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REVIEW ARTICLE

Current Treatments for Obesity: An Update

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ABSTRACT

Obesity is one of the biggest health problems in the world. It is not only a key developer of various dangerous diseases like coronary heart disease, type 2 diabetes mellitus, and sleep apnoea, but is also associated with high mortality and morbidity rate. In recent years, doctors have shifted their attention towards the prevention and treatment of obesity rather than letting the person move towards different diseases and then curing those multiple disorders. One of those strategies for obesity treatment includes bariatric surgery. This review paper encapsulates multiple other strategies like dietary, pharmaceutical, and surgical options available at present for the treatment of obesity.

Keywords: Obesity, weight, diabetes, heart disease.

INTRODUCTION

According to the definition of the World Health Organization, obesity is an abnormal fat accumulation in human tissues that poses a threat to human health, generally defined by the body mass index known as BMI. BMI is easy to calculate but it comes with certain barriers like muscle mass, age, and ethnicity can impact the results of BMI and its relationship with body fat. There are certain parameters of measurement to find the obesity ratio and calculate the person's risk to develop obesity-related diseases like T2Dm and CVD, like anthropometric measures in which waist to hip ratio, and skinfold thickness are calculated[1]**.**

As per the data of the WHO, the ratio of obesity is increasing like an epidemic with encompassing about 2 billion overweight people and 650 million obese people all around the globe.in 2016, a survey showed that in Europe 10% of children and 27% of adults were identified as obese, and it was found on the basis of this data that obesity-related health issues dropped a financial burden of £6.1 billion on the UK's health sector. The world's health institutes are dedicating their struggles and resources to tackling this issue that widely impacts societies of the world[2].

In 2013 a report was published with the title, "Action on obesity: Comprehensive care for all". The purpose of this report was to throw some light upon this global health issue and raise awareness among health professionals. The report stated that obesity and nutrition's impact upon health was inappropriately mentioned in undergraduate courses, whereas this is an issue not to be overlooked or taken lightly. Moreover, it was also highlighted in the report that professional training on this issue is inadequate. Therefore, this review paper has been devised on basis of current management strategies required for obesity and those that are in use at present.

Therapy through Diet: Weight gain or loss can be effectively managed by achieving a net kilocalories deficit. An estimated amount of energy expenditure per kg of an adult's body weight is almost 22 kcal. In order to achieve a net energy deficit, diet can be managed in several ways which are mentioned below:

Composition of Macronutrients: Fat, carbohydrate, and protein fall under the three main primary macronutrients category of diet. These provide the body with 9, 3.75, and 4 kcal energy/g, respectively. Among these three, fat is the one that has the maximum absorbing ability and is calorie-dense, owing to this it is on top of the targeted list of the doctors for weight loss strategies. According to a meta-analysis survey, a diet with less fat quantity in it has proved as the most effective one in reducing weight, after comparative evaluation with high-fat meals. [3] However, another comparative assessment of high-fat diet and high carbohydrate diet showed that weight loss is more prominent and effective in diets with fewer carbohydrate macronutrients as compared to diets with low fat. This was found significant owing to the loss of water and glycogen stores in the body which significantly reduced 1 to 2 kg of weight within the initial 14 days of diet therapy, however, this weight loss rate declines and becomes slow with time. Protein is known as one of the most satiating diets, and meals rich in protein are often used to replace high-fat and high-carbohydrate diets with the focus to reduce weight by preventing passive overconsumption. However, some recent studies have revealed that these high protein diets have low to no prominent effect on body weight[4,5].

Calorie Restriction: Another approach used in diet therapy is the restriction of calorie consumption. As per the dietary guidelines, low and very low-calorie diets (VLCD) encompass the energy intake to about 800- 1600 kcal per day, and less than 800 kcal per day, respectively. However, a very low-calorie diet is dangerous and it achieves short term weight loss in comparison to the low calorie diet (15kg in the former diet therapy and 9.8 kg in the latter). In almost 6 months 7 to 8% of total body fat is reduced primarily through a very low-calorie diet. Nonetheless, immediate weight loss is more prominent with VLCD, long-term benefits are not pronounced with it. The long term impacts of VLCD on weight loss are independent of its progress in the initial months and these impacts are undergirded with revised data of Franz[6]. According to it starting progress addressing weight loss is 16% in six months, then it falls to

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-10% in 12 months, and then to -5% at 36th month. So many reasons are behind this gradual decline in weight loss like metabolic adaptation, negligence with the dietary schedule, and viabilities of calorie counting.

