B-Patients with BMI more than 35 who have serious medical problems such as sleep apnea, that would be improved with weight loss.

9.4 Natural products for treatment of obesity

The potential of natural products for treating obesity is under exploration. This may be an excellent alternative strategy for developing future effective, safe anti-obesity drugs. A variety of natural products, including crude extracts and isolated pure natural compounds can induce body weight reduction and prevent diet-induced obesity. Therefore, they have been widely used in treating obesity [75].

6.7.1. Dietary photochemical

Dietary photochemical might be employed as anti-obesity agents because they may suppress the growth of the adipose tissue, inhibit differentiation of preadipocytes, stimulate lipolysis, and induce apoptosis of existing adipocytes, thereby reducing adipose tissue mass (table 3).

Table 3: Classes of dietary photochemical

Photochemical	Examples	Effects
Polyphones	Simple phenolic acids (e.g. ferulic, caffeic)	Ferulic acid has hypolipidemic effect and lowers the risk of high fat diet-induced obesity and reduces serum cholesterol [21]
	Stilbenes (resveratrol)	Resveratrol decreases LDL-cholesterol and prevents lipid oxidation [77]. Decreases adiposeness by downregulating adipocyte transcription factors, altering the expression of adipocyte specific genes[22]. In mature adipocytes, it increases lipolysis, induces apoptosis, and reduces lipogenesis, proliferation and lipid accumulation[23]. Dietary supplements of resveratrol, vitamin D, quercetin, and genistein reduce weight gain and body fat leading to potential novel therapies for obesity [24].
	Curcumins	Prevent lipid accumulation [25]. Regulate energy metabolism and decrease level of intracellular lipids [26]. In adipose tissues, curcumins suppress angiogenesis necessary for tissue growth [27]. Curcumins regulate transcription factors that play key roles in adipo- and lipogenesis [27]
	Lignans (e.g. secoisolariciresinol, matairesinol)	They are converted to mammalian lignans enterodiol and enterolactone that may reduce the risk of chronic diseases including obesity [27]
	Flavonoids (e.g. quercetin)	Attenuate *in vitro* adipogenesis by activating AMPK signal pathway in preadipocytes and decreasing expression of adipogenesis related factors [29]
Alkaloids	Capsaicin	Attenuates obesity-induced inflammation, obesity related metabolic disorders, and liver diseases[29]. Reduces food intake and increases energy expenditure and lipid oxidation [30]

Photochemical	Examples	Effects
	Ephedrine	Increases norepinepherine causing appetite suppression [31]. Produces thermogenic effect (increase basal metabolic rate) and energy expenditure [31]
	Caffeine	Stimulates fat breakdown, potentiates the anorectic and thermogenic effects in addition to its diuretic effect [32].
	Nicotine	Decreases food intake and increases fat oxidation and energy expenditure
Terpenoids	Abscisic acid (ABA)	Effective in treatment of diabetes and obesity-related inflammation
	Carotenoids	Carotenoids may prevent inflammation associated diseases such as obesity and atherosclerosis
	Lycopene	Lycopene rich diets lower the risk of CVD (inhibition of LDL oxidation and lipid peroxidation)
Organosulfur	Ajoene	Decreases cholesterol synthesis, lowers blood pressure, and stimulates non-specific immunity Decreases fat cell number suggesting some therapeutic possibility for obesity
Phytosterols	Diosgenin, Campesterol, Brassicasterol, Sitosterol	High inta kes of these sterols can protect against atherosclerosis and decrease LDL-cholesterol Phytosterols compete with cholesterol for micelle formation in the intestinal lumen and inhibit cholesterol absorption
	Protodioscin	Significantly reduces blood levels of TG, cholesterol, LDL and increases high-density lipoproteins
	Diosgenin	Inhibits accumulation of TG and expression of lipogenic genes

Suggestions and recommendations

A-Be active, walk for 30 min a day especially before breakfast to burn off fat. Exercise is the best way to get rid of excess body fat and to maintain good muscle tone.

B-Check with the doctor, underactive thyroid can cause obesity to be a problem.

C-Rotate foods and eat a variety of foods, ask dietitian to regulate your food intake and drink 6–8 glasses of liquids every day.

D-Cut down on salt, it makes you thirsty and causes retention of water.

E-Make sure bowels are regular. Use extra fibers in the diet every day. Put less food in your plate. Chew slowly.

F-Do not chews gum, because it starts the gastric digestive juices flowing and will make you feel hungry sooner, in addition to overworking your digestive system.

G-Never consume animal fats; butter, cream, ice cream, whole milk, rich dressing, mayonnaise, and fried foods.

H-Do not eliminates sources of good fat, containing unsaturated fatty acids, such as avocados, olive oil, and nuts.

I-Avoid white flour products, salt, white rice, or processed foods. Avoid fast food restaurants.

Do not consume sweets such as soda pastries, cakes, doughnuts, and candy. Eat complex carbohydrates that offer protein: lentils, plain baked potatoes, sesame seeds, beans, brown rice, and whole grains.

J-Eat fresh fruits and raw vegetables (good fiber sources). At least one meal a day should be only fruits and vegetables.

K-Make lunch the main meal of the day, no later than 3 PM to give the body time to burn some calories before bedtime.

Conclusion

Weight management is a life-long process and permanent weight reduction is difficult to achieve. The ultimate cause of obesity is an imbalance between calorie intake and energy expenditure resulting from complex interactions between many genetic and environmental factors. Obesity is a chronic disease that affects millions of people worldwide and contributes to substantial morbidity and mortality. A successful weight control program must balance calorie intake with energy expenditure. Diet and exercise have been the mainstays for weight control. Natural products can play a safe and effective role with obesity specially those containing fibers, polyphones, sterols, and alkaloids. In addition, they are a good supplement for vitamins and minerals. In general, natural products with potential action in treatment of obesity act as a general body cleanser, regulate metabolism, dissolve fat in the body, help to eliminate craving of food, stimulate glandular secretions, reduce water retention, boot energy and help in constipation. However, their use should be in conjunction with regular exercise, as well as dietary and behavioral modifications. The use of multiple photochemical might result in synergistic and enhanced effects.

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