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CONTEMPORARY WEIGHT LOSS MEDICATIONS: "A COMPREHENSIVE REVIEW ON THE THERAPEUTIC EFFICACY, SAFETY AND ADVERSE EFFECTS."

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ABSTRACT

This article critically evaluates and understands the weight loss medications or anti-obesity medicines to apprise the modern and traditional medication's safety, efficacy and the side-effects or ADRs. An excessive build-up of body fat is the hallmark of obesity, which is a long-term metabolic disorder that can have a detrimental impact on a person's body and increase their risk of developing certain chronic illnesses. This can be determined by examining the Body Mass Index (BMI), which normally equals 30 kg/m^2, according to the World Health Organization (WHO). Around the world, about 2 billion people are obese. Some unpredictable lifestyle changes, such as sleeping too little, consuming too many calories, and taking medications with weight-gaining side effects, can cause it. To address this problem, a few pharmacological agents or biologically active drugs have been approved by the United state food and drug administration (USFDA) and European medicines agency (EMA). Among these drugs are Orlistat, Phentermine/Topiramate, Lorcaserin, Naltrexone/Bupropion, and Liraglutide. Constipation and nausea are both possible side effects of these medications. One of the natural substances used to reduce weight is Curcumin. through a combination of medication, moderate physical activity, and dietary modifications. The side effects of all these medications can be decreased once treatment is discontinued.

KEYWORDS: Obesity, anti- obesity medications, causes of obesity, co-morbidities with obesity, traditional or natural components, rational use of AOMs.

INTRODUCTION

A number of co-morbidities and causes of death are associated with obesity, a chronic illness that has an adverse effect on people's health.[1,2,4] It is an epidemic of the modern era.The WHO states that BMI calculations can also be used to determine it. It is greater than or equal to 30 kg/m2. It is a recurrent, chronic illness that can be brought on by both genetic abnormalities and risk factors from the environment that have an adverse effect on an individual's health. sedentary behaviour, unhealthy diets, and poor lifestyle choices might also be to blame.[1, 2, 3 & 4]

Globally, 600 million people are obese and 1.9 billion people are overweight. In the US, one-third of the population—roughly 14% of men and 16% of women—have this illness. In India, 24% of women and 23% of men are overweight or obese. The US guidelines for managing obesity heavily promote lifestyle changes like calorie restriction, behavioural therapy, and moderate-to-intense exercise. Even though losing weight can reduce the risk of cardiovascular diseases, patients are frequently finding it difficult to keep it off. There are four Food and drug administration (FDA)-approved drugs for weight loss.[4, 5] by reducing appetite, Anti-Obesity Medications (AOMs), are used to slow the condition's progression.[5]

Function of Adipose Tissue: Adipose tissue primarily stores triglycerides as extra energy. Immune cells,

endothelial cells, adipocytes, and pre-adipocytes are just a few of the many cell types found there. When there is a positive energy balance, adipose tissue stores extra energy as triglycerides in the lipid droplets of the adipocytes through either hyperplasia or hypertrophy. The quantity of adipocytes in both lean and obese individuals is mostly established during childhood and adolescence and remains consistent throughout maturation, even after significant weight loss. Therefore, an increase in fat mass during maturity is mostly caused by hypertrophy.

Adipose tissue dysfunction caused by hypertrophy is believed to be a major factor in the development of metabolic diseases, considering the fact that metabolic illnesses are linked to general obesity.[6]

CAUSES

Lack of sleep: Sleep controls the neuroendocrine and glucose metabolism. Lack of sleep raises cortisol and ghrelin levels (and, consequently, appetite) while lowering insulin sensitivity, glucose intolerance, and leptin levels. Since exercise has long been linked to restful sleep and recent studies have demonstrated that insufficient sleep leads to low levels of physical activity, sleep and exercise are mutually beneficial. Additionally, one study discovered that by altering the impact of fat mass and obesity-associated gene (FTO) variations on BMI, a change in the average amount of sleep increased the risk of obesity.[7]

Overconsumption of calories: Obesity has long been thought to be an energy disorder. Post-absorbent hyper-insulation can also occur in people who consume diets heavy in carbohydrates, particularly sugary and starchy foods. This condition is brought on by the pancreas producing an excessive amount of insulin, which causes the body's fat cells to absorb calories instead of lean tissue, ultimately making the person feel hungry. As a result, there is a corresponding decrease in metabolism and hunger.[7]

