Asian Journal of Pharmaceutical Education and Research
Vol -13, Issue-3, July- September 2024
ISSN:2278 7496

REVIEW ARTICLE Impact Factor: 7.014

PHARMACOLOGICAL MANAGEMENT OF TYPE II DIABETES MELLITUS: REVIEW

Jagpreet Kaur Sandhu, Saurabh Sharma*, Rupali Bharti Sao, Smruti Ranjan Dash

Faculty of Pharmacy, Kalinga University, Naya Raipur, Chhattisgarh India (492101)

*Corresponding Author's E mail: saurabh.sharma@kalingauniversity.ac.in
Received 14 June. 2024; Revised 16 June. 2024; Accepted 22 June. 2024, Available online 10 July. 2024

Cite this article as: Sandhu JK, Sharma S, Sao RB and Dash SR. Pharmacological management of type II diabetes mellitus: review. Asian Journal of Pharmaceutical Education and Research. 2024; 13(3): 139-143.

https://dx.doi.org/10.38164/AJPER/13.3.2024.139-143

ABSTRACT

Diabetes Mellitus is a non-communicable disease caused due to hyperglycaemia. It possesses threat to millions of people worldwide and is the cause of morbidity and early mortality in individuals. Studies have shown links between diabetes mellitus and other comorbidities such as cardiovascular disorders, hypertension and renal disorders. Cognitive decline, functional disability and infections also follows. Insulin resistance has a direct metabolic effect on heart. Insulin sensitisers have a beneficial vascular effect. Nutritional therapy, weight management and appropriate class of medications should be provided to control these diseases. This review summarises the increasing risk of Diabetes Mellitus and the emerging complications due to it. How non communicable diseases in India are reaching an epidemic position. They can be reversed by taking appropriate measures and lifestyle changes and the with the advancement in medical technology treatment is possible to delay the effects of these diseases. However, it is important to realise that lifestyle modification as a therapeutic measure should be reinforced by the government and medical professionals as apart of educating the masses.

Keywords: Diabetes, hypertension, dyslipidemia, obesity.

INTRODUCTION

Diabetes is a condition in which blood sugar levels increase and leading to other health problems. Hyperglycaemia occurs when-

- Pancreas stop producing Insulin
- The body becomes resistant to Insulin
- Minimal Insulin is produced by the body.

It causes unusually high blood sugar levels. It is basically the result of stagnant lifestyle, obesity, genes, family history and physical inactivity. Type 2 is the most common form of diabetes (DM) [1,2]. When glucose builds up in the blood instead of going into cells, it can cause some problems such as -

- Hypoglycaemia - symptoms include shakiness, dizziness, sweating, hunger, headache, pale skin colour, tingling sensation around the mouth, difficult in paying attention or confusion. If not treated quickly, the person can pass out leading to emergency treatment. Quickest way to treat hypoglycaemia is to intake some form of sugar like- fruit juice, candies, sugar tablets.

- Hyperglycaemia - high blood sugar, high sugar in urine, frequent urination, increased thirst. Sugar level must be checked regularly, if an increase is observed it should be treated immediately, else it can lead to a condition called ketoacidosis. It is a condition where, due to lack of insulin the body is unable to breakdown sugar and to meet the energy requirements, it starts to break fats for energy.
- Ketoacidosis - Ketones as waste products are generated when the body breaks down fats for energy. Large amount of ketones cannot be tolerated by the body. This can lead to shortness of breath, nausea, vomiting and dry mouth, hallucinations, loss of vision, weakness on one side of the body.
- Hyperosmolar Hyperglycemic Non-ketonic syndrome - due to high sugar concentration in the blood, the body starts to remove it through urination. Leading to a dark colour urine with frequent urination. Person gets often thirsty due to removal of excess water. If it persists for a long time, can cause severe dehydration leading to seizure, coma or even death [3-5].

