

# Current Treatment Strategies for Obesity Including Indian scenario

Ram Kumar Sahu<sup>1</sup>, Deepak Prashar<sup>2</sup>

<sup>1</sup>Department of Pharmacy, Columbia Institute of Pharmacy, Raipur, Chhattisgarh, India, <sup>2</sup>Research Scholar, PAHER University, Udaipur, Rajasthan, India

## Abstract

**Aim:** The aim of the review is to recapitulate the existing treatment strategies for obesity including Indian scenario. **Materials and Methods:** The data are extracted from electronic databases and journal search, to find meta-analysis, systematic reviews and randomized, placebo-controlled trials for currently approved obesity medications. The evidence-based surgical and nonsurgical treatments for obesity is studied and evaluated. **Results and Discussion:** The outcome of the review work put forward the prevalence of nonrationalized treatment strategies for obesity management. Moreover, the review also suggested the current status of the anti-obesity agents in use. **Conclusion:** The present work concludes that current treatment methodologies are convenient for the treatment and management of obesity. But still, further clinical investigations are required for the proper selection of better treatment. The associated diseases and adverse drug reactions produced by currently used drug therapy plays a vital role in deciding the better curing options.

**Key words:** Allied ailments, Indian scenario, obesity, treatment strategies

## INTRODUCTION

Obesity is the most challenging threat faced by India. The most recent study by Press Trust of India indicates that India has the third-highest number of obese and overweight people (11% of adolescents, and 20% of all adults) after US and China.<sup>[1-3]</sup> In 2014, forthright inoffensive tidy high-spirited objective conducted the consumer survey (including 4100 participants out of which 46% were men, and 54% were women with age 18-75). The study was based on the guidelines by Indian Health Ministry.<sup>[4]</sup> The survey reports revealed that out of the total, 1/5<sup>th</sup> men (377 out of 1886) and 1/7<sup>th</sup> (316 out of 2214) of the women were extremely obese. The report also suggested that average age for the risk of obesity is 37 years in the case of men and 32 years in women. According to NDTV news in 2014, 41 million Indian populations are obese.<sup>[5]</sup> These alarming statistics are extremely significant as the prevalence of obesity and overweight will result in more adiposity-related diseases. These includes diabetes, high blood pressure, high cholesterol, heart disease, stroke, gallbladder disease, gastroesophageal reflux disease (GERD), osteoarthritis, sleep apnea, respiratory problems, cancer (endometrial, breast, colon, kidney, gallbladder, and liver), reproductive problems, mental illness such as

clinical depression, anxiety, and other mental disorders, body pain, and difficulty with physical functioning. Bleich *et al.* reported that only one-third of the obese patients undergoes weight related diagnosis and treatment.<sup>[6]</sup> There are many treatment methodologies available in the present time for the treatment and management of obesity. Dietary therapy, physical activity, behavior therapy, combined therapy, pharmacotherapy, surgery (gastric band surgery, gastric bypass surgery, sleeve gastrectomy, biliopancreatic diversion [BPD] and duodenal switch [DS]), electroconvulsive therapy (ECT), and gene therapy. In the present review, evidence-based surgical, and nonsurgical treatment strategy to overcome obesity is highlighted including Indian prospect. Key articles published over the last 20 years will be emphasized.

## OBESE DIVERSIFICATION IN INDIA

India is one among the most diversified countries worldwide. This diversification is the result of distinct religions, food,

### Address for correspondence:

Deepak Prashar, Research Scholar, PAHER University, Udaipur, Rajasthan, India.  
E-mail: pm\_vcp@rediffmail.com

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languages, customs, and beliefs. This diversification results in different types of food intake as well as the diverse lifestyle. Among the different states, Punjab ranked top as far as the obesity is concerned followed by Kerala and Goa, respectively [Table 1].

