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Commentary

Safety of the DPP-4 Inhibitor, α-glucosidase Inhibitors, Glitazones and SGLT-2 Inhibitors as Add-on Therapy with Metformin in Medication of Type 2 Diabetes Mellitus

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Abstract: Optimal successful management of type 2 diabetes mellitus (T2DM) remains an elusive goal ever. Add on therapies with metformin addressing the prime impaired insulin secretion shows promise in achieving strict and effective glycemic control. The aim of this study was to assess the efficacy of DPP-4 inhibitors, α-glucosidase inhibitors, glitazones and SGLT-2 inhibitors as add-on options with metformin to treat patients with T2DM. The primary outcome of this study was a reduction in diabetes and its associated complication along with strict glycemic control with add-on agents used with metformin.

Keywords: Diabetes Mellitus, SGLT-2 Inhibitors, Glitazones, α-glucosidase Inhibitors, Metformin

1. Introduction

Despite an emerging therapeutic option, optimal and efficient management of hyperglycemia in T2DM patients remains an elusive goal for researchers and clinicians [1]. Present scenario for the treatment of diabetes mellitus implicatesstep wise approach [2] initiating with lifestyle intervention and metformin as the first line of treatment followed by sequential add-on therapy such as oral antidiabetic drugs (OADs) and basal insulin. Type 2 diabetes is characterized by core defects of insulin secretion and insulin resistance that present itself long before the onset of frank diabetes [3-4]. Therefore early intervention with add-oncombinatorial approach of using OADs is the efficient rational therapeutic approach. Nowadays six classes of OADs presently available in pharmacological sector that includes biguanides (metformin), sulphonylurea (e.g. tolbutamide), thiazolidinediones (e.g pioglitazone), glinidines (e.grepaglinide), DPP-4 inhibitors (e.gsitagliptin, vildagliptin), SGLT2 inhibitors (e.g) and alpha-glucosidase inhibitors (AGIs) (e.gacarbose) [5-6]. The DPP-4 inhibitors belong to gliptins class that are relying on two incretin hormones glucagon-like peptide 1 (GLP-1) and gastric inhibitory polypeptide (GIP). Both of these stimulate insulin secretion from pancreatic beta cells after meals. Moreover, the GLP-1 molecule also additionally targets the post prandial hyperglycemia. However, GLP-1 and GIP has short half-lives and can't be implicated as such as pharmacological agents so DPP-4 inhibitors were used an alternative of both. The best studies DPP-4 inhibitors are sitagliptin and vildagliptin. Another class of AGIs inhibits the number of alpha-glucosidase enzymes (e.g maltase), which is devoid of pancreatic-centred mechanism action. It consequently delayed

the sugar absorption from gut [7]. The next class of OADs includes the glitazones that contribute to strict glycemic control. Several clinical trials showed that glitazone can either be used as monotherapuetic approach or can be used as combinatorial approach with metformin, sulfonylureas or insulin [8-10]. Sodium-glucose co-transporter 2 (SGLT2) inhibitors are a novel class of inhibitors used in the medicationof type 2 diabetes mellitus. SGLT-2 is a protein that facilitates the glucose reabsorption in the kidney, furthermore SGLT-2 inhibitors block the renal glucose reabsorption and increase glucose secretion that in turn lowers the post prandial glucose levels.

2. Safety of Add-on Combinatorial Therapies with Metformin

2.1. DPP-4 Inhibitors with Metformin

Continuous glucose-dependent insulinotropic effects of incretin-basedmonotherapy [11], the combinatorial approach of using sitagliptin or vildagliptin with metformin did not significantly present episodes of hypoglycemia. A more common event of weight gain on using metformin can be overcome by use of DPP4-inhibitors effectively [12]. Results from well-published studies (ADOPT and RECORD) showed the safety and efficacy of DPP4 inhibitors over metformin. DPP4-inhibitors was superior as combinatorial therapy in a way that it can't present events of hypoglycemia, weight gain, and CV events over monotherapy of metformin [13-14].

2.2. Alpha-Glucosidase Inhibitors (AGIs) with Metformin.

A meta-analysis and Cochrane systematic literature review reveal that AGIs are safer over metformin and other interventions in diabetes-related morbidities, mortalities, hypoglycemia, and weight gain [15].

2.3. Glitazone with Metformin

The use of glitazone over metformin has some deleterious effects when used as combinatorial approach with insulin or metformin. Patients with T2DM having episodes of heart failure should not use this combinatorial approach. This class presents weight gain, water retention and breathlessness in T2DM patients. This combinatorial approach also leads to increased risk of bone fractures, diabetic macular edema and liver damage [16].