Classification of medications used to treat T2DM:

- Sulphonylureas
- Meglinitide derivatives
- Biguanides
- Thiazolidinediones
- Alpha glucosidase inhibitors
- Long acting and short acting insulin

Since the 5 classes of drugs at in different ways to lower blood glucose levels, they may be used in combination. For example, a biguanide and sulfonylurea could be used together. There are many other combinations that can be taken together.

Although taking more than one drug can be costly and can increase the risk of side effects, combining oral medications can improve blood glucose control compared to taking only a single pill that does not have the desired effects [6,7].

Diabetes and Cardiac complications

T2DM patients have hyperglycemia, abnormal lipid levels, altered inflammatory mediators and thrombolytic parameters.

Hyperglycemia accelerates atherogenesis, endothelial dysfunction, formation of glycosylated proteins and advanced glycation end products and causes increase in active oxygen molecules. These direct consequences of hyperglycemia contribute to both macrovascular and microvascular disease. There are other important mechanisms implicated in the development of diabetic complications, in relation to co-existing hypertension and hyperlipidemia, activation of the renin angiotensin system, adipokinase production and protein folding.

Diabetes and Renal complications

10-40% of people suffering from T2DM will eventually suffer from renal complications. The early abnormality is glomerular hyperfilteration. It can be identified by a test of micro- albuminuria. The risk of diabetic neuropathy and mortality is increased in positive micro albuminuria group (AER). The levels of AER can be detected in early stage and prevent peripheral neuropathy and renal complications. It is potentially reversible [8-10].

Diabetes and Dyslipidaemia

Dyslipidaemia is an important aspect of diabetes as cardiovascular disease is the major cause of mortality in diabetes. There is 82% of prevalence of Dyslipidaemia in the diabetic population. Dyslipidaemia is the imbalance of lipids such as cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL)

and triglycerides (TGS). It may result from tobacco exposure, poor diet, unhealthy life style, consumption of high density fast foods, genetically passed and it leads to CVD. Diabetes is increasing and making India the epicentre of the global epidemic diabetes. The most common in T2DM is Atherogenic dyslipidaemia, it is characterized by high TGS, elevated HDL & LDL.

Major cause of diabetes is obesity.

Diabetes occur when the pancreas is working inefficiently and fails to produce sufficient amount of insulin which is required for the absorption of sugar and sometimes the cells are unable to absorb sugar from blood even with sufficient amount of insulin present in blood. And the glucose remains in the blood stream. It damages the body tissues and leads to the disorders of circulatory system, nervous system and the immune system [11,12].

This generally occurs due to obesity, physical inactivity family history, genetic mutation, hormonal imbalance, damage or removal of pancreas. Obesity is the global pandemic in today's world. Around 2billion people in the world suffer from obesity. It is the major cause of many diseases. Adipose tissue is an active tissue. Each cell produce numerous hormones affecting health and disease. When in balance fat cells provide us energy, imbalance results to insulin resistance. Obesity creates inflammatory environment in the body which affects other tissue, leading to diabetes, cardiovascular disease, hypertension and kidney diseases. It affects psychologically, economically, socially and physiologically [13,14].

It is the leading factor in the development of T2DM. visceral fat mass has the highest association with insulin resistance. Glucose and free fatty acids are increased leading to increased stress in pancreas and liver. Insulin signalling is altered because of free fatty acids. The constant damage to nephrons leads to chronic kidney disease which further leads to hypertension [15,16].

Hyperglycaemia and Hypertension damage the vessels of heart causing cardiovascular diseases. By mere prevention of obesity we will be able to achieve much more rather than treating the complications after obesity is acquired [17].

Pathways in the treatment of T2DM

Beta cell dysfunction- Decreased function of beta cells. Treated by incretins, suphonylureas, meglitinides.

Incretin effects- causes decrease in incretin effects in the body. Incretin is a gut derived peptide hormone which is released after ingestion of a meal. They stimulate beta cells in the pancreas to secrete insulin.

Alpha cell pathway- when there is increase in glucagon; incretins and pramlintidesa are used for treatment [18].