This clearly indicates that women populations in most of the states are more obese in comparison to male population. Figure 1 enlisted the top ten states with maximum obesity among the Indian population. It is more surprising to witness that Kerala with almost 100% literacy rate ranked second in this list. Ranjani *et al.*<sup>[8]</sup> through the systematic review presented the epidemiology of childhood overweight and obesity in India. The study concluded that obesity rate is also increasing in lower income groups were underweight still remains a major concern. Various researchers all over, India carried out the studies in different areas to support the increased obesity rates.<sup>[9-15]</sup>

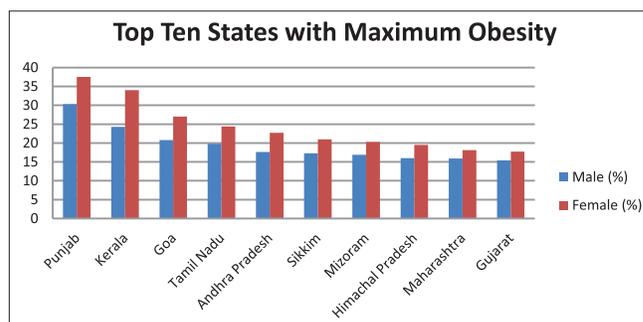
## CAUSES AND DISEASES ASSOCIATION WITH OBESITY

Treatment of obesity and overweight is by far the most difficult task for the physicians in the light of its unpredictable origin. Childhood obesity may result from undefined dietary pattern, greater availability of high-energy-dense food and sugar-sweetened beverages,<sup>[16]</sup> lack of breastfeeding and physical inactivity.<sup>[17-20]</sup> Adolescent obesity might result from overeating, family history, bad eating habits, medical illness, low self-esteem, depression, emotional problem, and stressful life. Gestational weight gain in the women can be related to hormonal imbalance, sedentary lifestyle, utilization of medications before, during and after pregnancy. Further, it is believed that abdominal obesity is caused by energy imbalance between consumed calories and its expenditure. Excess meat consumption may also be positively associated with abdominal obesity.<sup>[21]</sup> Maternal smoking, endocrine disrupting chemicals and diet containing estrogenic compounds might be the associated factors for abdominal obesity.<sup>[22]</sup>

Despite the nature of origin, obesity is associated with numerous disorders. Obligado and Goldfarb through their studies suggested that nephrolithiasis was associated with greater tendency to develop hypertension.<sup>[23]</sup> Available epidemiological data also provide the link of obesity and overweight with nephrolithiasis. Maruthur *et al.* presented the association of obesity with cervical cancer,<sup>[24]</sup> earlier the connection of obesity<sup>[25]</sup> with breast, cervical, and colorectal cancer in women was presented by Cohen *et al.* Darvall *et al.* also linked up obesity with thrombosis which promotes the cardiovascular disorders.<sup>[26]</sup> Anand and Katz after reviewing the accessible epidemiological data recommended that GERD is more prevalent in obese patients.<sup>[27]</sup> Bruno *et al.* marked the prevalence of asthma greater in obese patients in comparison to lean.<sup>[28]</sup> Further Kim *et al.* concluded through

**Table 1: State wise obesity diversification in India<sup>[7]</sup>**

State	Male (%)	Female (%)
Punjab	30.3	37.5
Kerala	24.3	34.0
Goa	20.8	27.0
Tamil Nadu	19.8	24.4
Andhra Pradesh	17.6	22.7
Sikkim	17.3	21.0
Mizoram	16.9	20.3
Himachal Pradesh	16.0	19.5
Maharashtra	15.9	18.1
Gujarat	15.4	17.7
Haryana	14.4	17.6
Karnataka	14.0	17.3
Manipur	13.4	17.1
Uttarakhand	11.4	14.8
Arunachal Pradesh	10.6	12.5
Uttar Pradesh	9.9	12.0
Jammu and Kashmir	8.7	11.1
Bihar	8.5	10.5
Nagaland	8.4	10.2
Rajasthan	8.4	9.0
Meghalaya	8.2	8.9
Orissa	6.9	8.6
Assam	6.7	7.8
Chhattisgarh	6.5	7.6
West Bengal	6.1	7.1
Madhya Pradesh	5.4	6.7
Jharkhand	5.3	5.9
Tripura	5.2	5.3



**Figure 1: List of top ten Indian obese states**

his studies that impairment of efferocytosis by macrophages in obese asthmatics along with immunological changes in adipose tissue may together play an important role in the mechanistic association of obesity with asthma.<sup>[29]</sup> Many researchers through their studies revealed that obesity is primary associated with diabetes both type-I and type-II.<sup>[30-32]</sup> Tukker *et al.* studied health problems of the lower extremities

such as osteoarthritis, pain, and disability. The results of the study suggested the effect of wear and tear on joint due to obesity.<sup>[33]</sup> In addition, the research concluded that greater the burden of fat greater the chance of trauma to joints with time.

