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Current Status of Weight Loss Therapy in Achieving Remission of Type 2 Diabetes Mellitus

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Abstract. Type 2 diabetes (T2DM) is a very big health problem all over the world. Obesity is the most important cause of T2DM, and more than 80% of people with this disease are overweight or obese. Obesity makes insulin resistance worse, hurts the function of pancreatic β-cells, causes long-term inflammation, and breaks the body's normal balance, and these things make T2DM start and get worse. Weight loss treatment has become a main way to help patients with obesity or overweight and T2DM get better. Today's ways mainly include lifestyle changes, medicine, and weight-loss surgery. These ways work together to help people lose weight and control blood sugar, but they use different methods. This paper carefully looks at how obesity and T2DM are connected, and it clearly explains how exercise for weight loss, Chinese and Western medicine, and weight-loss surgery work, how well they work in patients, and how they are used now. It also points out the problems with today's treatments, and using new research, it gives ideas for the future to help make personal weight-loss plans and promote more research in this field.

Keywords: obesity, type 2 diabetes mellitus, weight loss, insulin resistance, weight loss therapy

1. Introduction

The number of people around the world with type 2 diabetes (T2DM) is more than 400 million, and it will be 592 million by 2035 [1]. Obesity is one of the most important causes of T2DM [2], and more than 80% of people with T2DM are overweight or obese [3]. Overweight and obesity mean long-term inflammation, weak immune system, and poor body metabolism [4]. They are big health problems worldwide and are linked with many long-term diseases, and they are very important in causing T2DM [5]. These two health problems come from similar genes and living environment, and obesity makes genes and environment more likely to cause diabetes [6]. T2DM with obesity or overweight makes insulin resistance much worse [7], so insulin cannot lower blood sugar well, and blood sugar balance is broken [8]. At the same time, pancreatic β-cells do not work well, so sugar and fat metabolism is not normal [9], and this finally causes high blood sugar and T2DM [10]. Studies show that too much insulin because of obesity not only works on insulin receptors in pancreatic cells but also makes cells grow and live longer by activating the IGF-1 receptor [11]. It is thought that by 2045, about 700 million adults around the world will have diabetes, most will have T2DM, and 45% of these cases will be caused by obesity [12]. Obesity and T2DM have similar

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body disease processes. The 2024 American Diabetes Association rules say that patients with T2DM and obesity or overweight should try to lose weight [13] to control blood sugar better and use fewer diabetes drugs, so the body metabolism problems of T2DM can be improved [14]. Now, the treatment of obesity and T2DM is almost the same, including lifestyle changes, medicine, new medical tools, and weight-loss surgery. People care more about these treatments, and the skills are getting better and better [6].

2. Weight reduction improves diabetes mellitus

At present, therapeutic strategies that have demonstrated efficacy in both obesity and T2DM primarily include lifestyle interventions (such as dietary modification, increased physical activity, and behavioral therapy), pharmacological treatment, the use of related medical devices, and bariatric surgery [6].

2.1. Exercise-induced weight loss improves diabetes mellitus

Exercise is a very important way without medicine. It is used in hospital care and health plans to treat obesity and body problems caused by it [15]. Exercise can control blood sugar well, improve body fat and fat metabolism, and make blood sugar numbers much lower than people who do not exercise [16]. More exercise, less food, and weight loss are very important to make T2DM better [17]. Eating less energy is the main part of weight loss [18], but exercise is also very necessary. Exercise helps sugar, fat and protein work better in muscle, makes more mitochondria in muscle cells, makes more blood vessels, helps muscle cells take and use more sugar, and makes fat problems better. All these help control weight, control blood sugar and improve insulin resistance [19-21].

Not moving enough makes mTORC1 stay active all the time. This is an important step in getting T2DM [22]. Studies show that 8 weeks of aerobic exercise can make insulin work better in fat mice by helping blood release exosomes [23]. Aerobic exercise makes heart and lung stronger. Strength exercise makes muscle work better. Using both together can reduce fat and increase muscle at the same time [24]. This may be because exercise uses more muscle fibers, makes muscle bigger and stronger, makes more and better mitochondria in muscle, helps cells take and use more sugar, burns fat faster, uses more energy and uses energy better. All these help lose fat and weight [25].

But longer exercise does not always work better. More exercise time does not always help prevent or control disease better. This is because more exercise gives less extra good result, too much exercise is bad for body, and people feel tired mentally [26]. So we need to make personal and scientific exercise plans.

