

The Pathogenesis and Treatments of Diabetes, Questions and Answers

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Abstract

Diabetes Mellitus is an old disease but modern epidemics. Despite many improvements and benefits of diabetes mellitus treatments recently, many new and unresolved problems relevant to diabetes mellitus pathogenesis and therapy have been found; Pathogenesis and treatments study of diabetes currently is complicated and imperfect. Disease complications, such as cardiovascular symptoms, vision impairments, nephropathy, chronic leg infections etc are even more fatal than hyperglycemia control; Moreover, drug toxicities owing to long-term utilization of many chemical agents and drugs are equally harmful for patients. Furthermore, different doctors and drug manufactures hold different views on diabetes mellitus treatment options and financial interesting distributions. In this editorial, new ideas for building update diabetes mellitus therapeutic systems, new drug development pipelines and experimental and clinical models, possible future directions are proposed, addressed and highlighted.

Keywords:

Diabetes mellitus; Diabetes therapy; Insulin; Insulin-derivatives; Diabetes complications; Diabetes complications; Small molecular chemical; Bee extract; Qi-Gong, Cardiovascular complication; Hyperglycemia; Drug toxicity; Propolis; Genetics; Genomics; Pharmacogenomis; Nephropathy; Traditional chinese medicine

Introduction

Scenarios of global diabetes epidemics and different therapy options

Diabetes Mellitus is an old disease but modern epidemics. The epidemics of diabetes in China, developing and developed countries have been growing rapidly now. For this reason, medical expenses on diabetes diagnosis and treatments have been increased greatly worldwide now [1,2]. Despite many improvements and benefits of diabetes mellitus treatments, many new problems relevant diabetes mellitus pathogenesis and therapy have been emerged. Moreover, pathogenesis and treatments of diabetes is too complicated to be completely solved by present state-of-the-art techniques and licensed drugs. Disease complications, such as cardiovascular symptoms, vision impairments, nephropathy, mental retardation and chronic leg infections etc are even more fatal than hyperglycemia control; Drug toxicities owing to long-term utilization of many chemical drugs are equally harmful for patients. Many people of experienced medical personnel and many new comers all enthuse and chase their shares of academic credits and drug markets and incomes. Owing to the diversity of talents and educational backgrounds of researchers, scientific merits and usefulness of experimental or clinical study have been differed greatly. For many new comers, they commonly treat for superficial indicates (glucose uptake and blood concentrations) rather than targeting the origin of disease pathogenesis, such as insulin-

related or other genetic-related symptoms. Facing this dilemma, new initiatives and challenges must be pursued, promoted and highlighted with new twists. This editorial will address some of them.

New Insights

Building good educational systems worldwide

Developing to type 2 diabetes mellitus might undergo a long course of pathogenesis processes in susceptible human (many of them are family inheritance). Many preventive measures or control food intake can slow the disease progression and reduce morbidity rates. Some good and long-term educations, propaganda and wide-spread the basic knowledge and themes of diabetes pathogenesis and therapeutics will target and influence largest population of humans, especially to potential diabetes susceptible old persons. Good customs, such as reducing nutritional composition intakes, increasing body exercises etc will educate more people and might slow down disease progressions of potential diabetes susceptible patients. The prompt interventions of early stage diabetes patients are also a way of preventing the occurrence of fatal complications of diabetes. Overall, education to most people is an effective ways of reducing diabetes epidemics and helps the control of hyperglycemia.

Deep understanding about pathologic and pharmacologic points of views for diabetes treatments

Deep understanding about pathologic and pharmacologic points of views for diabetes treatments is necessary. For many new comers, they are focusing on control glucoses interfering or sabotaging normal food intake and digestions systems and offering other mono carbohydrate or sugar derivatives for substitute. For in depth points of views, most of these efforts are relatively superficial because the top culprits of disease progression are often not glucoses itself. The real pathogenesis causations of diabetes mellitus are mostly insulin-binding or -related functionality, such as loss functions of pancreas island β -cells [3], liver metabolism [4], insulin resistance [3,4] and other inheritable components (malfunctions of insulin-related molecules by gene mutations and inherent of family) (Table 1). According to this view, many in vitro glucose-related studies are especially questionable. Owing to these weaknesses and drawbacks in diabetes therapeutic study, the wide debate of new experimental or clinical results is indispensable.

Targets	Mechanisms	Personal opinions
Glucose	Exogenous polycarbohydrate lyses enzymes inhibitors	Skeptic Controversy Controversy

	Decrease glucose concentrations in animal and human by many metabolism interference Substitute food glucose intake with other mono carbohydrates or substitute glucose intake by glucose-derivatives	
Insulin	Human insulin and its derivatives Modulators of pancreatic island β -cell	First line therapy Potential
Disease complications	Cardiovascular complications Nephropathy Vision impairment Mental retardations Chronic leg infection	Potential and need to be improved
Hepatic functions	Ameliorate of damaged cells and metabolism	Future trend

Table 1: Current targets and mechanisms of different drugs for diabetes mellitus treatments

Design and apply personalized diabetes therapy (PDT)

Since the clinical symptoms and stages of diabetes mellitus patients vary greatly, treatments for different diabetes mellitus patients should not be uniformed. Personalized Diabetes Therapy (PDT) is a modern way and commonly offer better therapy for diabetes mellitus patients. Nonetheless, PDT is not restricted for pharmacogenetics (PG) studies alone [5-8]. At this stage of understanding and technical facility systems, PG study aims at prediction of drug dosage and concentrations in patients' plasma by detecting polymorphism of human metabolizing enzymes by PG or pharmacokinetics considerations. Since diabetes mellitus can be divided into type 1 and type 2, different disease-related molecules and complications in patients with type 2 diabetes mellitus ought to be treated individually. Bioinformatics and molecular detections of pathological profiles of diabetes is also the foundation of PDT because disease-related molecular information of disease progressions at present is more straightforward interpretations rather than genetic information sequencing alone (Figure 1).

