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Pharmacologically relevant drug interactions of α-glucosidase inhibitors

Abstract

The α-glucosidase inhibitors are antidiabetic agents suppressing the postprandial hyperglycemia and they include Acarbose, Miglitol and Voglibose. These drugs could be used alone or as add-on therapy to treat patients with type 2 diabetes taking other antidiabetic drugs. The gastrointestinal motility is increased by the administration of Acarbose, which may lead to decreased absorption of Digoxin and Metronidazole. The glucose lowering effects of antidiabetic drugs such as Metformin, Glibenclamide, Rosiglitazone, Vildagliptin and Dapagliflozin might be enhanced by the coadministration of α-glucosidase inhibitors, though there were reports of little or no alterations in the pharmacokinetics properties of them.

Keywords: Drug Interactions, α-glucosidase inhibitors, Acarbose, Miglitol, Voglibose

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Introduction

The α-glucosidase inhibitors are a class of oral antidiabetic drugs and they help the patients with type 2 diabetes to manage their blood glucose. They include Acarbose, Miglitol and Voglibose.[1] The postprandial glycaemia could be reduced by the administration of α-glucosidase inhibitors. The absorption of starch and other carbohydrates is delayed by the administration of Acarbose, which inhibits starch digesting alpha amylase and disaccharide digesting alpha- glucosidase. Whereas, Miglitol and Voglibose inhibit disaccharide digesting alpha-glucosidases alone.[2] Diabetes is a group of metabolic disorders and a major health threat to the global population. International Diabetes Federation (IDF) estimated that 451million are affected by Diabetes, in 2017 and it has been projected that the number of patients affected by diabetes would reach around 693million by 2045.[3] The patients with diabetes may take several medications to treat comorbid conditions such as hypertension, dyslipidaemias, obesity, cardiovascular disorder, neuronal disorder, kidney disease, liver disease and others along with their antidiabetic medications. Hence, the incidence of drug interaction is high among them.[4]

Drug interaction is defined as the modification of effects of one drug by the co administered drug(s), herb(s), supplements, food, tobacco smoke or alcohol.[5] Whereas, the Adverse Drug Interaction is defined as the drug interaction resulting in elevated risk of adverse effects or decreased therapeutic efficacy.[6]

As the α-glucosidase inhibitors delay the absorption of carbohydrates, they may interfere the absorption of certain drugs by altering gastric motility.

Digoxin

Digoxin is a cardiac glycoside and it is useful to manage the cardiac conditions like congestive heart failure, atrial flutter and atrial fibrillation.[7] Concomitant use of Acarbose and Digoxin resulted in decreased plasma concentrations of Digoxin.[8,9] It has been postulated that absorption of digoxin is interfered by the coadministration of Acarbose through increased gastrointestinal motility.[10] The interaction between Digoxin and Acarbose may not be clinically significant at therapeutic doses of Acarbose.[11] The absorption of Digoxin is not interrupted by the concurrent use of Voglibose, as it is not affecting the gastrointestinal motility.[12] It has been suggested to use Voglibose as preferred α- glucosidase inhibitor in patients with diabetes taking Digoxin.[13]

Warfarin

Warfarin is an oral anticoagulant used widely to prevent thromboembolic events in patients with venous thromboembolism, chronic atrial fibrillation, coronary artery disease and others.[14] International Normalized Ratio (INR) of a patient taking Warfarin was elevated after the initiation of Acarbose therapy. In addition, it has been hypothesized that Acarbose may increase the absorption of Warfarin.[15] It is recommended to monitor International Normalized Ratio (INR) while initiation or discontinuation of Acarbose in patients taking Warfarin. Moreover, Voglibose,[16] and Miglitol,[17] the other α-glucosidase inhibitors did not affect the pharmacokinetics and pharmacodynamics of Warfarin.