Meal Alteration: Meal replacement offers an effective way of achieving weight loss by partially or completely changing the meal. This includes low-calorie but nutritionally balanced meals. A meta-analysis of seven different studies has shown that partial weight loss by partial meal replacement gave interesting results, -3 kg in starting 3 months and -3.63 kg in 1 year with little attrition ratio.

It is important to note that weight loss by meal replacement improves the overall health of the individual and aids in remission of obesity-related complications like Type 2 diabetes. In another study, 300 patients were kept under observation and it was found that 74% of them showed remission of T2DM who were on low calorie diet replacement and lost more than 10 kg of weight in 12 months. This progress was appreciated. The reason behind this was improved hepatic insulin sensitivity, declined hepatic glucogenesis, and balanced hepatic glycogenolysis. Furthermore, betterment in triglyceride levels and blood pressure was also observed[8].

Pharmaceutical Therapy: Pharmacological treatment is also used for obesity but in rare cases. It is usually accompanied by optimum exercise and low calorie diet. However, medicine options are limited and many of the licensed drugs are only available for persons with a basal metabolic index above 27 kg/ m^2 or ≥30 kg/m^2. It is extremely important to monitor weight loss, and if it is less than 5% after 3 months then patients are advised to stop the use of drugs. A few common drugs a discussed below:

Orlistat: Orlistat works on the pancreas by irreversibly stopping the functions of pancreatic lipase. This prevents the breakdown of fats from meal into free fatty acids, thus reducing 32% of ingested fats to be absorbed in the body and increasing their excretion via feces. Use of this medicine comes with its own side effects like oily stool, fecal urgency, and lack of self-restraint (incontinence). In order to combat this, it is advised to consume low fat diet and consume the medicine with a meal or within 1 hour of meal taken.

A meta analysis of 40 random control trials depicted that with a mean therapy duration of 2 months to 3 years, a mean reduction in body weight of 2.3kg was observed[9]. Orlistat proved helpful in the significant reduction of triglyceride and cholesterol levels in the body.

Liraglutide (Saxenda): Glucagon-like peptide-1 (GLP-1) receptor agonist is used as medicine known as liraglutide. It is administered subcutaneously once a day. In the human body, GLP-1 is a hormone produced by the GI tract when this tract encounters glucose and fat ingestion following both peripheral (changes glucose homeostasis and decreases GI transit) and central (appetite reduction) movement. With the use of this medicine, side effects like gastrointestinal upset and acute pancreatitis in severe conditions are observed. Average weight loss has been observed with this drug usage of about 3.3 kg along with betterment in blood pressure, cholesterol, and glycemic control[10].

Liraglutide Evidence (SCALE) trials were carried out to demonstrate its safety levels and impacts upon weight loss by the Safety and Clinical Adiposity. A double-blind RCT on SCALE pre-diabetes and obesity showed positive results regarding weight loss. Significant weight loss in the drug administering group vs placebo was observed with -8.3 kg vs -2.9 kg loss, respectively in 1 year. A large number of patients under trial, who were on medicine lost more than 5% of their initial body weight, thus 63% vs 27%, respectively. Furthermore, another double-blind LEADER RCT demonstrated that chances of mortality due to cardiovascular causes, non-myocardial infarction, and nonfatal stroke associated with obesity also significantly decline, when it was comparatively assessed with the control arm[11].

