The Place of Sulfonylureas in the Modern Treatment of Type 2 Diabetes Mellitus: The End of an Era or the Beginning of a New One?

Sir,

The treatment of type 2 diabetes mellitus (T2DM) has been recently put on a new basis since novel classes of hypoglycemic agents have been introduced in the daily clinical practice. Dipeptidyl peptidase-4 inhibitors, glucagon-like peptide-1 agonists, and sodium-glucose cotransporter 2 inhibitors seem to be both effective and safe for the management of T2DM, while in recent trials, specific agents of the two latter categories demonstrated significant cardiovascular (CV) benefits.[1]

Sulfonylureas (SUs) were originally introduced in the therapy of T2DM in the 1950s; however, they are still considered as the second-most prescribed class of antidiabetic drugs, following metformin.[2] Treatment with SUs gifts certain advantages, with the most prominent being low cost, efficacy, and vast experience after many years of usage. Still, there are particular concerns related to SUs therapy, including side effects – mainly hypoglycemia and weight gain – and lack of long-term efficiency (due to beta-cell exhaustion provoked by the insulin-secreting mechanism of their action). Most importantly, CV safety of the class has been questioned by various studies, with evidence derived from meta-analyses pointing toward an association between SUs use, increased mortality, and a higher risk for stroke.[3]

Contrariwise, SUs are not all the same given that modern SUs (mainly gliclazide Modified Release (MR) and glimepiride) have demonstrated lower risk of all-cause and CV death, compared to conventional SUs.[4] Gliclazide MR was proved to significantly reduce major macro- and micro-vascular complications and renal events, in T2DM patients.[5] Furthermore, the results of a recent trial showed that modern SUs, when used appropriately with regard to patient selection and dosage present low rates of CV events similar to pioglitazone, as add-on to metformin therapy.[6] Finally, it should be noted that some of the potential risks attributed to SUs may be the result of bias in the design or interpretation of study outcomes, rather than an effect of this class of agents.[7]

Keeping the above in mind, the question arises whether there is a model of T2DM patient, who would be considered as the "ideal candidate" for the treatment with SUs in the time of modern antidiabetics. Obviously, we have to decide according to each patient's distinctive characteristics; still, non-obese individuals, being in low CV and hypoglycemia risk, for whom affordability of their antidiabetic treatment is a question, could possibly benefit from therapy with SUs. Besides, specific groups of diabetic patients, such as the elderly ones, in which experience with the new agents is still inadequate, can be safely managed with modern SUs, based on existing evidence. Careful choice of SU, individualized dosage, appropriate timing of administration, and proper patient counseling – regarding particularly the risk of hypoglycemia – are essential requirements for patients to enjoy the advantages of this well-established class of antidiabetic drugs.[8]

Hence, are we ready to bid adieu to SUs? The answer is probably no or at least, not yet. Newer antidiabetic therapies look appealing and promising, but there is still a long way to travel in terms of evaluating their long-term outcomes and safety, considering that relevant data are still limited. In addition, in today's era of universal financial insecurity, there is an increasing concern with regard to economic burden and cost-effectiveness of novel antidiabetic drugs. Under these circumstances, SUs use may further expand in the next years, signaling a new epoch for the class. Until results of ongoing and future studies can provide us with confident answers regarding the above uncertainties, it seems that there is still a place for SUs in the 21st-century management of T2DM, always in a setting of individualized and patient-centered therapy approach.

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Conflicts of interest

There are no conflicts of interest.

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