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Bioequivalence & Bioavailability International Journal
ISSN: 2578-4803

Advancements in Antidiabetic Therapy: An extensive study on the use of Polypills to treat type 2 diabetes

Parimita Kalita[1,2]*, Rajesh Jesudasan[2] and Chinmay Maut[1]

[1]Ayush Pharmacy Institute, India

[2]School of Pharmacy, Assam Kaziranga University, India

***Corresponding author:** Parimita Kalita, Ayush Pharmacy Institute, Jorhat, Assam, 785010, India, Email: parikalita1991@gmail.com

Short Communication

Volume 8 Issue 1

Received Date: April 04, 2024

Published Date: June 10, 2024

DOI: 10.23880/beba-16000234

Abstract

The hallmark of type 2 diabetes (T2DM) is elevated blood glucose levels brought on by insulin resistance or inadequate insulin synthesis. Oral hypoglycaemic medications and insulin therapy are two examples of pharmacological therapies used in conjunction with lifestyle changes like diet and exercise to manage type 2 diabetes. However, because T2DM is a complex disease and requires many drugs to regulate different risk factors, managing the condition can be difficult. Polypills, or cardiovascular fixed-dose combination pills, have the potential to alleviate the pervasive inaccessibility and noncompliance with established medications. Switching from existing individually taken drugs is usually required to begin polypill-based therapy. The impact of polypill treatment across various patterns of previous pharmaceutical regimen is of relevance due to the heterogeneity in usual care. Utilizing a polypill helps streamline drug schedules, lessening patients' burden with pills, and possibly increasing adherence. In type 2 diabetes, when controlling blood pressure, cholesterol, and blood glucose levels frequently necessitates the use of many drugs, this is especially crucial. Recommendations state that those with established cardiovascular disease are probably now receiving aspirin, a statin, and blood pressure (BP)-lowering drugs. It might be reasonable to combine these medications into a cardiovascular polypill for these patients in order to reduce prescription gaps and non-adherence. A sizable portion of individuals suffering from long-term cardiovascular conditions currently use a combination of prescription drugs. Introduce a polypill to high-risk patients to reduce prescription gaps and enhance adherence to recommended therapy.

Keywords: Polypill; Type2 Diabetes; Combination Pills

Abbreviations: BP: Blood Pressure; T2DM: Type 2 Diabetes; ADA: American Diabetes Association; DM: Diabetes Mellitus; VLDLs: Very Low Density Lipoproteins; CMs: Chylomicrons; TG: Tri Glycerides; FPG: Fasting Plasma Glucose.

Introduction

T2DM, also known as non-insulin-dependent diabetes mellitus or adult-onset diabetes, is a metabolic condition characterized by elevated blood glucose levels due to insulin resistance and relative insulin shortage. T2DM symptoms include frequent urination, increased thirst, lethargy, and weight loss. T2DM is caused by a mix of hereditary and environmental factors. Toxins in the environment may also be contributing to recent rises in the rate of T2DM. Having T2DM relatives significantly raises the likelihood of acquiring T2DM in the family. In addition to any genetic component, environmental factors, particularly nutrition and obesity, have a significant role in the development of T2DM. Insulin resistance occurs when human tissues do not respond effectively to insulin [1].

T2DM is a heterogeneous and progressive metabolic illness characterized by hyperglycaemia and induced by abnormalities in insulin secretion or action as a result of a

complicated network of clinical circumstances. There are numerous pathways that interact and mutually reinforce each other, increasing the risk of other diseases such as heart disease, peripheral arterial and cerebrovascular disease, obesity, and non-alcoholic fatty liver disease, among others. Diabetes mellitus (DM) is one of the most ancient diseases known to man. About 3000 years ago, it was first mentioned in an Egyptian manuscript. Type 2 diabetes mellitus (T2DM) is by far the most prevalent kind of diabetes, followed by type 1 diabetes mellitus and gestational diabetes [2].

Dysregulation of the metabolism of carbohydrates, lipids, and proteins is a hallmark of type 2 diabetes, which is brought on by either decreased insulin production, insulin resistance, or both. Type 2 diabetes is brought on by the interplay of behavioural, environmental, and genetic risk factors [2]. T2DM epidemiology is influenced by both genetics and the environment. Following exposure to an environment characterized by sedentary behaviour and high calorie intake, genetic variables take influence. Globally, the number of adult patients affected by T2D was anticipated to be 537 million in 2021, with a further increase to 783 million by 2045. T2D, being a chronic illness, is widely documented to have a number of negative repercussions, including macrovascular and microvascular problems. Although the etiology of T2D is still unknown, there is growing evidence that inflammatory pathways are key and common pathogenic mediators in the natural course of diabetes [3].

