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Does Pharmacogenetics Play a Role in the Treatment of Type II Diabetes Mellitus?

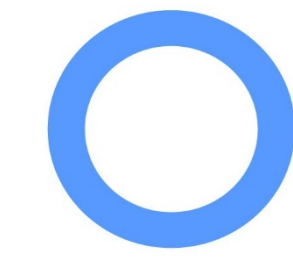
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Abstract

- Type 2 diabetes mellitus (T2DM) is a disease commonly presented in the family practice setting. Current therapies include one or multiple medications. Until recently, providers have used algorithms and medical expertise to control T2DM.
- Pharmacogenomics is a branch of pharmacology dealing with genetic variation on a medication response in an individual patient to discover medication compatibility, efficacy or toxicity.
- Analysis of genetic factors are still being discovered; however, this growing field may change the way medications are being prescribed for diabetes. This analysis investigated if pharmacogenetics is a useful tool for prescribing diabetic medications to T2DM patients. It was found that health care providers will be able to maximize therapy to those currently taking diabetic medication.
- The goal would be to personalize the treatment of T2DM by ensuring compatibility of the medication being prescribed. Although many genes have been implicated in the response to diabetic medications, the findings indicate that health care providers can improve the quality of care of patients taking diabetic medications by choosing the correct diabetic medication for the individual patient.

Introduction

Type 2 diabetes mellitus is a worldwide epidemic



- A multifactorial, heterogeneous metabolic disorder characterized by hyperglycemia and elevated insulin resistance.
- Results from both genetic and environmental factors.
- Multiple genes that are associated with the risk of developing diabetes
- Patients are often treated with more than one medication.
- Genetic testing could be employed to predict treatment outcome

Pharmacogenetic

- Studies focused on diabetic medications and a role of common drug-metabolizing enzymes and drug-transporters variants in therapy outcomes.



- The future of promoting safe and cost-effective individualized diabetes treatment, pharmacogenomics has a great potential to complement current efforts to optimize treatment of diabetes and lead towards its effectiveness and personalized care.

Statement of the Problem

- Since diabetes is not currently a curable disease, clinical guidance suggests the ability to tailor medications to the patients' needs may be the best compound the future of diabetes.
- Developing new medications is a lengthy process. The development of new medications which can take 10-20 years to develop and receive approval. Utilizing medications already in use to detect compatibility to each individual patient is still being developed.
- *Multiple genes associated with the risk of developing diabetes have been identified by gene analysis and genome scanning.*
- Markers together with clinical data, pharmacogenetics and other methods lead to the consideration of diabetes care being treated by genetic make-up of a patient.

Research Questions

Does Pharmacogenetics Play a Role in the Treatment of Type 2 Diabetes Mellitus?

- T2DM patients are often treated with more than one drug, including oral diabetic drugs.
- If genetic testing could be employed to predict treatment outcome, appropriate measures could be taken to treat T2DM more efficiently.

Literature Review

Biguanide

- In 2011, Zhou et al. found that common variants near the ataxia telangiectasia mutated (ATM) are associated with glycemic response to metformin in type 2 diabetes. Metformin is recommended as a first line therapy for type 2 diabetes in most international guidelines.
- Becker et al. 2009, examined the genetic variation in the organic cation transporter that is associated with metformin response in patients with diabetes mellitus.

Thiazolidinediones

- Aquilante et al. 2013, examined the influence of CYP2C8*2 on the pharmacokinetics of pioglitazone in healthy African American volunteers. The data in the study suggested a potential functional significance and merits further study.

Meglitinides

- Huang et al. 2010, examined IGF2BP2 variations influence repaglinide response and risk of type 2 diabetes in the Chinese population. Patients with the rs4402960 GT+TT genotypes exhibited an enhanced effect of repaglinide treatment on postprandial serum insulin compared with GG genotype subjects.

Sulfonylureas

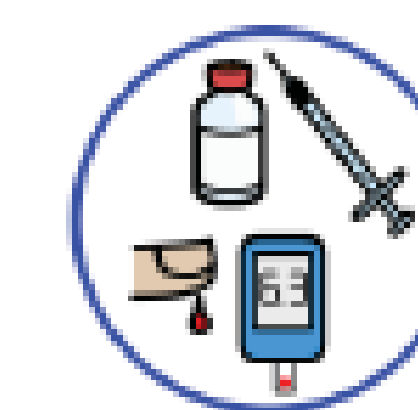
- Sulfonylureas are metabolized in the liver by CYP2C9.
- The major allele of this gene is CYP2C9*1.
- There are also two variants with reduced function, CYP2C9 *2 and CYP2C9*3, which are associated with decreased clearance in the liver with better effect of this medication

Discussion

- Multiple genes that are associated with the risk of developing diabetes or the risk of diabetes complications have been identified by candidate gene analysis and genome wide scanning.



- Pharmacogenetics can lead to the personalized treatment of type II diabetes.
- Known genes that cause diabetes have been reviewed and genotyping of an individual with diabetes could direct providers to accurate choices for diabetic therapy
- The genome-wide association studies (GWAS) have facilitated a substantial and rapid rise in the number of confirmed genetic susceptibility variants for type 2 diabetes.
- The result of Type 2 diabetes is many long-term adverse consequences. Chronic hyperglycemia results in microvascular complications such as retinopathy, nephropathy and neuropathy, and macrovascular complications such as cardiovascular disease, stroke and peripheral vascular disease.
- The goal of Type 2 diabetes treatment in men and non-pregnant women is to decrease periods of poor glycemic control and maintain hemoglobin (HbA1c) levels of less than 7%. Lowering glucose to near non-diabetic levels in Type 2 diabetes patients has been shown to reduce the risk of microvascular complications.



- There are several genes associated with diabetes and hyperglycemic medications with more studies being published every day.
- More evidence and studies will need to be conducted to see if pharmacogenomics will play a role in the future treatment of type 2 diabetes mellitus.

Applicability to Clinical Practice

- *Diabetes has increased disabilities and an enormous cost to the health care system while reducing the quality of life and life expectancy.*
- Strategies for personalized approaches to glycemic management discussed represents a personalized management approach to lowering blood glucose concentrations. The recent studies and advances in genetic and other molecular technologies creates a strong interest in more personalized approaches to diabetes management which will be the most effective for the patient.

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thanks . . .

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