The basal metabolic rate (BMR) is the main factor affecting energy expenditure. It is the amount of energy needed to sustain normal cellular metabolism when at rest. Last but not least, energy is needed for all types of physical activity as well as for food digestion. The central nervous system regulates both calorie intake and energy expenditure. The hypothalamus employs a number of chemicals and complex processes to stimulate appetite or satiety.[8]

Certain health issues or Medications: Doctors know extra pounds often show up with hormone-related conditions. Low thyroid activity can lead to increased body mass. So can Cushing's syndrome, where hormones go out of balance. In women with polycystic ovaries, trouble managing blood sugar might add to weight buildup.

Some medicines cause fast weight gain. Steroids do this often, just like certain depression treatments. One reason ties to how specific types work inside the body. Antipsychotic drugs differ widely in their impact. For example, lithium may add several kilograms, though slowly. Clozapine affects most people - between three out of ten and nine out of ten pack on pounds. Olanzapine users sometimes cross a five percent threshold in added mass. Quetiapine plays a role too, yet not always the same way. Haloperidol shows less change compared to others. Not every Selective Serotonin Reuptake Inhibitor (SSRI) stays neutral; citalopram shifts averages by up to seven kilos. Phenelzine does similar things over time. Blood pressure pills get overlooked here. Clonidine acts quietly. Atenolol joins that list. Diabetes controls aren't harmless either. Insulin pulls extra weight along. Sulfonylureas follow close behind. Thiazolidinediones complete the group known for tipping scales upward.[8]

THE CO-MORBIDITIESASSOCIATED WITH OBESITY ARE

Sleep disorders, hypertension, type-2 diabetes mellitus, hyperlipidaemia, stroke, osteoarthritis, certain types of cancer and other cardiovascular diseases, and even a modest 5% weight loss has been shown to improve cardio-metabolic risk factors like decreased systolic blood pressure and plasma triglyceride concentration and increased B-cell malfunction.[4, 9, 12, 13, 14]The gastrointestinal (GI) side effects, specifically nausea and vomiting, reported by trial participants have been examined in this review paper. The purpose of the studies was to ascertain if these adverse effects were related to the effects of Glucagon- like peptide-1 receptor agonists (GLP-1 Ras) on weight loss. According to data from the Sustain Clinical Trial Program, patients' weight loss was not significantly correlated with nausea or vomiting.[5]

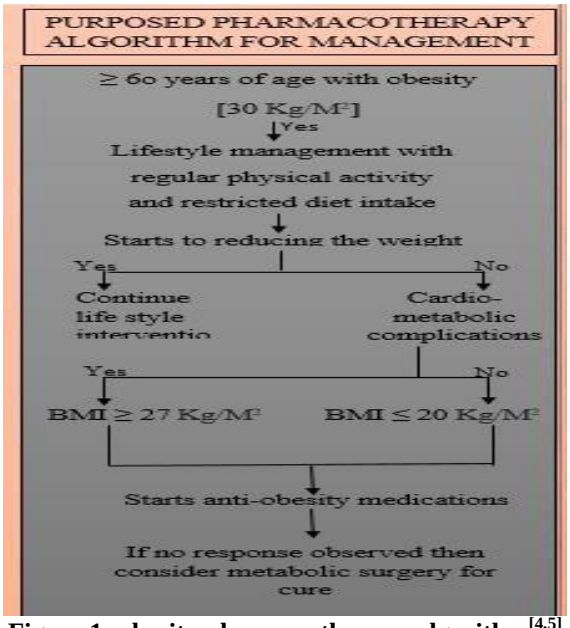

Figure 1: obesity pharmacotherapy algorithm[4,5]

FDA/EMA APPROVED ANTI-OBESITY MEDICATION[AOMs]