The clinical presentation, underlying pathophysiology, and disease progression in diabetic patients can vary greatly between individuals, and atypical symptom presentation can sometimes make T2DM classification problematic. Many people with T2DM are asymptomatic at the time of diagnosis, while others present with severe hyperglycaemia or even diabetic ketoacidosis. The American Diabetes Association (ADA) Consensus Conference10 advised that high-risk people with IGT or IFG levels (HbA1c >6.5%; BMI 30 kg per m2; age 60 years) be treated with metformin. Pioglitazone11, as well as the combination of low-dose metformin and rosiglitazone, are also particularly effective in reducing the progression of prediabetes to diabetes. Weight reduction and exercise, while initially helpful, are connected with weight rebound in the majority of people [2,4]. The organs involved in T2DM development include the pancreas (β-cells and α-cells), liver, skeletal muscle, kidneys, brain, small intestine, and adipose tissue.

Pathophysiology of Type 2 Diabetes Mellitus

β-Cell Dysfunction

β-cell dysfunction has typically been linked to -cell death. Overt T2DM, on the other hand, does not occur unless cells are unable to release enough insulin to compensate for insulin resistance. Excess FFAs and hyperglycaemia cause -cell dysfunction by causing ER stress via the apoptotic unfolded protein response (UPR) pathways [3,5].

Nutritional Factors

The high-calorie Western diet comprises high levels of fats and carbs, which raise blood glucose levels and increase the number of circulating very-low-density lipoproteins (VLDLs), chylomicrons (CMs), and their remnants (CMRs), which are high in triglycerides (TG). This causes an increase in reactive oxygen species (ROS) concentrations, which causes an aberrant production of inflammatory chemicals [6].

Physical Activity

Obesity and T2DM are linked by decreased physical activity and exercise training, as well as increased sedentary behaviors, which are related with elevated indicators of chronic low-grade systemic inflammation. In this condition, proinflammatory molecules such as interleukin 6 (IL-6), C-reactive protein (CRP), tumor necrosis factor-alpha (TNF-), or IL-1 are released into the bloodstream and produce an inflammatory state inside certain organ.

Gut Dysbiosis

The gut microbiota is made up of several bacteria species that influence human physiology and engage in various biological processes. Many metabolites are produced by gut resident bacteria that contribute to physiology in healthy persons. However, changes caused by both inherited and acquired factors such as age, nutrition, lifestyle, genetic predisposition, or underlying disorders can modify the number of metabolites generated by the gut microbiota, resulting in metabolic abnormalities that can lead to disease [5].

Mitochondrial Dysfunction

Oxidative stress, impaired mitochondrial biogenesis, genetic changes affecting mitochondrial integrity, and aging all promote mitochondrial dysfunction and are linked to the development of T2DM.

Diagnosis Procedure of Type 2 Diabetes Mellitus

An elevated random plasma glucose test (200mg per dl with classic hyperglycaemic symptoms), fasting plasma glucose levels (126mg per dl after at least an 8-hour fast), 2hour post-glucose-load glucose level (200 mg per dl after 75 g oral glucose), or HbA1c (6.5%) confirmed by repeat testing can all be used to diagnose T2DM. The fasting plasma

glucose (FPG) test is used by the ADA to diagnose diabetes, whereas the oral glucose tolerance test (OGTT) is used by the WHO. HbA1c and fructosamine are still effective for assessing blood sugar management over time [6].

Current Status of T2DM Treatment

T2DM is a chronic metabolic disorder characterized by high blood glucose levels due to insulin resistance or insufficient insulin production. The current treatment of T2DM involves lifestyle modifications, such as diet and exercise, and pharmacological interventions, such as oral hypoglycaemic agents and insulin therapy. However, the management of T2DM is challenging due to the complexity of the disease and the need for multiple medications to control various risk factors [7].

Polypill, A New Advancements in Antidiabetic Therapy

A polypill is a type of dosage form commonly targets for the treatment and prevention of chronic disease condition with multiple medications combined together. The word polypill refers the presence of more than one or multiple pill (fixed dose combination) in the form of tablet and capsules. The concept of a polypill was first introduced in the early 2000s as a way to simplify medication regimens and improve adherence to therapy. The use of a polypill has been proposed for the prevention of cardiovascular disease in patients with T2DM, as this patient population is at an increased risk of developing cardiovascular disease [8].

Improved Adherence: The use of a polypill can simplify medication regimens, reducing the pill burden for patients and potentially improving adherence. This is particularly important in T2DM, where multiple medications are often required to manage blood glucose levels, blood pressure, and cholesterol.

Prevention of Cardiovascular Disease: T2DM is associated with an increased risk of cardiovascular disease. A polypill containing aspirin, a statin, and blood pressure-lowering agents has been proposed for the prevention of cardiovascular disease in patients with T2DM. Studies have shown that the combined use of polypill components has increased over time, indicating its relevance in this patient population.

Cost-effectiveness: A study has demonstrated the cost-effectiveness and life-saving potential of a polypill in reducing cardiovascular disease. This suggests that a polypill approach may not only improve patient outcomes but also provide economic benefits by reducing the need for multiple medications.