## CURRENT TREATMENT STRATEGIES FOR OBESITY

The researchers implied that there are numerous causes of obesity depending on age, lifestyle, profession, and medical circumstances. Treatment of overweight is suggested only when patients have two or more risk factors (hypertension, high blood cholesterol, type 2 diabetes, coronary heart disease, and asthma, etc.) or a high waist circumference. The management of obesity should focus on producing significant weight loss over a prolonged period. The existence of comorbidities in overweight and obese patients should be considered while deciding treatment options. According to the clinical guidelines, the treatment of obesity and overweight is carried out through assessment and treatment management [Table 2].

Several modalities may be used to treat overweight and obesity. Their effectiveness on weight loss, loss of abdominal fat, and cardiorespiratory fitness can be assessed from the evidence generated by randomized control trials. These trials comprise of dietary therapy, physical activity, combined therapy, behavior therapy, pharmacotherapy, surgery, ECT, and gene therapy.

## DIETARY THERAPY

The dietary therapy is based on the criteria of decreased energy intake and increased energy expenditure to produce the negative energy balance. Researchers<sup>[34-37]</sup> are always looking up for generating balanced diet, which might prove productive to overcome obesity.

These weight loss regimens include vegetarian diet, low-calorie diets, and very low-calorie diets, diet with caloric restriction and diet with varying the combination of macronutrients.

## PHYSICAL ACTIVITY

Physical activities are considered among the best treatment for the obese and over weighted patients. This strategy requires regular workout in the form of aerobic and calisthenic exercise. The investigators through their studies and research have investigated that physical activities only helped in preventing the weight regain.<sup>[38]</sup> Thus the effectiveness of this strategy depends on upon the various factors such as lifestyle, associated disease conditions, and regularity in exercise.<sup>[39-41]</sup> This treatment policy is only effective in combination with balanced diet. Moreover, the long-term efficacy of physical activities in treatment of obesity is still not proven.

## BEHAVIOR THERAPY

Behavioral treatment approach helps individuals to achieve optimal weight. By developing a set of skills an individual can decide how to change through the use of goal setting, self-monitoring, and problem-solving. The goal setting literally means deciding the well-planned schedule for the working in connection with routine work out. Self-monitoring focusing on observing minute changes in body and body weight rather than expected large changes at initial stages. Behavior therapies include education, which helps in deciding individuals about a balanced diet with optimal calorie as per required. The use of internet-based programs (both short-term and long-term) helps to reduce obesity with cost-effectiveness. Slow eating techniques along with stimulus control (not distracted by television, books, or other materials) have shown the positive effect on weight loss.<sup>[42-45]</sup>

**Table 2: Factors for assessment, treatment, and management of obesity**

Treatment of obesity and overweight			
Assessment		Treatment management	
Degree of overweight	Risk status	Strategies reducing excess body weight	Measures to control accompanying risk factors
Body mass index	Disease conditions	Dietary therapy	Physical inactivity
Waist circumference	Other obesity-associated diseases	Physical activity	High serum triglycerides
	Cardiovascular risk factors	Behavior therapy	Patients motivation
		Combined therapy	
		Pharmacotherapy	
		Surgery	
		Electroconvulsive therapy	
		Gene therapy	

## COMBINED THERAPY

Combination therapies are always applicable when the single mode is unable to generate the desired results. In the treatment of obesity combination of diet and physical activities such as brisk walking, jogging, riding a stationary bicycle, and swimming may provide the results better than individual treatment technique. This combination of reduced-calorie diet and increased physical activity reduces the fat stored within the body and also prevents the regaining of weight.<sup>[46-48]</sup>

## PHARMACOTHERAPY

Pharmacotherapy is primarily suggested for obese patients with type 2 diabetes.<sup>[49-52]</sup> This is required because diabetes

results in overweight, which is needed to be counteracted using anti-obesity agents. Based on the mechanism of action anti-obesity drugs are classified under three groups: Appetite suppressants (phentermine, fluoxetine, sibutramine, rimonabant), inhibitors of fat absorption (orlistat), stimulators of energy expenditure (thyroid hormone), and thermogenesis (ephedrine with and without caffeine, terbutaline).<sup>[53]</sup>

According to Ioannides-Demos *et al.* 2-7.9 kg of weight can be reduced using pharmacotherapy.<sup>[54]</sup> There are several drugs available in the market for the treatment of obesity and overweight. Most of the drugs have established its practical effectiveness in the treatment of obesity. However, the associated adverse drug reactions confined the use of many drugs and may even have resulted in withdrawal [Table 3]. Dinitrophenol introduced in the 1930s was