Nowadays, medicines aimed at helping people lose weight are seeing wider use. Heavy emphasis on changing daily habits shows clear benefits when it comes to shedding pounds. One major study showed dropping just 5% of body mass led to better heart-related markers over time - things like blood pressure and cholesterol levels stayed improved. Five drugs have earned approval from American regulators: Orlistat, Phentermine paired with Topiramate, Lorcaserin, Naltrexone combined with Bupropion, and Liraglutide. Across Europe, only three of these treatments made the cut after review by their medical agency. Though nine anti-obesity medications now have approval, studies in older people mostly look at adding GLP-1 drugs like liraglutide, semaglutide, or tirzepatide. These medicines help cut weight and reduce heart-related risks without losing muscle.[4,10]

When standard care fails to bring down the numbers on the scale, some people turn to surgical fixes as a next move. These approaches often do lead to shedding pounds.[3, 4] Back in 2012, regulators gave the green light to two fresh options: one called Lorcaserine, another blending Topiramate with Phentermine in slow-motion form. By late 2014, yet another pairing - Bupropion plus Naltrexone - joined the list.[11]

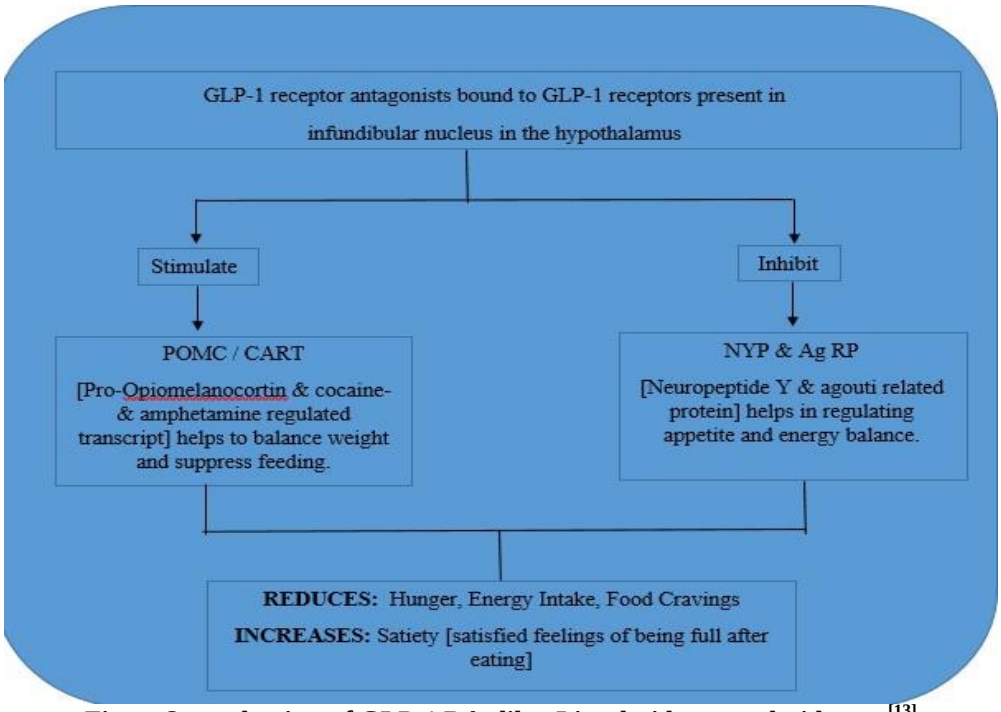

Figure 2: mechanism of GLP-1 RAs like; Liraglutide, semaglutide, etc.[13]

METHODS

To locate relevant research between 2018 and 2025, along with structured reviews focusing on obesity-related factors and treatment using approved anti-obesity medicines, searches were carried out across PubMed, Medline, and Google Scholar. Medications targeting obesity have gained approval from both the USFDA and EMA. Terms like "obesity," "pharmacotherapy of obesity," "therapeutic efficacy of AOMs," "side effects of these drugs," and "drug-based management of overweight and obesity" guided the search process. Studies selected involved peer-reviewed randomized controlled trials (RCTs), meta-analyses, and organized reviews featuring adults diagnosed with obesity (BMI $\geq$ 30 kg/m^2) receiving treatments cleared by the USFDA and EMA. Tracking how individuals reacted to therapy meant observing shifts in body weight, blood pressure (BP), blood sugar, cardiovascular patterns, sleep behaviour, and psychological state.[14, 17]