Literature Review on Polypill Treatment Strategy

Aspirin, a statin, and blood pressure (BP)-lowering medications are likely currently being given to individuals with established cardiovascular disease, according to recommendations. To decrease prescription gaps and non-adherence, it would be appropriate to combine these pharmaceuticals into a cardiovascular polypill for these patients. Our goal was to determine how frequently individuals with type 2 diabetes (DM2) or existing cardiovascular diseases (CVD) used aspirin, statins, and other BP-lowering medications between 1996 and 2009. A significant percentage of patients with chronic cardiovascular illnesses already employ a mix of pharmaceutical treatments. To decrease prescription gaps and improve adherence to recommended therapy, it might be possible to introduce a polypill in high-risk patients.

Considerations and Challenges

In T2DM, using a polypill can help to simplify drug regimens and increase adherence to therapy. The use of polypill components such as aspirin, a statin, and blood pressure-lowering medicines in combination has been advocated for the prevention of cardiovascular disease in T2DM patients. The usage of a polypill can lessen pill burden for patients and potentially enhance drug adherence. The combined use of polypill components has increased over time, showing their importance in T2DM patients [9].

Individualized Treatment: T2DM is a complex disease that requires individualized treatment approaches. While a polypill can simplify medication regimens, it may not address the specific needs of each patient. Tailoring treatment to individual patients' characteristics and preferences is essential for optimal management of T2DM.

Side Effects and Interactions: Combining multiple medications into a single pill increases the risk of side effects and drug interactions. Careful consideration should be given to the selection and dosing of medications in a polypill to minimize these risks and ensure patient safety.

Regulatory Approval: The use of a polypill in T2DM represents an innovative approach to enhance patient care and improve outcomes in the management of this chronic disease. The combined use of polypill components has shown an increasing trend over time, indicating its relevance in patients with T2DM. However, further research is needed to address individualized treatment approaches, potential side effects, and drug interactions. Regulatory approval and widespread availability of a T2DM-specific polypill are also

important considerations. Overall, the concept of a polypill in T2DM holds promise in improving medication adherence and simplifying treatment regimens [10].

Future Aspects of Polypill in Type II Diabetes Mellitus

In type 2 diabetic mellitus (T2DM), the future prospects of a polypill show promise in enhancing patient adherence and eliminating gaps between indicated and used therapy, improving medication adherence, and simplifying treatment regimens. The combined use of polypill components has increased over time, showing their importance in T2DM patients. More research is needed, however, to address specific treatment options, potential adverse effects, and drug interactions. Important considerations include regulatory approval and broad availability of a T2DM-specific polypill. Overall, the polypill concept in T2DM is a unique strategy to improving patient care and outcomes in the management of this chronic condition. T2DM management necessitates a combination of lifestyle adjustments, medication adherence, and frequent monitoring. Adherence to many drugs, on the other hand, might be difficult for patients, resulting in inadequate disease control. The idea of a polypill, which mixes many prescriptions into a single pill, has garnered traction as a viable solution for improving adherence and simplifying treatment regimens [4].

The Future Scope of the Polypill Approach in T2DM Treatment Includes

Development of New Polypills: The development of new polypills that combine various medications for the treatment of T2DM is an area of active research. The efficacy and safety of these polypills need to be evaluated in clinical trials before they can be used in clinical practice. Personalized Polypills: The development of personalized polypills that are tailored to the individual needs of patients with T2DM is another area of active research. These polypills can be customized to include medications that are specific to the patient's risk factors and comorbidities. Cost-Effective Treatment: The polypill approach can reduce the cost of T2DM treatment by reducing the number of medications required to control various risk factors and comorbidities. The development of cost-effective polypills can improve access to T2DM treatment for patients in low- and middle-income countries. Prevention of T2DM: The polypill approach can also be used for the prevention of T2DM by combining medications that target various risk factors associated with the development of T2DM. The polypill can simplify the prevention of T2DM by reducing the number of medications required for the prevention of various risk factors [5].

This strategy would increase the frequency of clinical examinations for vulnerable people while potentially raising costs; however, this increase could be mitigated by savings from fewer prescriptions and the anticipated reduction in adverse occurrences. As a result, clinical performance measures that combine therapy deintensification with correct clinical assessments and monitoring appear to be appropriate for safely terminating unnecessary and potentially harmful medicines while maintaining the benefits of vascular prophylaxis. This strategy will be crucial in establishing effective personalized preventive interventions for the aged and vulnerable [11]. Polypills are important in therapeutic practice, even if their contribution to increased adherence is small. A variety of other patient- and system-related characteristics, including as patient age, health literacy, socioeconomic level, disease and medication convictions, adverse effects, medical condition and degree, treatment expenses, and clinical outcomes, all contribute to positive outcomes [12]. However, reducing pill regimens, especially in cases when the number of tablets may be overwhelming for patients, may result in increased treatment adherence and, as a result, improved clinical results. Nonetheless, more long-term randomized controlled trials addressing a variety of medical problems will be needed to better understand the role of polypills in clinical practice [13,14].

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