2.2. Pharmacological weight loss improves diabetes mellitus

Clinical data show that almost two out of three patients with T2DM have abnormal body weight [27]. Although diet and exercise can improve health and lower disease risk in people with obesity, using these methods alone often leads to weight loss stopping, difficulty keeping weight off long-term, and weight and blood sugar going back up. For obese people who also have T2DM [6], medicine that helps both weight loss and blood sugar control has become an important addition to long-term care [28].

In terms of medicine, some drugs—including lorcaserin, orlistat, phentermine/topiramate, naltrexone/bupropion, and GLP-1 RAs—have rules against them because of possible cancer risks,

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and they have been stopped or limited by the U.S. FDA [29]. A study looking at 143 randomized controlled trials gives strong evidence for how well and how safely different weight-loss drugs work compared with each other [30]. These studies show that such drugs not only lower body weight but also improve problems with sugar metabolism, and lower blood sugar effectively [31]. By helping weight loss through medicine, belly fat is reduced, insulin resistance from fat tissue is improved, and sugar metabolism is controlled directly, making fasting blood sugar and glycated hemoglobin much lower.

It is important to know that medicine's control of body weight and blood sugar has a strong two-way relationship. Most diabetes drugs change body weight while they control blood sugar. For example, SGLT-2is lower blood sugar by letting sugar leave the body through urine, and they also help weight loss at the same time.

In general, most current treatments for obesity and T2DM work well together: weight-loss drugs can make T2DM better, and in some cases even improve the disease over time by keeping weight down.

2.2.1. Western pharmacotherapy

For patients with T2DM and obesity or overweight, we should first use drugs that help both lose weight and control blood sugar. Among the diabetes drugs we have now, metformin is still a very important drug for T2DM. It lowers blood sugar by stopping the liver from making too much sugar, reducing sugar absorption in the intestines, and helping body parts like muscles use more sugar. This makes insulin work better. Besides, metformin activates the AMPK pathway, helps the body burn more fat, breaks down fat, reduces fat accumulation, and reduces inflammation [32]. Metformin also makes muscle cells have more GLUT4, which helps the body take in more sugar from the outside. This way, it not only lowers blood sugar well but also helps lose weight by stopping the body from storing too much energy [33]. Because it works well to lower blood sugar and is safe, metformin is widely used in hospitals [34].

Besides this common drug, other medicines also have great potential. Pramlintide was approved by the U.S. FDA in 2005. It is used as an extra drug for both type 1 and type 2 diabetes. It is a safe form of the body's own IAPP (also called amylin) [35]. It works by slowing down stomach emptying, stopping the body from making too much glucagon [36], making people feel full, and reducing food intake. By lowering blood sugar after meals and helping lose weight, pramlintide helps control body metabolism better. Losing fat also helps reduce the fat's bad effect on insulin, makes insulin work better in the body, and makes weight loss and blood sugar improvement work together better.

SGLT-2 inhibitors [37] are another important kind of drug. They lower blood sugar well by stopping the kidneys from reabsorbing sugar and letting sugar leave the body through urine [38]. Losing calories through sugar in urine helps reduce fat accumulation and lose weight. What's more, these drugs protect the heart and blood vessels, and they are especially suitable for T2DM patients who also have heart or kidney disease.

In recent years, GLP-1 RAs have become a new kind of drug to lower blood sugar. They work well and are safe for treating T2DM and obesity [39]. They mainly work by stimulating insulin secretion, slowing down stomach emptying, and reducing appetite. This way, people eat less and blood sugar is lower [40]. Among them, long-acting semaglutide works very well: injecting 2.4 mg under the skin once a week can help obese people lose an average of more than 10% of their weight. Taking it for a long time makes the effect better, and it also greatly improves blood pressure, blood sugar, fat levels, and other body metabolism indicators [41]. It is important to note that professional

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obesity organizations suggest using these drugs together with comprehensive methods—including eating less calories, exercising regularly, and changing bad habits—to make sure weight loss lasts. If you need to stop taking the drug, you should reduce the dose slowly or change to another drug. This can reduce weight gain again and prevent blood sugar from getting worse because of weight changes [42].

The FDA has approved several weight-loss drugs for patients with T2DM who are obese or overweight. These include short-term drugs such as phentermine, and long-term drugs such as orlistat, phentermine/topiramate, liraglutide, and medicines that include semaglutide. The main goal of these drugs is to help people lose much weight, improve insulin resistance, and reduce or control the development of T2DM.

Orlistat is a drug that stops fat breakdown. It blocks some fat from food being taken into the body, so people take in fewer calories and lose weight. Less weight means less belly fat, less long-term inflammation and fat damage, better insulin resistance, and better fat metabolism [43-45]. More studies show that using orlistat with drugs like metformin works better to improve weight, fat distribution, and insulin resistance in patients with OB/OW-T2DM [46].

