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Evidence from Experience: Unity in Diversity

ABSTRACT

Diabetes in India presents unique challenges, which merit bespoke solutions. The early onset and rapid progression of diabetes, along with late presentation to the healthcare system, call for more proactive management strategies. At the same time, persons living with diabetes ask for convenient, uncomplicated treatment regimens, which offer comprehensive control with minimal dose frequency. The original research published in this issue highlights the relevance of fixed-dose combinations (FDCs) of sulfonylurea and metformin, as well as fixed-ratio combinations (FRCs) of rapid-acting and long-acting insulin analogs, in diabetes care. In this editorial, we highlight the similar preferences of oral and insulin medication, and explore the rationale behind this. We hope that this insight will encourage further discussion and research on ethnocentric pharmacotherapy in diabetology.

Keywords: Co-formulation insulin, diabetes, FDC, glimepiride, India, insulin, IDegAsp, type 2 diabetes

INTRODUCTION

India is a large country, united in its diversity. Type 2 diabetes is also a diverse syndrome, united not only in terminology, but in many other ways as well. Does the motto “unity in diversity” hold true for Indian diabetes care? We do see this in our epidemiology; similar trends are noticed across the country, and the entire nation seems to be marching towards an increased prevalence of diabetes.¹ We note unity in terms of the quality of care and control: diabetes targets are accomplished in only a minority of patients in every state.² Underlying this reality is the healthcare-seeking behavior and dietary preferences that are common to most of our fellow citizens. The baseline HbA1c is usually high at diagnosis² and patients report their preference for a high-carbohydrate diet, in all regions of the country.³ Yet another facet of healthcare-accepting behavior is the preference for minimal doses, of both oral and injectable drugs.⁴

QUESTIONS AND QUERIES

Are physicians united in diversity? Do they preferentially choose the same therapeutic options for persons living with type 2 diabetes? Are these preferences exhibited across various patient phenotypes, are they concordant between the oral and insulin therapeutic landscape, and can they be explained on the basis of current/contemporary knowledge of diabetes etiopathogenesis and natural history? This editorial explores subtle insights that come to mind while analyzing the results of the original research reported in this issue of the Asian Journal of Diabetology (AJD).

THE CHALLENGE

Indian diabetes care can be quite challenging. Earlier onset and rapid progression of disease, coupled with delayed presentation and erratic follow up of patients, makes it difficult for the treating physician to craft a therapeutic plan, which balances efficacy with safety. Heavy burdens, however, create strong shoulders, and this is what happens in our diabetes care ecosystem. Our physician-researchers, cognizant of the complaints, concerns and the clinical condition of their patients, are able to use evidence-based modern drugs to achieve optimal glucose control in a safe and smart manner.

THE EVIDENCE

Most Indian patients present with a high baseline HbA1c, which cannot be controlled by monotherapy.² Hence, a fixed-dose combination (FDC) of oral drugs, or a fixed-ratio combination (FRC) of dual-action insulin is usually required for glycemic management. This approach is supported by contemporary treatment guidelines.⁵ The choice of oral glucose-lowering drugs is based upon cardiovascular status, concerns about body weight, risk of hypoglycemia and cost.⁵

In this issue of AJD, Rao et al report the utility of glimepiride/metformin combination in young adults,⁶ while Ray et al report that it is a preferred choice in persons with

atherosclerotic cardiovascular disease (ASCVD)/high risk of ASCVD as well.⁷ Karmur et al find that different strengths of glimepiride/metformin FDCs are commonly prescribed in combination with insulin in patients with type 2 diabetes with favorable efficacy and safety profile.⁸

This issue also features a real-world study on the use of dual action insulin like insulin degludec/insulin aspart (IDegAsp) fixed ratio coformulation. Chatterjee et al show that in insulin-naïve Indian patients with type 2 diabetes inadequately controlled with oral antidiabetic drugs alone, initiating insulin therapy with IDegAsp was superior to insulin glargine (IGlar U100) in terms of glycemic control and also in managing postprandial plasma glucose excursions.⁹

THE PREFERENCE

Sulfonylurea and metformin combinations address insulin deficiency and resistance, both of which contribute to the pathogenesis of diabetes in Indian adults. FDC preparations provide the added advantage of economical, error-free, easy-to-use drug administration.¹⁰

These FDCs can be used along with virtually every non-insulin glucose-lowering drug, except repaglinide, and with certain insulins such as basal insulin.

A similar experience is noted in the insulin space in India. Dual action insulin, also termed as premixed or co-formulation insulin, has been found to be an effective, and efficient, way of achieving glucose control. Insulin preparation such as biphasic insulin, biphasic aspart, lispro mix and IDegAsp offer both prandial and basal coverage, while minimizing the number of injections needed.¹¹

THE EXPLANATION

The preferred choice of drugs, both oral and injectable, in Indian persons living with type 2 diabetes, bears uncanny resemblance. FDCs are preferred over oral monotherapy and FRCs over basal insulin. This seems to be a response to the complex pathogenesis of diabetes, which involves both insulin secretory defect and insulin resistance. It addresses the commonly encountered clinical presentation, which includes both fasting and postprandial hyperglycemia, and may be associated with symptoms. It is mindful of the carbohydrate-based Indian diet, as well as the expressed desire of our patients to achieve glucose control as swiftly as possible, in a safe and well-tolerated manner. The choice of therapy respects the Law of Therapeutic Parsimony,⁴ which enjoins us to manage diabetes with as few doses of drugs as possible.

SUMMARY

This issue of the AJD explores the evidence related to experiences of Indian diabetes care. Taken together, the studies highlight the consistency and concordance of physician's choices in both oral and injectable drug segments.

We emphasize this similarity, and suggest possible reasons for this. Clarification of this facet of diabetes pharmacotherapy will help us understand our response to the etiopathophysiologic complexity of type 2 diabetes and allow us to improve it further.

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