Metformin

Metformin is an antihyperglycemic drug preferred as a first-line agent to treat type 2 diabetes mellitus in overweight patients and it also helps to manage various conditions such as Prediabetes, Gestational diabetes mellitus (GDM), Obesity, Cancer, Polycystic Ovarian Syndrome (PCOS), and others.[18] The bioavailability of Metformin found to be decreased by the coadministration of Acarbose.[19] The dose of Metformin might be adjusted when the concomitant use of Metformin and Acarbose is necessary.[20] However, a meta-analysis indicated that addition of Acarbose to the Metformin therapy increases the antidiabetic efficacy in patients with type 2 diabetes.[21] A study found that the pharmacokinetics of Metformin is not affected significantly by the coadministration of Voglibose.[22]

Sulfonylureas

Sulfonylureas are the antidiabetic medications inducing the release of insulin from beta cells of islets of pancreas and they include the drugs such as glibenclamide, gliclazide, glipizide and others.[23] Concurrent use of Glibenclamide and Acarbose did not

alter the pharmacokinetics of Glibenclamide and it has been found as an useful addition to treat the patients with type 2 diabetes along with sulfonylurea antidiabetics.[24] Moreover, the pharmacokinetics of Glibenclamide was also not affected by the concurrent use of Voglibose the other α-glucosidase inhibitor.[25]

Thiazolidinediones

Thiazolidinediones (TZDs) are antidiabetic medications, which increase the insulin sensitivity, and they include Rosiglitazone and Pioglitazone.[26] A study demonstrated that the pharmacokinetics of rosiglitazone altered slightly and insignificantly by the coadministration of Acarbose.[27]

DPP4 inhibitors

Dipeptidyl peptidase-4 (DPP-4) inhibitors are antidiabetic drugs which block the breakdown of Glucagon-like peptide-1 (GLP-1) resulting in improved insulin secretion and decreased glucagon output. DPP4 inhibitors include Sitagliptin, Saxagliptin, Vildagliptin, Anagliptin, and others.[28] Administration of Voglibose to the patients taking Vildagliptin decreased the plasma levels of Vildagliptin. However, the clinical benefit was higher with this combination.[29] Concurrent use of Miglitol and Anagliptin decreased the pharmacokinetics properties of Anagliptin such as the maximum concentration (Cmax) and area under the curve (AUC) 0-24h. Nevertheless, this combination of drugs found more effective in reducing fasting and postprandial glucose levels than single use of either drugs.[30]

SGLT2 inhibitors

Sodium-glucose cotransporter-2 (SGLT2) inhibitors are newer antidiabetic drugs and they include Dapagliflozin, Canagliflozin and Empaglilfozin.[31] A study indicated that Voglibose did not alter the pharmacokinetics of Dapagliflozin and this combination does not require any dosage adjustment.[32]

Metronidazole

Metronidazole is an antimicrobial agent and its absorption found decreased in patients with diabetes taking Acarbose due to increased motility and adherence of Acarbose on to Metronidazole.[33]

Phenytoin

Phenytoin is an antiepileptic drug and the concomitant use of Miglitol and Phenytoin, did not affect the bioavailability of Phenytoin.[34]

Adsorbents

The use of adsorbents such as carbon spheres and polystyrene sulfonic acid cation exchange resins in patients taking Miglitol resulted in the adsorption of Miglitol on to the adsorbents and this interaction is not clinically significant, as it does not affect the pharmacokinetics and pharmacodynamics of Miglitol.[35]

Conclusion

The α- glucosidase inhibitors do not interact significantly with other drugs except few since they do not affect their pharmacokinetic properties except absorption. The absorption of Digoxin and Metronidazole found decreased by the coadministration of Acarbose. The INR of patients taking Warfarin might be elevated due to the addition of Acarbose. It has been found beneficial to use α- glucosidase inhibitors along with other antidiabetic agents such as Metformin, Glibenclamide, Rosiglitazone, Vildagliptin and Dapagliflozin, though there were reports of little or no alterations in the pharmacokinetics properties of them. The pharmacokinetics of Phenytoin and the adsorbents such as carbon spheres and polystyrene sulfonic acid cation exchange resins are not altered significantly by concurrent use of Miglitol.

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None.

Conflicts of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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