

Glyburide vs. Glipizide: Which is superior?
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Both glyburide and glipizide are second generation sulfonylureas. The drugs have slightly different pharmacokinetic characteristics.^{1,2} Although both are dosed once or twice daily, time to onset of the drug and duration of effect are slightly longer for glyburide (nonmicronized formulation), as is the serum half-life.³ These parameters may be seen in Table 1. Despite these differences, administration for both drugs is recommended approximately 30 minutes prior to a meal. Of note, absorption of glyburide is not affected by food intake, while absorption of glipizide is delayed by food. Both drugs are renally excreted (glyburide 50%, glipizide 80-85%); thus, conservative dosing with potential dosage adjustment is recommended for patients with renal insufficiency.

Table 1. characteristics of glipizide and glyburide.^{1,2}

Drug	Approximate equivalent dose (mg)	Serum t _{1/2} (h)	Onset (h)	Duration (h)
Glyburide-nonmicronized	5	10	2-4	16-24
Glyburide-micronized	3	~4	1	12-24
Glipizide	10	2-4	1-3	10-24

t_{1/2} = half-life

Regarding clinical efficacy, glyburide is more potent than glipizide,⁴ as evidenced by the fact that comparatively lower doses may be used to control hyperglycemia; however, the maximum effects attainable with glyburide are similar to those of glipizide as well as other sulfonylureas. Compared to glyburide, glipizide may produce a faster blood glucose-lowering effect and is eliminated more rapidly, suggesting a potential for lower risk of hypoglycemia. However, a difference in the risk for hypoglycemia between these 2 drugs has not been clearly substantiated.

Several trials have been conducted involving glyburide and glipizide, few with direct comparisons; additionally, most of the available literature is not recent. In 2000, Kitabchi et al performed a trial in which they compared the effectiveness and relative potency of glyburide and glipizide over a 15-month period in patients with type 2 diabetes mellitus (T2DM) who were unresponsive to lifestyle modifications.⁵ Their assessments included quarterly fasting blood glucose (FBG) and 2-h post-prandial glucose (PPG, after a standardized meal), and quarterly glycosylated hemoglobin (A1c). A total of 18 patients were randomized to receive glyburide, initial dose 2.5 to 5 mg once daily, or glipizide, initial dose 5 mg once daily. Dosages were increased every 2 weeks until fasting levels <140 mg/dL or 2-h PPG <200 mg/dL were achieved. Dosages were decreased with the occurrence of hypoglycemic episodes.

Patients in both groups experienced significant reductions in FBG, 2-h PPG, and A1c over the study period.⁵ Differences between the groups in FBG and 2-h PPG were significant at 6 months, with lower values observed

in the glipizide group (FBG: -42.08 mg/dL, $p=0.021$; 2-h PPG: -52.08 mg/dL, $p=0.033$); however, over the 15-month period, there were no significant differences between groups for these parameters. Regarding adverse events, there were 101 complaints of hypoglycemia in the glipizide group and 110 in the glyburide group – this difference was not statistically significant. All episodes were characterized as mild or moderate; neither group reported severe hypoglycemia. The investigators concluded that both drugs are effective in controlling hyperglycemia in patients with T2DM.

In a similar study, Birkeland et al evaluated differences among glipizide, glyburide, and placebo in glycemic control and insulin secretion in patients with T2DM over a 15-month period.⁶ A total of 46 patients were included in this study. The investigators observed a comparable reduction in A1c levels in the groups treated with sulfonylureas, relative to placebo, throughout the study period. Both sulfonylureas were found to reduce postprandial glucose levels and increase fasting and postprandial insulin levels compared to placebo. Birkeland et al concluded that glyburide and glipizide were effective in achievement and maintenance of glycemic reduction and insulin secretion over a 15-month period.

In another study, Sami et al compared the effects of glipizide and glyburide on metabolic parameters including FBG and A1c in patients with T2DM who had manifested failure to first generation sulfonylurea therapy.⁷ Patients had been receiving either chlorpropamide or tolazamide and were switched at the discretion of the physician to either glyburide 20 mg daily or glipizide 40 mg daily, both administered in 2 divided doses. Patients were monitored every 2 months for a total of 6 months. There were 55 patients included, of mean age 63 years (43 to 73 years) and with a mean duration of diabetes of 8 years (5 to 15 years). No significant changes were observed in FBG and A1c for the 29 patients on glipizide (FBG: 209 ± 31 mg/dL vs. 211 ± 34 mg/dL; A1c: $12.3 \pm 2.1\%$ vs. $11.7 \pm 1.8\%$, $p>0.05$ for both) and 26 patients on glyburide (FBG: 180 ± 16 mg/dL vs. 184 ± 20 mg/dL; A1c: $11.2 \pm 1.6\%$ vs. $11.0 \pm 1.5\%$, $p>0.05$ for both) over the study period. Although the investigators did not statistically analyze differences between the 2 treatment groups (i.e., glipizide vs. glyburide), they concluded that treatment with both agents was comparable and not superior to treatment with the first-generation sulfonylureas in this study.

Rosenstock et al compared the efficacy and safety of glyburide and glipizide in elderly patients with well-controlled T2DM.⁸ Patients >65 years of age with stable T2DM on a sulfonylurea for >3 months prior to enrollment were included. At baseline, patients were subjected to a washout phase, after which they were randomized to receive glyburide 1.25 or 1.5 mg/d or glipizide 2.5 or 5 mg/d. Dosages were titrated over a 4- to 8-week period and maintenance doses then administered for a total of 4 months. Drug efficacy was assessed using FBG and A1c levels. A total of 139 patients were included in the study. Most patients in both treatment groups attained satisfactory glycemic control with no significant differences between groups in FBG or A1c at any time during the study. At the study endpoint, mean doses of glyburide and glipizide were 8.5 mg/d and 15.4 mg/d, respectively. Both regimens were determined to be well-tolerated with low incidences of hypoglycemia.

Of note, several guidelines are available addressing the management of patients with T2DM, including those of the American Diabetes Association, American Association of Clinical Endocrinologists, and the National Institute for Health and Clinical Excellence.⁹⁻¹² Recommendations for preferential use of glipizide or glyburide were not found in any of these guidelines.

In summary, while there are pharmacologic differences between glipizide and glyburide, there does not appear to be a clear consensus that 1 drug is superior to the other.

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