Naltrexone/ bupropin: Naltrexone is a combination of drugs that were given to patients for adjustments in diet and lifestyle. However, at present, it is not recommended by NICE as its long-term impacts are unknown. Naltrexone is licensed for alcohol management and opioid dependency because it is itself an opioid. On the other hand, bupropion is an antidepressant that prevents noradrenaline and dopamine uptake. The latter was licensed to provide help in stopping smoking. Together both these drugs are involved in appetite suppression, however, their united action is still cloudy. It has been postulated that both these medicines might have synergistic impacts on hunger sites in the hypothalamus, as a result, hunger is suppressed. In a multicenter double-blind placebo-controlled study in phase 3, about 1700 patients were added. Their body weight and mean change were observed as -6% in comparison to the placebo group -1.3%. However, out of 100%, only half 50% of the patients completed the therapy of 56 weeks, and they faced side effects like nausea, headache, and constipation[12].

New Drugs: Recently, many drugs have been removed from the category of medicine used for obesity due to their adverse side effects and safety concerns. These drugs were found to be affecting the central nervous systems like rimonabant and sibutramine, moreover similar drugs were also found in increasing the risk of suicide, cerebrovascular events, and myocardial infarction. New drugs which are available in the market are:

- Lorcaserin: it is a serotonin agonist that suppresses appetite. It prevents the rise of CVD risks and aid in achieving weight loss.
- Topiramate/ phentermine: a combination of both these drugs is used which increases energy utilization[13].

Intragastric Balloon: Since 1985, the intragastric balloon is commonly known as a useful intervention against obesity. It involves an endoscopically developed silicone balloon inflated in the stomach for a period of about 6 months, filled with saline. Intragastric balloon is used for weight loss as a substitute for bariatric surgery in patients who are not fit to undergo a surgical procedure. However, based on the Cochrane study, little evidence is present to support its effectiveness in gaining weight loss in comparison to conventional medical management for obesity.

Bariatric Surgery: Bariatric is the choice opted for treating obesity when all other methods have failed. Despite the type of bariatric surgery performed, it is quite effective in achieving appropriate weight loss, and co-morbidities

linked with it are superior in comparison to non-surgical methods.

In the world's health sector, the Swedish Obesity Study (SOS) provides one of the largest evidence-based data on the effects of bariatric surgery upon obesity, the health of individuals and its long-term consequences. Their study encapsulated 4000 patients and divided them into the surgical and controlled group, and observed better and greater weight loss in the former group along with betterment in obesity-associated co-morbidities. Remission of T2DM after 2 years was observed at a rate of 73% which fell to 36% in the next 10 years. Many other studies have also shown positive results in favor of bariatric surgery as a therapy for obesity and diabetes rather than the use of conventional medicines for diabetic obese persons. Moreover, it is estimated that surgery can lead into the coming 4 years towards the decline in drug usage for diabetic patients, and the increase in the duration of the healthy period of the individual away from diabetic complication, and it can positively impact the financial status by saving almost £18.1 million.

In recent years, the focus has been shifted more towards mechanistic efforts of enteric gut hormones after gaining positive results for diabetic obese patients from bariatric surgery. Hormones like GLP-1 and pancreatic polypeptide YY are of major concern because these are involved in the maintenance of homeostatic processes like gut motility, appetite, plasma nutrient regulation, and absorption of nutrients. Evidence has been found regarding these hormones and alterations in them leading towards beneficial impacts upon bariatric surgery[14].

Given below are the current guidance advice provided by NICE for bariatric surgery to fulfill the criteria:

- BMI ≥40 kg/m^2
- BMI ≥35 kg/m^2 along with linked conditions that can boost weight loss
- BMI of 30–34.9 kg/m^2 for those who are recently identified with T2DM
- Surgery opted as an option when other medical options for weight loss have failed to show progress
- Patients will get service based weight loss program under an intense management system
- The patient is healthy enough for anesthesia and surgery
- The patient is willing to abide by the follow-up schedule

Dumping Syndrome: This syndrome is a complication of the gastrointestinal tract that originated due to the malabsorptive surgical process. In it gastric quickly empties which causes vasomotor and gastrointestinal symptoms. This syndrome is divided into early and late phases, in the former meal is dumped within 30 minutes of consumption. This is associated with multiple signs and symptoms like pain in the abdominal region, diarrhea, borborygmi, and bloating. However, in the latter late dumping phase, dumping occurs after 1 to 3 hours of meal consumption and is linked with reactive hypoglycemia which causes even worse symptoms like fatigue, dizziness, sweating, and weakness. The main issue faced by doctors here is the maintenance of appropriate nutritional levels in the body of the patients because in severe cases protein wasting is observed. Dietary modification is extremely important in dumping syndrome by adding small and more frequent meals full of fiber, fats, and proteins to fight these issues.