Weight loss numbers, pulled from studies lasting twelve months or more, showed these results when comparing certain obesity drugs to placebos: Phentermine combined with Topiramate led to 6.8%, Liraglutide reached 5.4%, Naltrexone paired with Bupropion brought about 4.0%, Orlistat gave 2.9%, while Lorcaserin managed 3.1%. Trouble arose for Lorcaserin after a safety review uncovered higher chances of developing cancer, so United State regulators demanded its removal on February 13, 2020. Right now, approval stands for only four long-term treatments - Liraglutide, Phentermine plus Topiramate, Naltrexone-Bupropion combo, and Orlistat. Cost climbs high for each one. Unwanted effects show up in some individuals too. Because benefits differ across users, decisions around starting medication need careful weighing before beginning treatment in those living with obesity. twelve months onward, weight loss beyond placebo sat between 2.9 and 6.8 percent with newer obesity drugs. Phentermine paired with Topiramate led at 6.8 percent. Liraglutide followed,

trimming 5.4 percent. Naltrexone joined with Bupropion managed 4.0 percent. Orlistat brought up the rear at 2.9 percent, while Lorcaserin showed 3.1 percent. Yet on February 13, 2020, USFDA pulled Lorcaserin from shelves. A safety review had flagged higher cancer odds. Today, Orlistat, Phentermine-Topiramate, Naltrexone-Bupropion, and liraglutide remain cleared by the FDA for extended use against obesity. Cost runs high. Side effects can show up. Given these factors, using medicine needs weighing risks alongside benefits before starting treatment in those with obesity.[15]

THE AOMs APPROVED BY USFDA & EMA FOR ITS MANAGEMENT ARE

This table lists the names of medications used to treat obesity along with their pharmacokinetics, FDA and EMA approval, therapeutic activity, and adverse drug reactions.

Table1: Anti-obesity medications approved by FDA & EMA: MOA, ROA, approval, therapeutic use and ADRs.[14, 20, 21, 22]

No.	Drugname	MOAs	ROA	Dose	Approvalyear by FDA & EMA	ADRs	Therapeutic uses
1.	Orlistat	Lipaseinhibitor& decreases fat absorption	PO	60-120mgTD	FDA1999&EMA1998	Oilyrectalleakage, steatorrhea, abdominal	Reducefat absorption upto 30 %
2.	Phentermine/ Topiramate	GABAreceptor modulator &sympathomimetic	PO	7.515/46-92mg/ day	FDA2012	ElevatedBP, metabolic acidosis, CNSdisorder	Decreaseappetite
3.	Naltrexone/ Bupropion	Opioidantagonists	PO	32/360 mg/ day	FDA2014&EMA2015	GIdisturbance, headache,insomnia	Decrease appetite& cravingsofunhealthy foods
4.	Liraglutide	Decreaseappetite& GLP-1 RAs	SC	3mgperday	FDA2014&EMA2015	Increased HR, Hypoglycaemia,GI disturbance	Increase fullness&satiety
5.	Semaglutide	Decreaseappetite& GLP-1 RAs	SC	2.4mg oncea week	FDA2021&EMA2021	Abdominalpain,GI disturbance, headache	Reduce appetite&improve fullness
6.	Tirzepatide	Increasefullness& GLP1 RAs	SC	2.5-15mgweek	Under consideration by FDA	Decreasedappetite, GIdisturbance,dyspepsia	Increases satiety
7.	Setmelanotide	MC4receptor agonists	SC	2-3 mg/day	FDA2020& EMA2021	Hypersensitivity, hyperpigmentation,GI-disturbance	Reducesthe hunger

[Abbreviations: MOA- mechanism of action, ROA stands for route of administration, ADRs stands for Adverse drug reactions, GABA means gamma-aminobutyric acid. Glucagon-like peptide 1 receptor antagonist goes by GLP-1 RAs. Melanocortin-4 receptor is short for MC4R. Dopamine shows up as DA. The European Medicines Agency answers to EMA. Food and Drug Administration gets tagged FDA. Subcutaneous? That's SC. IV stands in for intravenous. Norepinephrine hides behind NE. Three times daily becomes TD]

EFFECTIVE NATURAL COMPONENTS THAT USED TO TREAT THIS CONDITION

Curcumin: The yellow root called turmeric holds a compound known for calming inflammation, slowing cell overgrowth, and balancing internal reactions. Instead of sugar pills, people taking 1500 mg daily saw drops in weight and better response to insulin. Their pancreas cells worked more smoothly too. Findings showed.

