ISSN 2959-409X

Comparative Analysis of Therapeutic Methods for Type 2 Diabetes Mellitus

Zhihao Lei

Wuhan University of Technology, Wuhan, Hubei, 430070, China
Corresponding author: lei13308038705@whut.edu.cn

Abstract:

Type 2 Diabetes Mellitus(T2DM) is known as the most common metabolic disordered disease in the world now. Nowadays, research about T2DM is focused on treating the T2DM indirectly, such as, increasing the secretion of insulin or promoting the use and monitoring of insulin. However, there are still a lot of problems for monitory the dose of insulin or medicine, so most of medicine can cause low blood glucose levels or other common side effects caused by using too much or less medicine. This review has reviewed three different parts of medicine, and then compared the mechanism and the side effects of this therapeutic method. After that, come up with some conclusions about how the advantages and disadvantages of different methods. The meaning of this preview is to find out the effective method for T2DM nowadays and search the potential directly for caring for T2DM. In the last, after comparing the side effects of different therapeutic methods of T2DM, monitoring and control become two essential direct for improving the treatment of T2DM. So artificial intelligence could be a potential way for caring for T2DM.

Keywords: T2DM; Therapeutic methods; insulin secretion.

1. Introduction

Type 2 Diabetes Mellitus (T2DM) is known as the most common metabolic disordered disease in the world now. T2DM is a heterogeneous condition disease. T2DM is generally caused by 2 main factors, on one hand, pancreatic beta-cell is disabled, leading to defective insulin secretion. On the other hand, insulin-sensitive tissues are disabled or insensitive, body can't tell the quantity of insulin, Without the sense of the quantity of insulin, pancreatic beta-cell can't secret insulin directly. These factors are usually triggered by genes or environment, such as the hyperglycemia can cause the metabolic to be disordered, this disorder appears to the pancreatic beta-cell don't secret enough insulin or peripheral tissues show resistance to insulin. In order to solve this question, many different therapeutic methods are applied now.

The therapy methods were generally classed in two different directions: Insulin based therapies, which are usually preprandial injections of insulin directly and modify the postprandial level of blood glucose, and Non-based insulin oral therapies, in which the hormones or proteins are used as therapies for T2DM indirectly (Repurposing anti-inflammasome NRTIs for improving insulin sensitivity and reducing type 2 diabetes development [1]). There has been more and more research and development of innovative therapeutic methods recently. It seems Non-insulin based and some new directions of therapeutic methods of T2DM will become the development focus of T2DM in new era. In order to improve the comprehension of the recent treatment of Type 2 Diabetes Mellitus (T2DM) and give the following researchers useful suggestions.

This review will compare different therapeutic methods in the mechanism of each substance and the potential value in the therapeutic methods, The advantages of using each therapeutic method of T2DM, And the side effects of each therapeutic method. In the last, this review comes up with a result of each therapy's advantages and disadvantages conclusions about differences from each therapy, and some suggestions for patients who have different requirements. The end of this article talks about some unavoidable problems (such as some comments from different patients that may not be objective enough), some useful suggestions about how to choose suitable T2DM therapy for new researchers or someone who is interested in T2DM therapies.

2. Organization of the Text

2.1 Non-insulin Based Therapeutic Method

2.1.1 Insulin secretagogues

Insulin secretagogues, generally sulfonylureas and meti-

glinides. First generation sulfonylurea are Tolbutamide, Chlorpropamide, Tolazamide, Acetohexamide and Second generation sulfonylurea includes Glibenclamide, Glipizide, Glimepiride [2].In recent years, sulfonylureas (SUs) have been important drugs in the antidiabetic therapeutic method. Both combination therapy and monotherapy have been applied to them. The debate over the effectiveness and safety of SUs has been sparked by worries about newer medications and the possibility of severe hypoglycemia and weight gain with some of them. However, here is one thing important that several contemporary SUs, including glimepiride and gliclazide modified release, are linked to improved safety profiles, it is not appropriate to attribute the negative occurrences connected with SUs to the class as a whole. Additionally, individualized therapy plans that combine SUs with other medications, closely monitor patients, and provide patient education guarantee the greatest possible benefits with the fewest possible adverse effects. The current guidelines encourage the prudent and safe use of SUs in conjunction with other glucose-lowering medications. They were created by specialists from Africa, Asia, and the Middle East [3].