Adipose tissue pathway- causes insulin resistance and increased Tipolysis. Metformin and thiazolidinediones are used for treatment. Liver - increased glucose production and reduced insulin production. Controlled by metformins and thiazolidinediones [19,20].

Brain- causes increased apetite, decreased morning dopamine surge and increase sympathetic tone. Treatment include in cretinism, dopamine agonists and appetite suppressants.

Stomach / small intestine- Increased glucose absorption. Treated with incretins, pramlintide, alpha glucosidase inhibitors.

Kidney pathway- Increased glcose reabsorption. Treated with SGLT2 inhibitors (sodium glucose co-transporters).

Diagnosis

- By determining blood sugar levels.
- A fasting plasma glucose measuring 126 mg/dL or higher.
- A 2 hour plasma glucose level of 200 mg/dL or higher.
- A-random glucose level of200 mh/dL in a person suggests the occurrence of Diabetes [21-24].

CONCLUSION

Over time, high blood sugar can damage and cause problems with your Heart and blood vessels. You're up to twice as likely to get heart disease or have a stroke, and at a younger age. If your kidneys are damaged or you have kidney failure, you could need dialysis or a kidney replacement. High blood sugar can damage the tiny blood vessels in the backs of your eyes. If this isn't treated, it can cause blindness. Affects the nerve this can lead to trouble with digestion, the feeling in your feet, and your sexual response. Your blood doesn't circulate as well, so wounds heal slower and can become infected. Only people with type 2 diabetes can use pills to manage their diabetes. The pills work best when combined with meal planning and exercise. It is not safe for pregnant women to take oral diabetes medications.

REFERENCE

1. Irwin N. New perspectives on exploitation of incretin peptides for the treatment of diabetes and related disorders. World J. Diabetes. 2015; 6: 1285–1295.
2. Drucker DJ. The biology of incretin hormones. Cell Metab. 2006; 3: 153–165.
3. Drucker DJ. Deciphering metabolic messages from the gut drives therapeutic innovation: The 2014 banting lecture. Diabetes. 2015; 64: 317–326.
4. Toft-Nielsen MB, Damholt MB, Madsbad S, Hilsted LM, Hughes TE, Michelsen BK and Holst JJ. Determinants of the impaired secretion of glucagon-like peptide-1 in type 2 diabetic patients. J. Clin. Endocrinol. Metab. 2001; 86: 3717–3723.
5. Xu G, Kaneto H, Laybutt DR, Duvivier-Kali VF, Trivedi N, Suzuma K, King GL, Weir GC and Bonner-Weir S. Downregulation of GLP-1 and GIP receptor expression by hyperglycemia: Possible contribution to impaired incretin effects in diabetes. Diabetes 2007; 56: 1551–1558.
6. Pathak V, Vasu S, Flatt PR and Irwin N. Effects of chronic exposure of clonal β-cells to elevated glucose and free fatty acids on incretin receptor gene expression and secretory responses to GIP and GLP-1. Diabetes Obes. Metab. 2014; 16: 357–365.
7. Højberg PV, Vilsboll T, Rabol R, Knop FK, Bache M, Krarup T, Holst JJ and Madsbad S. Four weeks of near-normalisation of blood glucose improves the insulin response to glucagon-like peptide-1 and glucose-dependent insulinotropic polypeptide in patients with type 2 diabetes. Diabetologia 2009; 52: 199–207.
8. Piteau S, Olver A, Kim SJ, Winter K, Pospisilik JA, Lynn FC, Manhart S, DeMuth HU, Speck M, Pederson RA, et al. Reversal of islet GIP receptor down-regulation and resistance to GIP by reducing hyperglycemia in the Zucker rat. Biochem. Biophys. Res. Commun. 2007; 362: 1007–1012.
9. Asmar M, Tangaa W, Madsbad S, Hare K, Astrup A, Flint A, Bülow J and Holst JJ. On the role of glucose-dependent insulintropic polypeptide in postprandial metabolism in humans. Am. J. Physiol. Endocrinol. Metab. 2010; 298: 614–621.
10. Esposito K, Mosca C, Brancario C, Chiodini P, Ceriello A and Giugliano D. GLP-1 receptor agonists and HBA1c target of of >7% in type 2 diabetes: Meta-analysis of randomized controlled trials. Curr. Med. Res. Opin. 2011; 27: 1519–1528.
11. Pocai A. Unraveling oxyntomodulin, GLP1's enigmatic brother. J. Endocrinol. 2012; 215: 335–346.
12. Amori RE, Lau J and Pittas AG. Efficacy and safety of incretin therapy in type 2 diabetes: Systematic review and meta-analysis. J. Am. Med Assoc. 2007; 298: 194–206.
13. Day JW, Gelfanov V, Smiley D, Carrington PE, Eiermann G, Chicchi G, Erion MD, Gidda J, Thornberry NA, Tschöp MH et al. Optimization of co-agonism at GLP-1 and glucagon receptors to safely maximize weight reduction in DIO-rodents. Biopolymers. 2012; 98: 443–45.

