Proceedings of the 2nd International Conference on Biological Engineering and Medical Science (ICBioMed 2022), Part I
DOI: 10.54254/2753-8818/3/20220378

Pharmacological Therapy for Obesity

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Abstract. Obesity is the main obstacle to human health in the world today, and it is more and more popular in the world.There are many methods to treat obesity in modern society, such as behavioral therapy, surgical treatment and pharmacological therapy.The author aims to give a review of pharmacological therapy for obesity based on existing literature research results and data. This paper mainly introduces the three drugs which are Phentermine, Sibutramine and Orlistat their mechanism.The result shows that these three drugs are applicable to moderate and severe obesity, and they can not be overused. Sibutramine, which can increase the risk of serious cardiovascular and cerebrovasular diseases, has been banned. The remaining two drugs, Phentermine and Orlistat, can be taken normally as long as they are under the guidance of doctors.

Keywords: phentermine, sibutramine, orlistat, pharmacological therapy, obesity

1. Introduction

Obesity has become a social disease that the public is worried about and has attracted great attention from the medical community. Some data show that since the 21st century, more people in the world have died of obesity than of starvation. In addition, by 2030, one billion people worldwide, including one in five women and one in seven men, will be obese, according to the World Obesity Atlas 2022, issued by the World Obesity Federation[1]. Obesity is now divided into three categories in society:1) Primary obesity; 2) Secondary obesity: secondary obesity is a kind of disease caused by an endocrine disorder or metabolic disorder, which is rare in clinics and only accounts for 2% ~ 5% of obese people. 3) Drug-induced obesity: while some drugs treat diseases, they also have adverse phenomenon that make people fat. There are also many harms brought by obesity, for example, it will harm many systems: the digestive system, respiratory system, metabolic system, circulatory system, and so on. At present, there are many studies on obesity. For example: 1)Surgical treatment provides the only feasible long-term weight loss and maintenance treatment option for obese patients. Gastric bypass surgery is the most commonly used operation at present. Weight loss after surgical treatment resulted in significant improvement[2]. 2)Ketogenic diet therapy refers to a diet with high fat, low carbohydrate and proper protein to accelerate the metabolism of fat into ketone bodies. When carbohydrate function is insufficient, fat and sugar are metabolized to produce glycerol and converted into sugar. Ketone bodies will be produced in this process and discharged into the body with urine to achieve the purpose of treating diseases or reducing weight. Studies have demonstrated the advantages of a prolonged ketogenic diet. Body weight and body mass index of the patient were dramatically lowered[3]. The theme of this paper is pharmacological therapy for obesity. The research has many

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social significance, such as improving people's health, reducing the waste of material resources and unnecessary social and economic expenditure, etc..

2. Obesity

The body mass index is the most used tool for determining if a person's weight is healthy(BMI). An index used to gauge a person's height is their body mass index. The best way to determine how obese someone is overall is to use their BMI[body mass index = weight(kg)/Height²(m²)]. BMI ranges from 18.5 to 24.9 for most persons, 25 to 29.9 for those who are overweight, 30 to 39.9 for those who are obese, and 40 or more for those who are very obese[4]. As a result, Phentermine, Sibutramine, Orlistat, and treatment were used as keywords in the author's search[5].