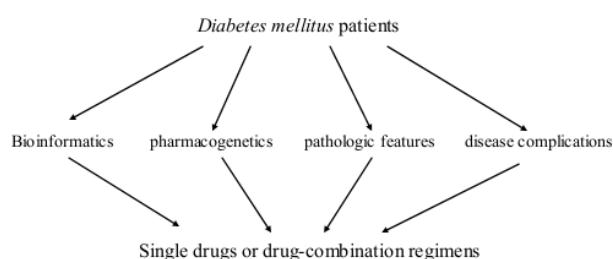


Figure 1: Proposed diagram of personalized diabetes mellitus therapy

Development of more effective and less toxic drugs

Development of more effective and less toxic drugs is always the ultimate goals of drug developments and manufactures. Likelihood, it is one of the major avenues of diabetes mellitus treatment study and clinical applications [9-16]. Many chemical synthetic diabetes mellitus treatment drugs, especially those chemicals for decreasing glucose concentrations in living bodies are toxic to patients when they are long-term applications in clinics. Despite insulin and insulin-derivatives are the safest and first-line anti-hyperglycemia therapeutic options and can be used in both type I and type II diabetes mellitus patients [11], it also has some obvious deficiency. The most conspicuous one is that needle injection is needed every day, which leads to treatment inconvenience and physical burden for diabetes mellitus patients.

Currently, oral intake of drugs is the most welcoming and environmental-friendly drug administration options for all patients. Thus, some small-molecular chemicals having the insulin-configurations or insulin receptors binding activity might be potential oral anti-hyperglycemia drugs for surrogating insulin or insulin-derivatives. In future, we can compare, simulate and calculate insulin-configurations or insulin receptors binding activity from large-pool of small-molecular chemicals pipelines by computing or experimental work. If this type of researches can help our finding new chemicals, we might produce, develop, approval and license insulin-like small-molecular drugs for patients' oral intake.

Seeking solutions outside of normal therapeutic arsenals

To test and study some new initiatives such as propolis is also good options [17]. Propolis is bee extracts of waxy-like and other components. It has been discovered for anti-bacterial, anti-fungal or anti-tumors [17]. In China, it has been licensed as healthy-promoting agents. Now it has been largely sold for treatment of diabetes mellitus and received widely acclaiming for its efficacy in China. Many renowned-brands of long history Chinese Pharmaceutical Companies are almost all manufactured and sold propolis widely. Nonetheless, large-scale, double-blind systematic clinical investigations are needed in future. Some similar alterations should also be initiated, cooperatively studied, testified and verified by more experimental, preclinical or clinical investigations worldwide.

Helping and encouraging diabetes mellitus patients to do more exercise along with proper treatments is a proved good way. In previous work and study, large body of publications and research projects show that proper exercise is very useful for control of hyperglycemia [18]. Furthermore, more diabetes mellitus patients should be encouraged to do more exercise. Exercise in diabetes mellitus patients is as equal importance as chemical or biological drugs for hyperglycemia control.

Pay more attentions on disease complications control

Diabetes complications are sometimes very serious. Large parts of disease complications are difficult to be successfully controlled or eradicated. Diabetes mellitus complications treatment study and applications should be drawn more attentions in futures

Discussion and Future Directions

Since a lot of people are agonized and suffered with hyperglycemia and related complications worldwide, current diabetes mellitus therapy

needs to be improved. Many persistent efforts and novel ideas are all welcomed. Table 2 illustrates roadmap and many avenues for diabetes mellitus treatment study and clinical usefulness in future (Table 2).

Development and production of more effective and low toxicity anti-hyperglycemia chemical drugs
Educate more normal people to understand the basic knowledge of diabetes. So diabetes mellitus can be properly noticed and treated once the disease just begins. To deepen fundamental and comprehensive mechanism study to make licensed anti-hyperglycemia drugs more reliable and versatility
Genetic or molecular study of pathogenesis of disease progression, drug pharmacological mechanisms of action and drug toxicities in living bodies along with different individuals, ethnic groups and largest populations. Lesson from history—traditional Chinese medicine, Indian medicine or Middle-east medicine etc Perfecting the personalized diabetes therapy (PDT) study and applications
To test and study some new initiatives and natural products such as propolis
To set a more rigorous toxicity baseline for anti-hyperglycemia drugs development, approval and license in developing countries, or even in developed countries.

To find some small-molecular chemicals for simulating insulin functions and receptors-binding activities

Table 2: Possible roadmap and landscape for future anti-hyperglycemia study [9].

Conclusions

Many therapeutic options for late-stage diabetes patients are less effective and mostly unsatisfactory. For example, treatments for chronic leg infections are commonly lacking now. In future, clinical study and new challenges relating to improve therapeutic outcomes for late-staged diabetes mellitus patients is urgently needed. In addition, PDT might be increasingly used and perfected by persistent experimental and clinical investigations and systematic studies.

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Author Contributions

This article is mainly plotted and written by Dr Da-Yong Lu and Jin-Yu Che, Prof Ting-Ren Lu and Hong-Ying Wu discussed many details of the article. The contribution of the first and second authors is equal.