14. Lynch AM, Pathak N, Flatt YE, Gault VA, O'Harte FP, Irwin N and Flatt P. Comparison of stability, cellular, glucose-lowering and appetite supressing effects of oxyntomodulin analogues modified at the N-terminus. Eur. J. Pharmacol. 2014; 743: 69–78.
15. Meek CL, Lewis HB, Reimann F, Gribble FM and Park AJ. The effect of bariatric surgery on gastrointestinal and pancreatic peptide hormones. Peptides. 2016; 77: 28–37.
16. Laferrère B. Bariatric surgery and obesity: Influence on the incretins. Int. J. Obes. 2016; 6: 32–36.
17. Bhat VK, Kerr BD, Vasu S, Flatt PR and Gault VA. A DPP-IV-resistant triple-acting agonist of GIP, GLP-1 and glucagon receptors with potent glucose-lowering and insulinotropic actions in high-fat-fed mice. Diabetologia. 2013; 56: 1417–1424.
18. Chepurny OG, Bonaccorso RL, Leech CA, Wöllert T, Langford GM, Schwede F, Roth CL, Doyle RP and Holz GG. Chimeric peptide EP45 as a dual agonist at GLP-1 and NPY2R receptors. Sci. Rep. 2018; 8: 1–14.
19. Hasib A, Ng MT, Khan D, Gault VA, Flatt PR and Irwin NA. Novel GLP-1/xenin hybrid peptide improves glucose homeostasis, circulating lipids and restores GIP sensitivity in high fat fed mice. Peptides. 2018; 100: 202–211.
20. Lu Y, Griffen SC, Boulton DW and Leil TA. Use of systems pharmacology modeling to elucidate the operating characteristics of SGLT1 and SGLT2 in renal glucose reabsorption in humans. Front. Pharmacol. 2014.
21. JLiu J, Lee TW and DeFronzo RA. Why do SGLT2 inhibitors inhibit only 30–50% of renal glucose reabsorption in humans? Diabetes. 2012; 61: 2199–2204.
22. Busch RS and Kane MP. Combination SGLT2 inhibitor and GLP-1 receptor agonist therapy: A complementary approach to the treatment of type 2 diabetes. Postgrad. Med. 2017; 129: 686–697.
23. Pranjul Shrivastava*, Khushboo Gupta. (2022). Therapeutic significance of carica papaya as an anti-inflammatory modulator. Journal of East China University of Science and Technology, 65(2), 303–307.
24. Divesh Pandey, Khushboo Gupta*, Saurabh Sharma, Pranjul Shrivastava, Bulletin of Environment, Pharmacology and Life Sciences Bull. Env. Pharmacol. Life Sci., Vol 12 [10] September 2023: 436-445 ©2023 Academy for Environment and Life Sciences, India Online ISSN 2277-1808.