3. Phentermine

3.1. Drug mechanism and utility analysis

Phentermine can enhance adrenergic signals in the brain and surrounding tissues. It is an adrenergic re-uptake inhibitor[6]. It increases neurotransmitters through induction γ-. The activity of aminobutyric acid and the regulation of voltage-gated ion channels can suppress appetite and increase satiety. It is mentioned in some articles that phentermine and topiramate can be used together to treat obesity more effectively[7]. High doses of fentramine topiramate can reduce body mass index by an average of 10%, which is the result of a randomized experiment. Twenty percent of American teenagers are obese. Obesity is quite common in the United States, which can be reflected in another reported data. It is reported that by 2030, nearly half of American adults will have a body mass index(BMI) of more than 30. In other words, at least 35 percent of adults in each state are obese. Usually, the reasons for their obesity are as follows: 1) the United States is economically developed. Fast food processing is very popular. 2) Diet is heavy oil and salt. Salad, the source of vitamin intake, should also be covered with high calorie sauce. The effect of the non-surgical intervention on obesity in this population is limited. The combination of fentramine and topiramate is effective for adult obesity, but the FDA has not approved its use in adolescents, and it is uncertain whether it is safe and effective for adolescents. In this study funded by the pharmaceutical manufacturer, 227 obese adolescents(age range: 12-16 years old; average body mass index[BMI], 37.8 kg / m²) who were otherwise healthy were randomly divided into three groups. The three groups given placebo, medium-dose fentramine topiramate(7.5 mg / 46 mg) or high-dose fentramine topiramate(15 mg/92 mg) for one year. In the intention to treat analysis, adolescents who received high-dose or medium-dose fentramine topiramate lost an average of 9.2 kg and 5.5 kg, respectively, while adolescents who received the placebo gained 6.5 kg. In the two fentramine topiramate groups, 43% and 32% of the participants, respectively, lost at least 10% of their weight. Both doses were associated with a small improvement in blood lipid. In addition to significant weight loss, waist circumference shortening, total cholesterol and non-high-density lipoprotein cholesterol levels will also decrease. These results ultimately reduce the risk of cardiovascular disease[8].

3.2. Side effect

This medicine will also bring some adverse reactions to people: it may cause urticaria and may cause pulmonary hypertension; and if this drug is used with other anorexic drugs(such as fenfluramine or dexfenfluramine), and there is a heart valve defect. At the same time, insomnia is also a common negative effect.

4. Sibutramine

4.1. Drug mechanism and utility analysis

Sibutramine, a monoamine reuptake inhibitor, enhances adrenergic, serotonergic, and dopaminergic signaling in the brain. Sibutramine's weight loss machenism mainly includes: first, it can increase the

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sense of physiological satiety, reduce appetite and reduce the amount of diet by inhibiting the reuptake of monoamine neurotransmitters such as 5HT and norepinephrine by cells; second, it can increase the thermogenic reaction, increase energy consumption and reduce the amount of fat accumulation. It is mainly used for the treatment of obese patients who cannot reduce and control their weight through diet control and exercise[9]. If Sibutramine is included in the family's behavioral weight control plan, can this practice effectively reduce adolescents' obesity? Some experiments have been conducted based on this idea. One experiment lasted for 6 months, involving many experiments, such as randomized experiment, double blind experiment and placebo control experiment. The subjects of the experiment are mainly teenagers. Teenagers are between 13 and 17 years old. Their BMI is 32-44. These teenagers will receive open label treatment. The treatment period is 7-12 months. The total number is 82. After the experiment, the data will be analyzed and sorted according to the experimental results. The main indexes of the experiment were systolic blood pressure, hunger feeling and diastolic blood pressure. Another major control was their BMI changes. After the experiment, after comparative analysis, it was found that the average weight loss of participants in behaviour therapy group and Sibutramine group was 7.8 kg and 6.3 kg. This result was significantly higher than the 3.2 kg(6.1 kg) weight loss in the BT and placebo groups. 8.5% and 6.8% were their body mass index, which was also higher than 4.0%(5.4%) in behavior therapy group and placebo group. Additionally, recipients of both BT and Sibutramine reported significantly less hunger($P = 0.002$). The adolescents initially receiving Sibutramine treatment gained 0.8 kg(10.5 kg), which is the data from the 7th month to the 12th month. The drug continued to be used at the same time, and the results showed that the adolescents who changed from placebo to Sibutramide lost 1.3 kg(5.4 kg) of weight. They were asked to reduce the dose or stop the drug in order to prevent the increase in blood pressure, pulse rate or other symptoms. The final experimental result was that Sibutramine significantly reduced body weight compared with behavioral therapy and placebo[10]. Although the cost of Sibutramine is low, it can also achieve the effect of treating obesity.