These category of drugs' mechanisms are combined with sulfonylurea receptor (SUR) of ATP sensitive potassium channel on pancreatic beta-cells [4] then they can increase the secretion of insulin from pancreatic beta-cell. The 2nd generation sulfonylurea compared with 1st generation, 2nd generation sulfonylurea are more rapid and can have longer time to act.

However, this medicine may cause side effects such as low blood glucose levels, and it will appear as dizziness, sweating, or even nervous and it may cause hunger or stomach upset (They maybe caused by patient taking excessive sulfonylurea or not having regular diet). But it can also cause weight gain, skin reaction, and dark-colored urine. This symptom maybe depend on different patient.

2.1.2 Insulin sensitizers

"Insulin Sensitizers" is a direct name that is more comprehensive. Insulin sensitizers are one part of nuclear hormone receptor superfamily ---- Peroxisome proliferator-activated receptors (PPARs), it has three subtypes: PPARα, PPARγ, and PPARβ/δ. When PPARα is active, it can reduce the level of triglyceride and keep the balance of energetic system. When PPARγ is active, it can enhance the metabolism of glucose and the pancreatic beta-cells sensitivity of insulin. When PPARβ/δ is active, it can enhance the fatty acid metabolism. Meanwhile, here is a category of well-established antidaibetic drugs which are called Thiazolidinediones, also named as glitazones. Thiazolidinedione structure is the most interesting and essential part in researches, as for creating and developing novel medications to treat type 2 diabetes. Numerous studies on the mechanism of action and structural prerequisites have demonstrated that the agonistic effect on the nuclear receptor superfamily member peroxisome proliferator-activated receptor (PPAR) is responsible for the expected antidiabetic efficacy in type 2 diabetes [5]. Glitazones show a particular affinity for PPAR γ, one of the PPAR subtypes. A few substances in development exhibit dual agonistic activity of PPARα/γ, suggesting potential benefits in the treatment of obesity and diabetic cardiomyopathy. As the preceding part has mentioned, these three subtypes are now only used or combined with each other and used as the Non-insulin therapeutic method of T2DM, such as Glitazones, one of PPARγ, increase the sensitivity of cells to insulin. They also decrease systemic fatty acid production and their uptake. Enhance the cells' sensitivity to insulin. They also decrease the synthesis and absorption of systemic fatty acids. It has been demonstrated that PPARγ/γdual agonist responds to blood glucose regulation, and PPARγ ractivation enhances glucose absorption by skeletal muscles and reduces glucose synthesis by delaying gluconeogenesis. However, there are many insulin sensitizers that may cause weight gain, plasma volume expansion, bone loss, harm to heart, and even cause cancer after long-time use by patients. So, research and development of PPARs is still a problem.

2.2 Research Progress of Therapeutic Method for T2DM

2.2.1 Bariatric Surgery

Bariatric surgery is an indirect method to treat T2DM patients Because there are more than 75% T2DM patients are considered to be overweight [6], so there are some researchers come up with using bariatric surgery. This surgery's primary goal is to alter the upper gastrointestinal tract (GIT), which can enhance blood glucose metabolism. It's unclear exactly how bariatric surgery results in treatment for type 2 diabetes, though. There are some research that has proved bariatric surgery to be effective and sustainable in the long-term weight loss and remission of metabolic disorders. The gastrointestinal tract is altered during bariatric surgery, either physically or functionally, changing the metabolism of bile acids. Bile acids, rather than digestive juice, are signaling molecules that have been linked to metabolic control, according to a growing body of research. The majority of the benefits to metabolism are mediated via the membrane receptor TGR5, nuclear receptor FXR, and reciprocal impact on gut flora. Animals are also subjected to bile diversion procedures in an effort to summarize the advantages of bariatric surgery. It seems that modifications to bile acid play a significant role in bariatric surgery and offer a viable avenue for

treating metabolic diseases [7]. However, the surgery has shown obviously individual differences, different patients with T2DM have different physical conditions. Bariatric surgery seems just to be a special therapeutic method for very little amount of T2DM patients. It is not suitable for every T2DM patient.