2.4. SGLT-2 Inhibitors with Metformin

The SGLT-2 inhibitors reduce blood pressure and body weight [13]. Few studies have compared the metformin over SGLT-2 inhibitors, however, previously published studies showed the safety of SGLT-2 inhibitors as combinatorial approach over metformin as monotherapuetic approach [13]. It reduces blood pressure, body weight, and HbA1c more efficiently than metformin alone as a monotherapy.

3. Conclusion

Despite advances in pharmacotherapy, type 2 diabetes, and its associated complications remains a tales for scientist and physicians. Intensive studies and better approach with minimal complications in the combinatorial approach with metformin may be implicated in the treatment of Type 2 diabetes mellitus. Pros and cons are associated with the every add-on therapies with metformin, but we have to choose the add-on with minimal loss and sufferings so that we can save the future generations.

References

[1] Saydah SH, Fradkin J, Cowie CC. 2004. Poor control of risk factors for vascular disease among adults with previously diagnosed diabetes. JAMA 291:335–342.

[2] Nathan DM, Buse JB, Davidson MB, Ferrannini E, Holman RR, Sherwin R, Zinman B. 2008. Management of hyperglycemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy: update regarding thiazolidinediones: a consensus statement from the American Diabetes Association and the European. Association for the Study of Diabetes. Diabetes Care 31:173–175.

[3] Nathan DM, Davidson MB, DeFronzo RA, Heine RJ, Henry RR, Pratley R, Zinman B. 2007. Impaired fasting glucose and impaired glucose tolerance: implications for care. Diabetes Care 30:753–759.

[4] DeFronzo RA, Fleck PR, Wilson CA, Mekki Q. 2008. Efficacy and safety of the dipeptidyl peptidase-4 inhibitor alogliptin in patients with type 2 diabetes and inadequate glycemic control: a randomized, double-blind, placebo-controlled study. Diabetes Care 31:2315–2317.

[5] Vilsboll T, Agerso H, Krarup T, et al. 2003. Similar elimination rates of glucagon-like peptide-1 in obese type 2 diabetic patients and healthy subjects. J ClinEndocrinolMetab, 88:220–4.

[6] Nathan DM, Davidson MB, DeFronzo RA, et al. 2007. Impaired fasting glucose and impaired glucose tolerance: implications for care. Diabetes Care, 30:753–9.

[7] Campbell LK, White JR, Campbell RK. 1996. Acarbose: its role in the treatment of diabetes mellitus. Ann Pharmacother, 30:1255–62.

[8] Akanuma Y, Kosaka K, Toyoda T, et al. 1996. Clinical evaluation of a new oral hypoglycemic agent CS-045 in combination with insulin [abstract]. Diabetologia; 39 (suppl 1): A232.

[9] Fonseca VA, Valiquett TR, Huang SM, et al. 1998. Troglitazonemonotherapy improves glycemic control in patients with type 2 diabetes mellitus: a randomized, controlled study. J ClinEndocrinolMetab; 83:3169-3176.

[10] Horton ES, Whitehouse F, Ghazzi MN, et al. 1998. Troglitazone in combination with sulfonylurea restores glycemic control in patients with type 2 diabetes. Diabetes Care; 21:1462-1469.

[11] Mikhail N. 2006. Exenatide: a novel approach for treatment of type 2 diabetes. South Med J, 99:1271–9.

[12] Mikhail N. 2008. Incretinmimetics and dipeptidyl peptidase inhibitors in clinical trials for the treatment of type 2 diabetes. Expert Opin Investig Drugs, 17:845–53.

[13] Singh AK. 2014. Deciding oral drugs after metformin in type 2 diabetes: An evidence-based approach. Indian Journal of Endocrinology and Metabolism.; 18(5):617-623. doi:10.4103/2230-8210.139214.

[14] Benjamin M. Scirica,2016. The Safety of Dipeptidyl Peptidase 4 Inhibitors and the Risk for Heart Failure. JAMA Cardiol. 1(2):123-125.

[15] Van de Laar FA, Lucassen PLBJ, Akkermans RP, et al. 2006. Alpha-glucosidase inhibitors for people with impaired glucose tolerance or impaired fasting blood glucose. Cochrane Database Syst, Rev doi: 10.1002/14651858.CD005061.pub2.

[16] http://www.nytimes.com/health/guides/disease/type-2-diabetes/medications.html.