Nutritional Concerns: There are different methods of bariatric surgery and all of them are found to leave negative impacts upon the nutritional intake. These can also affect the absorption process of micro as well as macronutrients. Many of the patients who have undergone bariatric surgery will need nutrient supplements for a lifelong time along with modification in a balanced diet. Multivitamins and minerals like iron, zinc, copper, selenium, folate, B12, calcium and vitamin D are usually prescribed. For patients with duodenal switch procedures, fat-soluble vitamins are also prescribed to maintain optimum health status.[15]

Psychological Effects: Studies have demonstrated that many patients who underwent bariatric surgical procedures have depicted more harmful and suicidal behaviors in comparison to patients who were on medicinal therapy. The biological and behavioral reasons are still unknown behind this. The possible hypothesis states that this might be due to changes in the absorption mechanism of drugs and imbalances in the body's hormones, glucose, and peptide levels. Evidence on post-operation eating disorders has also been found which shows that it keeps on developing inpatient like anorexia nervosa and bulimia nervosa. A habit of binge eating was also observed being developed in patients who had bariatric surgery and the reason behind this was described as a consequence of changes in eating patterns. It is imperative to provide counseling services to patients who undergo a bariatric surgical procedure to prevent any future incidents.

Emerging Treatments:

Pharmacological Interventions: In recent years, numerous pharmacological advancements have been made to tackle the issue of obesity. However, some of these drugs are under clinical trial phases before they are launched in the market, some of them are given below:

- Gut specific agents: Pancreatic lipase inhibitor-Cetilistat, dual GLP-1 agonist receptor and glucagon receptor precursor- oxyntomodulin, and DGAT-1 as sodium-dependent glucose co-transporter and diglyceride acyltransferase inhibitors.
- Central nervous system agents: Inhibitors of monoamine reuptake such as tesofensine, although it was initially formulated for neurodegenerative disorders, the combination of zonisamide- bupropion where the former was developed for epilepsy disorder. Additionally, some drugs like D_3 dopamine antagonists, AgRP blockers, Neuropeptide YY5 receptor opposers like velneprit, andμ-Opioid inverse agonists are also formulated for treating obesity[16].
- Systemic agents: Activators, such as resveratrol, of molecules sirtuin 1 which is drove by calorie restriction and beloranib which is methionine aminopeptidase 2 restrictor[16].

Endoscopic Interventions: Recently, many endoscopic developments have also held the group for the treatment of obesity. These interventions are either adjuncts to bariatric surgical procedures or are used as another option for patients who are not medically sound to under surgery due to declined health status or are prone to have surgery-associated complications, or for those who want to have less surgical invasion treatment. A variety of mechanisms

have been devised like reduction of gastric contents or its capacity, or exclusion of proximal small intestine thus decreasing the impacts of surgery. However, the issue with these interventions is that they are effective for a limited short period after which their removal is required, and they provide limited benefits to the patients.

CONCLUSION

Obesity continues to be the biggest health concern in the world. This issue is increasing like an epidemic affecting the economies and health sectors of all societies of the world. It encompasses specifically low to middle-income countries and is common among youth and adolescent populations. For its treatment and management, conventional therapies like diet and lifestyle modification along with pharmaceutical approaches, have remained the main options but these come with their limitations and side effects. Recently, bariatric and metabolic surgeries have been in trend and they proved to be an effective treatment, especially for diabetic obese patients. These also provide significant improvement in complications associated with type 2 diabetes mellitus. Indeed, many of these recent interventions are under clinical trial phases but their results are showing positive outcomes in combat against obesity in the long run.

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