2.2.2 Anti-Obesity Drugs

There are studies demonstrated the favorable and significant effect of Anti-Obesity Drugs on weight loss, blood pressure reduction, glycemic control (A1C reduction), and CVD mortality. [8]In the other words, Anti-Obesity Drugs are beneficial for treatments of T2DM in some extent. For example, there is a drug called orlistat, which has been proved for chronic weight management by the Food and Drug Administration (FDA), furthermore, in addition to increasing the secretion of two gut hormones, GLP-1 and GIP, it can decrease visceral fat and stop the digestion of free fatty acids, which raises hepatic and peripheral insulin resistance. GLP-1 is an incretin peptide that stimulates insulin secretion and inhibits glucagon secretion. Evidence, primarily from animal models, suggests that GLP-1 plays a role in increasing beta-cell proliferation and differentiation while decreasing beta cell apoptosis. Thus improving insulin release. However, the orlistat has caused gastrointestinal side events, including: Episodes of hypoglycemia and other common side effect such as nausea, headache, and constipation, which is related to the consumption of dietary fat and orlistat's inhibition of gastrointestinal lipase activity [9]. Thus lead to poor patient compliance.The FDA authorized the combination of naltrexone, an opioid receptor antagonist, and bupropion, a dopamine and norepinephrine reuptake inhibitor. Anorectic alpha-melanocyte stimulating hormone is released and anorexigenic POMC neurons are stimulated more when these two factors are combined [10]. The use of it has been demonstrated to be safe in terms of the risk of MACE, but it has comparable dose-dependent side effects to orlistat, such as nausea, headaches, and constipation [11].

2.3 Equipments for Replacing the Pancreas or Monitoring Glycemia Level

2.3.1 Early detection of T2DM using machine learning-based prediction models

These days, data mining is used in many scientific domains, including medicine and healthcare. Pattern recognition, illness prediction, and classification utilizing different data mining approaches are often used [12]. Many methods, including logistic and Cox proportional hazard regression models, Random Forest, and boosted ensembles, have been utilized to develop prediction models and models for early illness detection in response to the rising prevalence of T2DM. To reduce their risk factors with medication and/or lifestyle changes, those at high risk of acquiring type 2 diabetes can be identified using screening techniques. Most screening tools are used to do predictive modeling, which will be mentioned in later part. Conventional screening methods that aim to detect people with undiagnosed type 2 diabetes rely on common regression analysis methods. It's critical to look at if applying machine learning-based techniques can produce better outcomes than the techniques that are already in use. The analysis of electronic health record (EHR) data can now be used to test a number of significant advancements in machine learning techniques, such as AdaBoost, random forest, support vector regression, decision trees, and neural networks based on stacked denoising autoencoders (SDA), for predictive modeling [13].

2.3.2 Artificial pancreas

In recent years, there are many new product that looks like insulin pumps with many functions (such as detectors and sensors) have been developed. The FDA authorized the MiniMed 670G hybrid closed-circuit system in 2016, which is sometimes referred to as a "artificial pancreas" and was intended for patients with Type 1 diabetes. However, a completely closed-circuit artificial pancreas system has not yet been fully created [14]. Although there are many differences between T1DM and T2DM, when T2DM patients whose pancreas function is lost. They also have the necessity to change an "artificial pancreas". Numerous studies have examined the effectiveness of MiniMed 670G in controlling blood sugar levels. According to the data, most people in Europe who used the MiniMed 670G system were able to minimize hypoglycemia while achieving the internationally recommended goals of glycaemic control, which include a TIR (percentage of time spent within) of more than 70% and a GMI (glucose management indicator) of less than 7%. This was made possible by automating the distribution of basal insulin, which takes into account each user's unique insulin requirements in real time [15].

However, the surgery for changing pancreas or adding human-made equipment is still in the stage of exploration, most equipment now are insulin pumps with some monitoring method.