Phentermine/topiramate is a stronger weight-loss treatment. Phentermine is a drug that affects the brain and reduces appetite [47]. Topiramate makes people feel full in many ways. Together, they can make people eat much fewer calories and lose up to 13% of their weight for a long time [48]. This treatment is safe for the heart, and better body composition improves insulin resistance and helps control T2DM better.

In the GLP-1 RA group, liraglutide and semaglutide [49] are two drugs that lower blood sugar and help weight loss. They are often used for T2DM or obese patients with fat problems. These drugs stop too much glucagon, reduce sugar made by the liver, help the body make better insulin, and help the body use more sugar. So both morning and after-meal blood sugar becomes lower. At the same time, they slow stomach emptying and reduce appetite in the brain. People eat fewer calories, lose weight, have less belly fat, and insulin works better in muscles and liver. Many good clinical studies [50] prove they work very well. For example, in a 68-week study, patients who took 2.4 mg semaglutide every week lost about 9.6% of their weight, and blood sugar control also got better. We should know that nausea, vomiting and other stomach problems are common during treatment and need proper medical care.

2.2.2. Traditional Chinese medicine and its formulations

Traditional Chinese medicine (TCM) has a long history of preventing and treating obesity and related T2DM. TCM medicines often have many parts, and they help lose weight by working together on many targets and ways. These effects can improve insulin resistance and make the body metabolism of T2DM patients better, and they are also less toxic. However, most studies on how they work are based on basic experiments now, and there is not much evidence from human clinical trials. We still need large-scale, long-term clinical trials to prove these effects.

Studies show that many useful substances in TCM can effectively control key disease processes, such as inflammation and insulin resistance, to reduce fat and help lose weight, thus reducing or even improving T2DM. In obese people, intestinal cells are easy to have bad insulin signals because of inflammatory substances. This makes cells take in too much sugar and fat, making fat accumulation and blood sugar problems worse. The Jianpi Qinghua formula can obviously reverse this process [51] by restoring normal intestinal metabolism, reducing fat accumulation, and then repairing insulin signals after weight loss. Coptis (Huanglian) [52] and its main useful part berberine [53] can reduce inflammation by adjusting chemokine expression and improving macrophage

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infiltration in fat tissue. This effect helps break down fat to lose weight, and directly improves insulin resistance and fat metabolism, thus helping control blood sugar.

In addition, widely existing plant substances such as quercetin [54] and hypericin [55] have been shown to improve inflammation in white fat tissue and restore bad insulin signals. These substances stop fat cells from growing too much to reduce fat accumulation, and at the same time make insulin work better in the body, achieving the effect of losing weight and controlling blood sugar together. Baicalin, a useful part of Scutellaria baicalensis, can also adjust macrophage polarization, reduce fat tissue inflammation [56], and help obese diabetic mice reduce body fat and blood sugar. Other substances, including curcumin and its derivatives [57] and sesamol, can promote macrophage polarization to the anti-inflammatory M2 type, reduce systemic inflammation, help break down fat to lose weight, and improve insulin resistance and sugar-fat metabolism. Curcumin can also stop liver inflammatory pathways such as JNK/NF-κB, reduce proinflammatory cytokine production, and make insulin work better [58].

In terms of TCM medicines, classic prescriptions such as Gegen Qinlian decoction work through many useful parts targeting different pathways. These medicines improve insulin resistance in fat tissue, liver and muscles, enhance sugar and fat metabolism, reduce fat accumulation, and comprehensively improve blood sugar problems in T2DM patients [59].

It should be noted that weight gain again after stopping TCM treatment is basically caused by the complex physiological mechanisms that control energy balance. It should not be simply regarded as treatment failure. To achieve long-term weight control and continuous T2DM management, it is most effective to combine long-term TCM treatment with continuous lifestyle and behavior changes. In addition, if patients do not understand how TCM helps lose weight and lower blood sugar and its clinical significance, their willingness to take TCM will be greatly affected, which will then reduce the treatment effect [60].

2.3. Bariatric surgery for improving T2DM

Although lifestyle changes are the first treatment choice for obesity and T2DM, they often do not work well for weight control in the long term. Patients often stop losing weight, and lifestyle changes alone cannot stop the bad development of T2DM [47]. So bariatric surgery has become a very effective treatment for OB/OW-T2DM [6]. Its main way is to help people lose much weight and keep it low. This greatly improves insulin resistance and makes T2DM better or even gone. At the same time, it improves body metabolism and reduces inflammation all over the body [61].

