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Sulfonylurea: Personalized Medicine for Type 2 Diabetes

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Recently, new drugs targeting different glucose-regulating mechanisms have been brought to market and the pharmacological treatment of type 2 diabetes has become complex and more controversial. Clinicians can be confused about how to manage their patients optimally. Consequently, the American Diabetes Association and European Association for the Study of Diabetes published a consensus algorithm for managing type 2 diabetes patients. This position statement is an evidence-based recommendation that recommends choosing a specific anti-hyperglycemic agent based on several considerations: (1) glycemic effectiveness; (2) effects on long-term complications; (3) safety profile; and (4) patient preference [1].

Sulfonylureas have long been used for the treatment of type 2 diabetes and were the first oral anti-hyperglycemic agents to be introduced into clinical practice. They are still widely used and are first- or second-line drugs if the hemoglobin A1c (HbA1c) target is not achieved after metformin monotherapy [1,2]. Sulfonylureas stimulate insulin secretion by inhibiting the potassium flux through ATP-dependent potassium channels (K_{ATP}) in pancreatic β-cells and are most effective in patients who have had diabetes for less than 5 years, and who have residual endogenous insulin production [3]. These drugs have potent and rapid hypoglycemic effects; however, these effects are short-lived and HbA1c eventually increases over time [4]. In addition, there are some safety issues, including hypoglycemia, weight gain, and possibly risk of cardiovascular disease [5].

In this issue, Min et al. [6] investigated the clinical characteristics of patients who are dependent on sulfonylurea treatment for adequate glycemic control. The authors retrospectively selected 19 patients whose HbA1c was maintained below 7.5% with a small dose of sulfonylurea (glimepiride ≤2 mg/day or equivalent dose). The HbA1c level increased after discontinuing the sulfonylurea, but fell again after resuming treatment. The average age of the patients was 67±11 years and there was no gender difference. The mean body mass index was 25.1±3.1 kg/m^2 and 73% of the patients had a first-degree family history of type 2 diabetes. In addition, although the patients had relatively long durations of diabetes (18±10 years), β-cell function was preserved; fasting C-peptide level was 3.9±2.6 ng/mL.

To date, there has been much effort to determine who best will respond to a specific anti-hyperglycemic agent and which drug is the best option for certain type 2 diabetes patients for optimal glycemic control. Despite these efforts, selecting the best anti-hyperglycemic agent for an individual with type 2 diabetes is still complicated. Furthermore, there is no way to determine who will show good glycemic control after discontinuing sulfonylureas. Although Min et al. [6] did not report the proportion of sulfonylurea-dependent patients among all patients receiving sulfonylurea treatment, and did not compare clinical characteristics between sulfonylurea-dependent patients and sulfonylurea-independent patients, there is arguably a population of type 2 diabetics who can best benefit from sulfonylurea treatment for optimal glycemic control. Future studies need to characterize patients with type 2 diabetes who show a good response to sulfonylureas and are dependent on sulfonylurea treatment for adequate glycemic control.

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CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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