ORIGINAL ARTICLE

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The Effect of DPP4 Inhibitor on Glycemic Variability in Patients with Type 2 Diabetes treated with twice-daily Premixed Human Insulin*

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Abstract

Objective. To evaluate the effect of adding DPP4 inhibitor (DPP4-i) on glycemic variability (GV) in patients with type 2 diabetes mellitus (T2DM) treated with premixed human insulin (MHI).

Methodology. We conducted a prospective study in patients with T2DM on twice-daily MHI with or without metformin therapy. Blinded continuous glucose monitoring was performed at baseline and following 6 weeks of Vildagliptin therapy.

Results. Twelve patients with mean (SD) age of 55.8 (13.1) years and duration of disease of 14.0 (6.6) years were recruited. The addition of Vildagliptin significantly reduced GV indices (mmol/L): SD from 2.73 (IQR 2.12-3.66) to 2.11 (1.76-2.55), p=0.015; mean amplitude of glycemic excursions (MAGE) 6.94(2.61) to 5.72 (1.87), p=0.018 and CV 34.05 (8.76) to 28.19 (5.36), p=0.010. In addition, % time in range (3.9-10 mmol/l) improved from 61.17 (20.50) to 79.67 (15.33)%, p=0.001; % time above range reduced from 32.92 (23.99) to 18.50 (15.62)%, p=0.016; with reduction in AUC for hyperglycemia from 1.24 (1.31) to 0.47 (0.71) mmol/day, p=0.015. Hypoglycemic events were infrequent and the reduction in time below range and AUC for hypoglycemia did not reach statistical significance.

Conclusion. The addition of DPP4-I to commonly prescribed twice-daily MHI in patients with T2DM improves GV and warrants further exploration.

Key words: glycemic variability, dipeptidyl peptidase 4 inhibitors, premixed human insulin, continuous glucose monitoring, type 2 diabetes mellitus

INTRODUCTION

Glycemic variability (GV) has become an emerging target for optimal glycemic control in patients with diabetes independent of HbA1c.[1-3] Recent studies have highlighted the association of GV to hypoglycemia and its associated adverse consequences.[4-6] In addition, there are increasing data in the literature supporting association of GV to microvascular and macrovascular diabetic complications although definitive evidence on hard clinical outcomes remains limited.[1,6-9] Nonetheless, with the advent of continuous glucose monitoring (CGM), the focus of glycemic management in diabetes has moved beyond HbA1c to include reduction of GV and hypoglycemic events.

Type 2 diabetes mellitus (T2DM) is a progressive disease and many patients will require insulin therapy in order to achieve glycemic control. In Asia, premixed insulin, often in combination with metformin, is commonly used for the treatment of T2DM.[10,11] While more convenient for the patients, premixed insulin with a fixed ratio of prandial and intermediate insulin is less flexible and may be associated with more hypoglycemic risk and greater GV. In addition, in resource-limited countries and public institutions, premixed human insulin is still commonly prescribed. Premixed human insulin may further increase the GV compared to premixed insulin analogues due to its less physiological pharmacokinetic profile.[12,13] Hence, a strategy to reduce GV in patients on premixed human insulin is highly desired.

Incretin-based therapies especially the dipeptidyl peptidase 4 inhibitors (DPP4-i) have been increasingly used for the treatment of T2DM. Few studies have shown DPP4-i to be effective in reducing GV in patients treated

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