Based on early clinical evidence, international diabetes organizations have issued joint statements recommending that metabolic and bariatric surgery (MBS) be incorporated into treatment plans for patients with a BMI ≥35 kg/m² and T2DM [62]. The mechanisms underlying its effects can be summarized in three main pathways: (1) restriction of gastric volume, which directly reduces food intake and rapidly decreases fat accumulation; (2) modulation of gut hormone secretion, which regulates appetite signals and glucose–lipid metabolism, promoting weight loss while enhancing insulin sensitivity; and (3) reduction of intestinal nutrient absorption efficiency, which limits caloric accumulation to consolidate weight loss, complemented by lifestyle modification to sustain weight reduction and glycemic stability [63].

Bariatric surgical techniques have undergone significant evolution. Vertical banded gastroplasty (VBG) and Roux-en-Y gastric bypass (RYGB), proposed by the U.S. National Institutes of Health consensus in 1991, are now less commonly used due to limitations in efficacy and safety. Currently, minimally invasive sleeve gastrectomy performed via laparoscopy or robotic assistance has become the mainstream clinical choice, offering advantages such as procedural simplicity, minimal trauma,

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and rapid recovery [64]. Clinical data confirm that both RYGB and minimally invasive sleeve gastrectomy achieve superior long-term T2DM outcomes compared with pharmacotherapy alone [65]. Compared with non-surgical interventions, metabolic bariatric surgery demonstrates better medium- to long-term safety, efficacy, and durability [66,67] in terms of weight loss and glycemic control [68], and is more effective than conventional medications for long-term T2DM management [68], while also significantly reducing overall mortality [64].

Among these procedures, laparoscopic sleeve gastrectomy (LSG) involves resection of a portion of the stomach to reduce gastric volume, directly limiting food intake and modulating gut hormones related to appetite. LSG produces significant weight loss, alleviates most obesity-related comorbidities, is technically simpler than other procedures, and preserves normal gastrointestinal anatomy, resulting in a markedly lower complication rate. Postoperatively, patients typically experience decreased appetite and hunger, leading to reduced body fat, decreased visceral adiposity, alleviation of adipose tissue inflammation and lipotoxicity, improved insulin resistance, and consequent regulation of blood glucose in T2DM patients.

Long-term follow-up data have confirmed the metabolic benefits of surgical intervention via weight reduction, which can partially relieve T2DM. A multicenter randomized controlled trial reported that the proportion of patients achieving T2DM remission 10 years postoperatively far exceeded the 18% and 12% remission rates reported in adults at 7 and 12 years after bariatric surgery [69]. Studies have shown significant improvement in metabolic indicators and extended life expectancy in postoperative patients, with T2DM patients benefiting particularly due to improved glycemic control and reduced risk of complications [70]. A large meta-analysis showed that surgery can make people live 6.1 years longer on average [71]. Metabolic and bariatric surgery is also safe and effective for young people under 18 years old. It can help them keep weight loss and improve T2DM and other related diseases [64]. Recent clinical data show that children as young as 5 years old can keep long-term weight loss and recover from related problems after surgery [72]. Five years after surgery, the T2DM remission rate in young people was 27% higher than in adults [47]. This means early surgery may help the body respond better and control disease for a longer time.

Although current clinical evidence does not support strict age limits, doctors should choose patients carefully based on health and other signs to make sure surgery is safe and works well [64]. In short, bariatric surgery can keep weight down for a long time, reduce insulin resistance effectively, and help T2DM patients control blood sugar well for a long time. So T2DM can be treated with metabolic surgery.

3. Conclusion

In the future, as more and more people around the world have T2DM, weight-loss treatment has become an important way to make the disease better [73], which shows its great value in medical treatment. However, there are still many things we need to study further. Now, structured exercise is known to be good in hospitals, but it is hard for people to keep doing it for a long time. Western medicines like GLP-1 RAs and SGLT-2is work well to help lose weight and lower blood sugar, and common drugs like metformin are widely used. TCM medicines, which work on many parts of the body, have great potential, but there is not enough clinical evidence to make them widely used. Bariatric surgery is a long-lasting and effective treatment for people with moderate to severe obesity and T2DM; minimally invasive surgeries like laparoscopic sleeve gastrectomy have become the main choice. However, weight gain again after surgery and the need to closely check for related problems are still challenges. All weight-loss methods have problems that need to be solved. Future research should focus on important clinical issues and existing gaps. First, we need to fully assess

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patients and make personal exercise and diet plans to help people keep doing them for a long time [13]. Second, we need to do more clinical studies on TCM medicines to make clear how they work and how well they treat diseases. Third, we need long-term follow-up studies on new weight-loss and blood sugar-lowering drugs to check their safety, possible drug resistance, and which patients are most suitable for them. Fourth, we must improve the postoperative management system to prevent health problems caused by weight gain again [74].

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