**Table 3: List of anti-obesity drugs with mechanism of action<sup>[53]</sup>**

Drug	Mechanism of action	Brand name	Current status
Phentermine	Reducing food intake: Sympathomimetic amine	Adipex-P Lonamin	Short-term use (<12 weeks)
Diethylpropion	As above	Tenuate Tepanil	Short-term use (<12 weeks)
Fluoxetine	Reducing food intake: Selective serotonin reuptake inhibitor	Prozac Sarafem	Short-term use (<12 weeks)
Sibutramine	Reducing food intake: Combined norepinephrine and serotonin reuptake inhibitor	Meridia	Withdrawn
Orlistat	Reducing fat absorption: Lipase inhibitor	Xenical Alli	Marketed
Rimonabant	Reducing food intake: Selective CB1 receptor blocker	Acomplia	Withdrawn
Dinitrophenol	Uncouples oxidative phosphorylation in mitochondria	Dinitriso Nitromet Dinitrenal	Withdrawn
Amphetamine	Increases the neurotransmitters dopamine, noradrenaline, and serotonin in brain	Evekeo Adzenys XR-ODT Dyanavel XR	Banned as an anti-obesity drug
Aminoxaphen	Indirect sympathomimetic action	Aminorex	Withdrawn
Phenylpropanolamine	Central $\alpha_1$ -adrenergic receptor agonist	Accutrim Dexatrim	Banned in the USA
Fenfluramine, dexfenfluramine	Selective serotonin reuptake inhibitor	Pondimin Redux	Withdrawn
Lorcaserin	Selective 5-HT <sub>2C</sub> receptor agonist	Belviq	Recently approved
Topiramate+phentermine	Topiramate blocks voltage-dependent sodium channels, glutamate receptors and carbonic anhydrase, and augments GABA activity; phentermine is sympathomimetic	Qsymia	Recently approved
Tesofensine	Norepinephrine, dopamine and serotonin reuptake inhibition	-	Not approved
Cetilistat	Lipases inhibitor	Cetislim	Not approved
Bupropion+naltrexone	Bupropion increases the activity of POMC neurons. Naltrexone blocks opioid receptors on the POMC neurons, preventing feedback inhibition and increasing POMC activity	Contrave	Still under investigation

POMC: Pro-opiomelanocortin, GABA: Gamma-aminobutyrate

withdrawn from the market with risk of neuropathy and cataract. Amphetamines derivatives such as dexamphetamine and methamphetamine resulted in dependency and abuse potential along with cardiovascular adverse effects, which restricted its use. Aminorex introduced in 1965 was withdrawn in 1968 with resulting pulmonary hypertension. Fenfluramine and dexfenfluramine were also withdrawn in 1997 with associated valvular heart disease and pulmonary hypertension. Rimonabant drug was available in European countries since 2006 but after 3 years was withdrawn in 2009 due to possible serious psychiatric disorders. Sibutramine too was temporarily withdrawn in 2002 but was able to overcome the allied adverse effects. In the present scenario orlistat and sibutramine are the only two drugs with are available in the market for the long-term treatment and management of obesity.<sup>[55-58]</sup> Other to be available drugs in the near future are under phase-III trials.

## SURGERY

This is one among the most reliable therapy as far as the overweight and obesity treatment is concerned. Weight loss surgical treatment or bariatric surgery is based on the concept of restricting the quantity of food the stomach can clutch and causing the least absorption of nutrients. Laparoscopic surgery is one among the invasive technique used for this by adopting the procedure, including gastric bypass, adjustable gastric band, sleeve gastrectomy, and BPD with DS. This procedure is opted for the patients with body mass index (BMI)  $\geq 40$  or weight more than 100 pounds. The surgery can also be carried out for patients with BMI  $\geq 35$  with at least two comorbidities such as fatty liver, heart disease, hypertension, and type II diabetes. The bariatric surgical procedure helps in treating obesity either by changing the anatomy of gastrointestinal area or by producing the physiological change (hormonal change) with decreases the appetite.<sup>[59-61]</sup> However, no surgery is without risk and weight-loss surgery also carries the same for the future. The complications and risks of weight loss surgical treatment vary according to the age, sex, and BMI [Table 4].

