

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 implicates step 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-on combinatorial 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.g. repaglinide), DPP-4 inhibitors (e.g. sitagliptin, vildagliptin), SGLT2 inhibitors (e.g.) and alpha-glucosidase inhibitors (AGIs) (e.g. acarbose) [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 as 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 monotherapeutic 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 medication of 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-based monotherapy [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 monotherapeutic 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.

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