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Letter to the editor

The Current Status of New Antidiabetic Drugs

Sudhakar Pemminati[1]*, Richard Mark Millis[2], Ashwin Kamath[3], Ashok Kudgi Shenoy[4], Vasavi Rakesh Gorantla[5]

[1] Department of Medical Pharmacology, American University of Antigua College of Medicine & Manipal University, St. John's, Antigua and Barbuda
[2] Department of Medical Physiology, American University of Antigua College of Medicine, St. John's, Antigua and Barbuda
[3] Department of Pharmacology, Kasturba Medical College, Manipal University, Mangalore, India
[4] Department of Pharmacology, Kasturba Medical College, Manipal University, Mangalore, India
[5] Department of Behavioural Sciences and Neuroscience, AUA College of Medicine, St. John's, Antigua and Barbuda

Key Words

lifestyle, multimodal treatment, metabolic syndrome

Dear Editor,

Type 2 diabetes mellitus (T2DM) is a world-wide public health problem [1]. As such, the Food and Drug Administration (FDA), pharmaceutical companies and medical researchers/practitioners should be discussing the costs vs. the benefits for economically-disadvantaged populations that are disproportionately affected by T2DM and, therefore, suffering the most [2]. The current debate about new antidiabetic drugs is focused mainly on pharmacological efficacy and does not take into account the multimodal mechanisms and treatments for this complex disease [3]. Whether the statistically-significant positive results demonstrated for these drugs translate into real benefits for patients in real-life clinical settings has yet to be established.

The multimodal principle of treatment, although well-taught in most medical schools, is often ignored in real-life, particularly when expensive drugs are readily available. For example, treatment of T2DM should start with the least costly, yet effective, nonpharmacological interventions, such as diet/exercise/lifestyle changes, thereafter progressing to first-line gluconeogenesis suppressors, such as metformin and later sulfonylureas. Only after such interventions have failed should the newer, very expensive GLP-1 agonists and SGLT2 inhibitors be introduced [3, 4].

Research should be carefully designed to determine whether the newer drugs benefit patients after diet/lifestyle changes and standard treatments have failed. Such studies of multimodal treatment for T2DM should include not one, but several, intensities of diet/lifestyle modifications even before standard drug treatments are employed. Likewise, several intensities of standard drug treatments should be used in the presence and in the absence of different intensities of diet/exercise/lifestyle modifications. The newer antidiabetics should be similarly added to the experimental regimens. Early introduction of SGLT2 inhibitors without trying the safer treatment options first may result in unnecessary harm [5], as well as increased cost to patients for whom diet/lifestyle and standard drugs may work in the correct combinations. Indeed, this approach is in accordance with the principles of personalized medicine, one of the most promising goals of 21st century medical practice.

In the recent past, a rapid rise in the prevalence of metabolic syndrome has been observed globally, especially in developing countries like India. This increased prevalence of metabolic syndrome is thought to be an important predisposing factor for the current epidemic of T2DM [6, 7]. Complex environment-gene interactions give rise to most, if not all, human diseases, and metabolic syndrome is no exception. For example, two single-nucleotide polymorphisms (SNPs) of apolipoprotein C3 (APOC3), T > C 455 and C > T 482, alone or in combination with the fatty acid binding protein-2 (FABP2), Ala54Thr SNP, appear to be associated with a high risk for developing metabolic syndrome [8]. Even in populations such as those in India with low-fat diets, individuals with these genetic risk factors do not usually escape metabolic syndrome. This knowledge

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*Corresponding Author
Sudhakar Pemminati. Department of Medical Pharmacology, American University of Antigua College of Medicine, St. John's, Antigua and Barbuda.
Tel: +1-268-484-8900 Fax: +1-268-484-8910
E-mail: pemmineti@yahoo.com

has evolved from basic research in medical science combined with genetic and clinical epidemiological research, an approach that must become more widely used if we are to effectively stem the tide of the current T2DM epidemic.

When properly added to a progressive, carefully-designed treatment regimen, the newer antidiabetic drugs may have limited value, with the cost to the patient being disproportionate to the benefit. What is needed is more information about the long-term safety and efficacy of these new antidiabetic drugs, which can only be gleaned from the right kind of multimodal clinical trial. This should be the subject of the current debate on T2DM.

Conflict of interest

The authors declare that there are no conflicts of interest.

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