Noninsulin Antidiabetic Agents Effects on Blood Glucose

Table 1. ***Differential effects of noninsulin antidiabetic agents on premeal and postmeal glucose*****[1-3]**

Intervention	Premeal Glucose	Postmeal Glucose	Typical A1C Reduction
Oral agents			
Metformin	√√	√	1.0 percent to 2.0 percent
Sulfonylureas	√√	√√	1.0 percent to 2.0 perrcent
Glinides*	√	√√	0.5 percent to 1.5 percent
Thiazolidinediones	√√	√	0.5 percent 1.4 percent
DPP-4 inhibitors	√	√√	0.6 percent to 0.9 percent
α-Glucosidase inhibitors	—	√√	0.5 percent to 0.8 percent
Colesevelam	√	√	0.5 percent
Injectable agents			
GLP-1 agonists†	√	√√√	0.5 percent to 1.5 percent
Pramlintide	√	√√√	0.5 to1.0 percent

Effects: —, none; √, mild; √√, moderate; √√√, marked

*Repaglinide has a more prominent effect on premeal glucose than nateglinide and also yields higher A1C reductions

†Liraglutide has a more prominent effect on premeal glucose than exenatide and also yields higher A1C reductions

As shown in Table 1, agents that primarily reduce fasting glucose are generally associated with more robust A1C reductions. For this reason, agents that target postprandial hyperglycemia will not get patients to goal when added to existing therapy if the baseline A1C is > 8 percent. However, given the disproportionate contribution of postprandial hyperglycemia to overall glucose at lower A1C levels, use of therapies that lower postmeal glucose can help achieve A1C targets. In a prospective study involving patients with type 2 diabetes and a baseline A1C ≥7.5 percent, 64 percent of patients who met FPG (<100 mg/dL) but not PPG (<140 mg/dL) targets achieved an A1C <7 percent. In contrast, 94 percent of the patients who met both targets achieved the A1C goal.[4] Another reason to address postprandial glucose excursions is that they have been associated with endothelial dysfunction. [5-7]

The relative contributions of pre- and postmeal glycemia are important therapeutic considerations for two reasons:

- **Different noninsulin antidiabetic agents affect different aspects of diurnal glycemia—some mainly lower fasting glucose, while others specifically target postprandial glucose (Table 1).**
- **An A1C level <7 percent may be difficult to achieve without incurring hypoglycemia unless a treatment strategy is used that addresses both fasting and postprandial glucose elevations.**

Table 4. ***Mechanisms of Action of Noninsulin Antidiabetic Agents***

Intervention	Mechanism	Primary Target	
		Insulin Deficiency	Insulin Resistance
Oral agents			
Sulfonylureas	Stimulate insulin secretion independent of glucose	√	
Metformin	Suppress Hepatic glucose output Increase glucose uptake in muscle		√
Glinides*	Stimulate mealtime insulin secretion independent of glucose	√	
Thiazolidinediones (TZD's)	Increase glucose uptake in muscle and fat Suppress hepatic glucose output		√
DPP-4 inhibitors	Stimulate glucose-dependent insulin secretion Suppress postprandial glucagon and hepatic glucose output	√	
α-Glucosidase inhibitors	Slow carbohydrate absorption from intestine	—	—
Colesevelam	Slow absorption from intestine	—	—
Injectable agents			
GLP-1 agonists†	Stimulate glucose-dependent insulin secretion Suppress postprandial glucagon and hepatic glucose output Delay gastric emptying Enhance satiety	√	
Pramlintide	Suppress postprandial glucagon and hepatic glucose output Delay gastric emptying Enhance satiety	—	—

*Repaglinide has a more prominent effect on premeal glucose than nateglinide and also yields higher A1C reductions

†Liraglutide has a more prominent effect on premeal glucose than exenatide and also yields higher A1C reductions

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