## GENE THERAPY

Researchers have well established the fact that abnormalities in specific genes might be directly or indirectly responsible for obesity.<sup>[62-67]</sup> Monogenic forms such as leptin, leptin receptor, pro-opiomelanocortin, pro-hormone convertase-1, and melanocortin-4 receptor genes are responsive for human obesity. In the majority of cases, polygenic factors are accountable for this defect. In a study published in Journal of Clinical Invest, 2001 signifies that selective deletion of leptin receptor genes or mutation of leptin leads to overeating, massive weight gain, insulin resistance, diabetes.<sup>[68]</sup> Further literature also sustains the same with additional development of a variety of neuroendocrine abnormalities in rodents and humans.<sup>[69]</sup> These published works also suggested that through genetic engineering or genetic recombinant technique, this mutation can be progressively overcome. This therapy too is associated with some risk factors like selecting proper therapeutic gene and maintaining the sustained expression of the transgene during gene silencing in obesity treatment.<sup>[67]</sup>

## ELECTROCONVULSIVE THERAPY

The patients with the psychiatric disorders such as depression and mania are prescribed atypical antipsychotic medication. Continuous consumption of these medications over a long period results in side effects, such as obesity, cardiovascular disease, type 2 diabetes, and hypertension. A part from these medications the patients with severe major depression and catatonia are recommended ECT (electric shock). Moss and Vaidya reviewed the charts of ten patients who have received maintenance ECT over the last 10-year period.<sup>[70]</sup> The results from their studies revealed that five of ten patients were obese pre-ECT, all of whom had a significant weight loss after ECT. Patients with normal weight pre-ECT did not experience weight loss. This finding suggests that ECT is a possible alternative for overweight patients with mood disorders. Earlier, Gleiter *et al.* carried out the similar research using rats and put forward the hypothesis that repeated electroconvulsive shock (ECS), as treatment is

**Table 4:** Represents the risks associated with weight loss surgical treatments

Type of Surgery	Future complications
Gastric band surgery	It may slip and erode through the wall of stomach and becomes ineffective
Gastric bypass surgery	Leak may develop at point where small intestine is connected to stomach and may require further surgery Intestine is bypassed in the surgery which leads to deficiency of vitamins and minerals
Sleeve gastrectomy	Since the side of stomach is removed and narrow tube is left hence patients have to consume much lesser meals in future
Biliopancreatic diversion	The upper part of intestine is bypassed which prevents the absorption of fats and carbohydrates. Moreover, this type of surgery results in flatulence and foul-smelling stool
Duodenal switch	This is a long surgery requiring general anesthesia which increases the risk of developing blood clot in legs and on lungs Flatulence, foul-smelling stool, and less protein absorption result in protein calorie malnutrition

known to change the body weight. ECS once-daily over the period of 10 days significantly reduced weight gain in rats with hypothalamus related body weight and obesity.<sup>[71]</sup> Eldor *et al.* also strengthened the hypothesis of use of ECT/ECS for the alternative treatment of obesity.<sup>[72]</sup> Hughes *et al.* studied 72 patients submitted on ECT and reported that 83% of the total patients showed improvement.<sup>[73]</sup> Freeman and Kendell carried the same type of study on 166 patients and concluded that 57.2% find this ECT useful.<sup>[74]</sup> However, another study carried out by Malekian *et al.* demonstrated that satisfaction with ECT was independent from treatment outcome.<sup>[75]</sup> Moreover, further research is required to evaluate safety criteria on the utilization of ECT as anti-obesity treatment.

Patients suffering from obesity may decide on anyone of the available treatments. The psychiatric patients may opt for ECT, while the genetic obesity can be treated with gene therapy. Obese patients with BMI  $\geq 40$  or weight more than 100 pounds may go for laparoscopic surgery. The current review encourages the use of anti-diabetic drugs for the treatment of obesity as well as diabetes. The findings of the review will prove to be beneficial for the entire scientific community and patients to decide the better alternative for obesity treatment in the near future.

## CONCLUSION

Diversification in India is one among the major problem for the uniform treatment plan for obesity. Some areas in India have a very sedentary lifestyle because of weather conditions while some areas have traditional fat rich diet schedules. The selection of better treatment strategies is required to overcome and manage the present condition. Pharmacotherapy is the best option for the long-term treatment of obesity, but available present medications have some limitations. The surgery and ECT also provided the good alternate, yet their positivity need to be strengthened. Gene therapy is the latest field to treat obesity and require some more time, especially in Indian to prove productive. The present review suggested the necessity of further clinical interventions for the better treatment of obesity.

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