3. Conclusion

Nowadays are tons of research of T2DM therapeutic method. This review has talked about three different therapeutic method to T2DM. The first one is the non-insulin therapeutic method, the second one is the Research progress of therapeutic method, and the third one is the equip-

ment for replacing the pancreas or monitoring glycemia level. In non-insulin therapeutic part, here are two mean parts are mentioned: insulin secretagogues and Insulin Sensitizers, and then talk about the side effects. In the research progress of therapeutic method part, bariatric surgery and Anti-Obesity Drugs are two interesting methods, they use the weight loss medicine or therapeutic method to reduce the blood glucose level and then help the T2DM patient indirectly. In equipment for replacing the pancreas part, here are two different equipment are mentioned, which can do the part of monitoring and secret insulin (by insulin pump) for T2DM patients. In conclusion, there are many mature therapeutic methods that can help the T2DM patient effectively, however, side effects are still a problem, most therapies contain side effects that can cause weight gain or low blood glucose level, which means most therapeutic method should be more humanized and easily controlled. However, the conclusions proposed in this review need to be verified by further experiments. Due to the limitations of the original data, the data mentioned in this article will need further updates and inflammation. As a suggestion for future research, some hormones that increase insulin secretion may still be of value to researchers.

References

[1]Ambati J, et al. Repurposing anti-inflammasome nrtis for improving insulin sensitivity and reducing type 2 diabetes development. Nature Communications, 2020, 11(1).

[2]Sola D, Rossi L, Schianca G, et al. State of the art paper Sulfonylureas and their use in clinical practice. Arch Med Sci, 2015, 4: 840–848.

[3]Kalra S, et al. Consensus Recommendations on Sulfonylurea and Sulfonylurea Combinations in the Management of Type 2 Diabetes Mellitus – International Task Force. Indian Journal of Endocrinology and Metabolism, 2018, 22(1): 132.

[4]Seino S, Sugawara K, Yokoi N, Takahashi H. β-Cell signalling and insulin secretagogues: A path for improved diabetes therapy. Diabetes Obes Metab, 2017, 19: 22–29.

[5]Nedelcu M, Loureiro M, Skalli M, et al. Laparoscopic sleeve gastrectomy: Effect on long-term remission for morbidly obese patients with type 2 diabetes at 5-year follow up. Surgery, 2017, 162(4): 857–862.

[6]Holst JJ, et al. Mechanisms in Bariatric Surgery: Gut Hormones, Diabetes Resolution, and Weight Loss. Surgery for Obesity and Related Diseases, 2018, 14(5): 708–714.

[7]Kane J, et al. Cardiovascular Risk Reduction Associated with Pharmacological Weight Loss: A Meta-Analysis. International Journal of Clinical Research & Trials, 2019, 4(1).

[8]Kelley DE, Bray GA, et al. Clinical Efficacy of Orlistat Therapy in Overweight and Obese Patients With Insulin-Treated Type 2 Diabetes: A 1-year randomized controlled trial. Diabetes Care, 2002, 25(6): 1033–1041.

[9]Saunders KH, et al. An Update on Naltrexone/Bupropion Extended-Release in the Treatment of Obesity. Expert Opinion on Pharmacotherapy, 2016, 17(16): 2235–2242.

[10][Sposito AC, et al. Cardiovascular Safety of Naltrexone and Bupropion Therapy: Systematic Review and Meta-analyses. Obesity Reviews, 2021, 22(6).

[11][Rahimloo P, Jafarian A. Prediction of Diabetes by Using Artificial Neural Network, Logistic Regression Statistical Model and Combination of Them. Bulletin de la Société Royale des Sciences de Liège, 2016.

[12]Basu S, Narayanaswamy R. A Prediction Model for Uncontrolled Type 2 Diabetes Mellitus Incorporating Area-level Social Determinants of Health. Medical Care, 2019.

[13]Miotto R, Li L, Kidd BA, Dudley JT. Deep patient: An unsupervised representation to predict the future of patients from the electronic health records. Sci Rep.

[14]Dahl RA. Communicative Constitution of Technology: A Sociomaterial Analysis of Data, Communication, and Control in the Design of an Open-Source Artificial Pancreas System [dissertation]. The University of Utah, 2021.

[15]Da Silva J, et al. Real-World performance of the minimedTM 670g system in Europe. Diabetes, Obesity and Metabolism, 2021, 23(8): 1942–1949.