



Sulfonylureas in the Treatment of Type 2 Diabetes Mellitus: A Fresh Look and New Insights

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Key Summary Points

In this editorial, the issues raised in each of the articles included in this supplement issue of *Diabetes Therapy* are introduced, including their focus on reappraisal of sulfonylureas (SUs) in the treatment of type 2 diabetes mellitus (T2DM).

SUs have been available for over 50 years, with the latest generation of SUs associated with effective antihyperglycaemic efficacy but a lower risk of adverse effects relative to earlier generations of SUs.

The wide clinical benefits of SU treatment in T2DM are reviewed in this supplement, as well as how international and national guidelines recommend their use in patients with T2DM.

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In recent years, remarkable changes have taken place in the treatment of type 2 diabetes mellitus (T2DM). The introduction of many new and exciting medications and drug classes have enriched and expanded the choice of therapies available to treat this increasingly prevalent and burdensome disease. In addition, the general approach to disease management has evolved from a strictly physician-driven treatment approach to an all-inclusive patient-centred care [1]. In the midst of the current change and adjustment however, it is incumbent upon us to reappraise the role of established medications, such as the sulfonylureas (SUs), in order to define their rightful place in this dynamic treatment landscape of T2DM therapies.

Since their first introduction into clinical practice over 50 years ago, SUs have incredibly maintained a consistent and strong presence as valuable agents in the treatment of T2DM [2]. The class itself has undergone structural and “generational” changes over the years, yielding modified medications that offer maximised efficacy with minimised risks of adverse effects [2]. SUs, especially later-generation ones, effectively lower blood glucose levels and have well-defined adverse events and cardiovascular safety profiles relative to other therapies [3–7].

A recent symposium, entitled “SUs in the treatment of T2DM: a fresh look and new insights” held on Wednesday September 18, 2019 during the 55th Annual Meeting of the European Association for the Study of Diabetes (EASD) in Barcelona, Spain, presented recent data for SUs, with the aim of going beyond the low cost and affordability of SUs to determine the main scientific evidence and wider clinical benefits behind the popular use of SUs in the treatment of T2DM. This supplement of *Diabetes Therapy* provides summaries of the three presentations made during the symposium by three international experts in the field.

In the first of these presentations, Dr Aslam Amod discusses his personal perspective of SUs, examining how this therapeutic class has performed in both local and international guidelines. In the second presentation, Professor Lawrence Leiter addresses the question of whether SUs have lived up to expectations on cardiovascular safety when directly tested against comparator agents in cardiovascular outcome trials. Finally, in the third presentation, in the context that T2DM is a progressive disease that commonly requires > 1 drug to control the disease, Dr Miao Yu discusses whether SUs are a good team player and examines the likely implications of using SUs alone early in the disease, or in combination with other agents, on glycaemic outcomes and net side effects.

In conclusion, the old image of SUs as a source of troublesome hypoglycaemia and chequered cardiovascular adverse outcomes in the past is no longer considered tenable. A new generation of SUs deserves to be seen in a better light as clinical experience and a growing body of scientific evidence, including favourable results from recent cardiovascular outcome trials (CVOTs), indicate that modern SUs stand out clinically as safe and effective therapeutic agents in the treatment of T2DM. The fact that these agents also happen to be affordable should be seen as an added advantage, not an indication to limit their use to poor or underprivileged T2DM patients. Furthermore, head-to-head CVOTs comparing SUs with newer medications are currently lacking. Until this has been scientifically addressed, the burden of proof for clinical superiority should not

necessarily be laid on SUs or other comparator therapies. Future outcomes of the ongoing GRADE study [8] may shed further light on the metabolic benefits of SUs and their likely repositioning in the cascade of therapies used to treat T2DM. Revisiting SUs today is like catching up with an old and trusted friend, and we hope that the readers will find this fresh look at SUs to be informative and relevant to clinical practice.

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Compliance with Ethics Guidelines. This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by the authors.

Data Availability. Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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