4.2. Side effects

However, this drug has many side effects, involving the nervous system, circulatory system, digestive system, endocrine and other systems. That its safety is unknown, so it has been banned by most countries. 1) Nervous system: if you take it for a long time, you may have insomnia, headache, ease to wake up, limb spasm and other uncomfortable symptoms. 2) Circulatory system: symptoms such as increased heart rate and blood pressure. 3) Digestive system: taste decreased, constipation, diarrhea and decreased appetite.

5. Orlistat

5.1. Drug mechanism and utility analysis

The pancreas' lipases are temporarily inhibited by Orlistat(brand name Xenical®). Orlistat is a useful medication for managing obesity in adults with or without comorbidities. It needs to be used in combination with a low calorie diet and moderate exercise to achieve the effect described above[11]. The mechanism of this medicine is mainly the absorption of excess fatty substances to achieve the goal of weight loss. According to some data, changing patients' lifestyles is far from enough, and it may be necessary to continue this treatment for a long time to avoid weight recovery. In the United States, Sibutramine and Orlistat are two drugs approved for long-term treatment of obesity. Clinical studies have demonstrated that both medications are capable of causing and maintaining weight loss in people who also have comorbid conditions such type 2 diabetes or hypertension. To fully benefit from this medication, patients must utilize them in conjunction with behavioral modification and structured food planning[12].

5.2. Side effects

In addition to normal weight loss, Orlistat also has a series of side effects. Gastrointestinal adverse

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reactions are common side effects such as increased gastrointestinal exhaust, diarrhea, watery stool, increased stool, fatty stool, abdominal pain, nausea and vomiting. Occasionally, adverse reactions such as upper respiratory tract infection, influenza and urinary tract infection will occur. However, another adverse phenomenon that rarely occurs is that it will cause severe liver injury to the patient. A 15-year-old Thai woman, who had no history of obesity, took Orlistat for 7 consecutive days. The dose is 3 times a day, 120 mg in total. A week later she was taken to the emergency room. The reason was that she had abdominal pain and diarrhea. She did not take any other poison, nor did she take any other medicine or herbal medicine. The body temperature is 37.5 ℃, and the body mass index is 20.0%, which means that she gets the physical condition when she is awake. 1.3 mg/dl total bilirubin level, 65 mg/d1 is her total cholesterol, the international standardized ratio of prothrombin is 2.98, and the level of immunoglobulin E is 486 IU/ml. After screening for viral hepatitis and autoimmune markers(antinuclear antibody and antimitochondrial antibody), the results showed that both were negative. Five days after intravenous injection of vitamin K, she slowly improved, and then the liver function test showed that the time to return to normal was within one month[13].

6. Discussion

Through searching the literature and summarizing, it can be concluded that the cost of Sibutramine is the lowest among the three drugs. For the mechanism of action, Phentermine and Sibutramine are both an appetite inhibitor, and Orlistat is the only pancreatic lipase inhibitor. In general, sibutramine and Orlistat are used more, but Sibutramine has been banned in most countries. The side effects of these three drugs are mainly concern rate and blood pressure. For example, Sibutramine has side effects on many systems.

7. Conclusion

In general, the common role of these three drugs is to help patients treat obesity, but each drug will cause different degrees of side effects, such as psychological aspects and digestive systems aspects. There are some shortcomings in the research of this paper. It is necessary to carry out a series of experimental operations in the laboratory to test three different drugs with different kinds of crowd populations, so as to improve this thesis.

Acknowledgment

First of all, I will express my deepest gratitude to the teachers who guide my thesis and to the teachers and professors who are responsible for scientific research projects. In addition, I want to thank my classmates, friends, teachers and parents for their encouragement and companionship. Without their guidance and help, as well as their enlightenment, I would not be able to complete my thesis.

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