•Homeostasis evaluation of β-cell function (HOMA) scores of 136.20 against.

•105.19, HOMA-IR values of 4.86 versus 6.04, adiponectin levels of 14.51 versus.

•10.36, BMI readings of 25.94 versus 29.34, and leptin levels of 9.42 versus 20.66. A 12-month randomised controlled experiment involving obese individuals with type 2 diabetes mellitus (T2DM) revealed this. Curcumin treatment may be helpful for these people.[18]

Genistein: Foods such as soybeans and products derived from them carry this compound. Found in legumes, it acts on metabolism in multiple ways. A type of isoflavonoid, it binds to oestrogen receptors selectively. Known scientifically as a Selective Estrogen Receptor Modulator (SERM), its role influences hormonal pathways.[18]

B**erberine [BBR**]: Roots of a plant called Coptic chinensis make up Huang Lian, used in old healing practices from China. That root holds berberine, its main active compound. This substance helps manage high blood sugar levels while influencing heart health through vessel relaxation. Fat buildup slows down when it enters the system. Inflammation markers drop during its presence in the body. Oxidative stress sees reduction thanks to its chemical behaviour. Cholesterol numbers often shift lower after consistent exposure.[18]

OBSERVATION

Some weight-loss drugs work differently, so doctors often pair them with changes in daily habits. Gastrointestinal issues may appear with Orlistat, since it interferes with fat absorption in the gut. Sudden bowel urges and oily stool show up in more than one out of four people using it. Brain-targeting treatments like Naltrexone-Bupropion or Phentermine-Topiramate sometimes reduce hunger signals. Constipation affects roughly a fifth of those on these central-acting options. Some medicines bring varied unwanted reactions - nausea shows up more often than tingling skin. Drugs built on hormone action, including Tirzepatide, Liraglutide, and Semaglutide, copy signals our body uses to manage appetite while offering certain heart and metabolism perks tied to losing weight. Upset stomach hits 28% to 44%, runs affect 9 out of every 50 people, and trouble moving bowels lands between 11% and nearly one in four. Studies using pooled data have compared how well these treatments work for adults dealing with obesity.

CONCLUSION

Half of India nearly, close to two out of every five, carry excess weight that harms health. A bit less in the U.S., yet still high - around four in ten face the same struggle. This condition spreads now like wildfire across nations, lasting years, sometimes lifetimes. Medicine, when chosen well, brings down numbers on scales slowly. Some pills help bodies reset, making daily living easier for those trapped by size. Doctors reach for these tools not just to shrink waistlines but to block heart failure, diabetes, and worse outcomes before they start. Few medicines work better for this job, yet bring along unwanted reactions - dizziness, upset stomach, trouble with bowel movements, shifts in mood or sleep. Once the pills are discontinued, those issues tend to fade on their own. Taking the drug while adjusting meals and moving more each day often boosts results. Dropping just five to ten percent of total weight can ease strain on the heart, stabilize blood sugar levels.[16]

DISCUSSION FOR THE RATIONALE USE OF AOMs

The drugs used to treat obesity need to have success means shedding pounds while fixing prior excess weight issues. Proof of how body handles side effects is necessary here. Just like similar drugs, staying clear of dependency matters most. What makes it work should stay private knowledge. Known science behind function fits better when cost stays fair.

The following are some ideas that are essential to any debate of the justification for the use of anti-obesity drugs.

- Changes in food choices along with daily habits help make medicine work better. Medicines on their own simply encourage people to stick more closely to those changes. Stillness breaks routine just enough.
- Stopping the pills means the extra pounds come back. Medication only works while someone keeps using it. Once intake ends, the body shifts toward gaining again. Pills do nothing unless swallowed each day,so when they go unused, weight climbs once more.
- Anti-obesity drugs must be administered under ongoing medical supervision.
- The choice of drug and course of treatment is based on the individual patient. The danger of obesity persistence must be balanced against the possible harms of medication use.
- Only when treatment is deemed safe and beneficial for the patient can it be started.

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