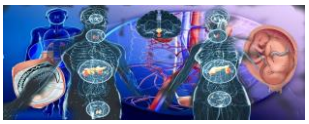
International Journal of Endocrinology and Disorders

www.alcrut.com

Short Review Article **International Journal of Endocrinology and Disorders** **Open Access**

Oral Anti Antihyperglycemic Therapy for Treatment of Diabetes Mellitus: A Prospective Study

Donnan F*, Tunceli G, Chibrikov T, Johnson R, Casciano G

Department of Medical Science, Yenangyaung University, Myanmar

***Corresponding Author**: Donnan F, Department of Medical Science, Yenangyaung University, Myanmar.

Received Date: September 08, 2022; **Accepted Date:** **September 28**, 2022; **Published Date:** September 30, 2022

Citation: Donnan F, Tunceli G, Chibrikov T, Johnson R, Casciano G, Chronic Autoimmune Disease: Type 1 Diabetes Pathophysiology and Management, J. International Journal of Endocrinology and Disorders, V1(4).

Abstract

Diabetes Mellitus Is a Chronic Disease that is growing in prevalence worldwide. Pharmacologic therapy is often necessary to achieve optimal glycemic control in the management of diabetes. Orally administered antihyperglycemic agents (OHAs) can be used either alone or in combination with other OHAs or insulin. The number of available OHAs has increased significantly in the last decade, which translates into more therapeutic options and complex decision-making for physicians.

Keywords: Diabetes Surveillance Strategy; antihyperglycemic agents; insulin sensitizers; postprandial elevations

Introduction

Diabetes mellitus is a chronic disease that is growing in prevalence worldwide. Canadian data from the National Diabetes Surveillance Strategy demonstrate a prevalence of 4.8% among adults, with the vast majority having type 2 diabetes. With the growing elderly Canadian population, the rising prevalence of obesity and the alarming increase in childhood and adolescent type 2 diabetes, the burden of this disease will continue to grow. Aggressive glycemic control has been demonstrated to decrease microvascular and perhaps macrovascular complications, although the latter claim remains controversial. The Canadian Diabetes Association 2003 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada recommends a target hemoglobin A_{1c} concentration of 7.0% or less for all patients with diabetes and, for those in whom it can be safely achieved, a target hemoglobin A_{1c} concentration in the normal range (usually ≤ 6.0%).Although nonpharmacologic therapy (e.g., diet, exercise and weight loss) remains a critical component in the treatment of diabetes, pharmacologic therapy is often necessary to achieve optimal glycemic control.

Pathogenesis of Diabetes

Postprandial elevations in serum glucose levels stimulate insulin synthesis and release from pancreatic β cells. Insulin secreted into the systemic circulation binds to receptors in target organs (skeletal muscle, adipose tissue, liver). Insulin binding initiates a cascade of intracellular signal transduction pathways that inhibits glucose production in the liver, suppresses lipolysis in adipose tissue and stimulates glucose uptake into target cells (muscle and fat) by mechanisms such as the translocation of vesicles that contain glucose transporters to the plasma membrane.

Type 2 diabetes is a metabolic disorder that results from complex interactions of multiple factors and is characterized by 2 major defects: decreased secretion of insulin by the pancreas and resistance to the action of insulin in various tissues (muscle, liver and adipose), which results in impaired glucose uptake. The precise molecular mechanism of insulin resistance is not clearly understood, but deficits in the postinsulin receptor intracellular signalling pathways are believed to play a role.

Novel drugs were less frequently used as initial therapy. Incidence of patients with dual combination of MET + DPP-4 inhibitors was the highest but remained unchanged (5%). Incidence of patients with monotherapy with GLP-1-RA increased from 1% to 4%, that of DPP-4 inhibitors from 2% to 3% and that of SLGT-2 inhibitors from 1% to 2%. Incidence of patients with dual combination of MET + SGLT-2 inhibitors exhibited a continuous increase over time from <1% to 3%

The number of patients with initial MET monotherapy was 113,256. Novel drugs with cardiovascular/renal benefit were less frequently added than other drugs in the subsequent six year after MET initial monotherapy (incidence rates of patients with GLP-1-RAs: 2%, 3%, and 4%; with SGLT-2 inhibitors: 4%, 6%, and 8%; for comparison incidence rates with DPP-4 inhibitors: 7%, 11%, and 14%; with SU: 11%, 17%, and 21%; with INS: 2%, 4%, and 5%, at months 24, 48, and 72, respectively)

Metformin

Traditional medicine used French lilac for treating diabetes for centuries, and guanidine compounds were derived from its extract in 1920s. These compounds exhibited hypoglycaemic effects in animals but were later withdrawn due to hepatotoxicity in patients. The biguanides, phenformin and MET are derived from guanidines and were introduced in 1950's.

Traditional medicine used French lilac for treating diabetes for centuries, and guanidine compounds were derived from its extract in 1920s. These compounds exhibited hypoglycaemic effects in animals but were later withdrawn due to hepatotoxicity in patients. The biguanides, phenformin and MET are derived from guanidines and were introduced in 1950's.

Cardiovascular safety

Although the UKPDS reported reduced mortality in the SU arm of intensive treatment, many authorities are concerned that SUs have not been subject to rigorous cardiovascular evaluation. This concern was raised as early as 1970 when a report from the University Group Diabetes Program (UGDP) found that the mortality of non-insulin-dependent patients treated with tolbutamide was approximately 2 ½ that of those treated with diet alone.

Mechanism of action and efficacy

This group of insulin secretagogues works through binding sites on beta cells that are both distinct and similar to those of SU. These drugs work by

stimulating first-phase insulin release but not second-phase release. Thus, these drugs are less likely to produce late or fasting hypoglycaemia compared with SUs. These drugs exert this effect as they close the potassium channels of the beta cell and open the calcium channel, thus inducing insulin exocytosis.

Conclusion

Their use should be individualized according to the health status and preference of the patient, keeping in mind their efficacy and side effects. Metformin remains the drug of choice in monotherapy, and the others are added to it. However, SUs is becoming less favourable as they may produce hypoglycaemia. Cardiovascular risk has received more attention and should be investigated thoroughly before licensing newer agents.

References

1. Bayraktar M, Van Thiel DH, Adalar N. A comparison of acarbose versus metformin as an adjuvant therapy in sulfonylurea-treated NIDDM patients. Diabetes Care 1996;19:252-254.
2. Hoffmann J, Spengler M. Efficacy of 24-week monotherapy with acarbose, metformin, or placebo in dietary-treated NIDDM patients: the Essen-II Study. Am J Med 1997;103:483-90.
3. Stades AM, Heikens JT, Erkelens DW, Holleman F, Hoekstra JB. Metformin and lactic acidosis: cause or coincidence? A review of case reports. J Intern Med 2004;255(2):179-87.
4. Torgerson JS, Hauptman J, Boldrin MN, Sjostrom L. XENical in the prevention of diabetes in obese subjects (XENDOS) study: a randomized study of orlistat as an adjunct to lifestyle changes for the prevention of type 2 diabetes in obese patients. Diabetes Care 2004;27(1):155-161.
5. Tsapas A, Karagiannis T, Kakotrichi P, et al. Comparative efficacy of glucose-lowering medications on body weight and blood pressure in patients with type 2 diabetes: a systematic review and network meta-analysis. Diabetes Obes Metab 2021;23:2116–2124.
6. Donnan JR, Johnston K, Chibrikov E, et al. Capturing adult patient preferences toward benefits and risks of second-line antihyperglycemic medications used in type 2 diabetes: a discrete choice experiment. Can J Diabetes 2020;44:6–13.