

Endogenous Insulin Secretion should be priority in Type-2 Therapy

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Abstract

It is argued - why the preferred method to maintain euglycemia in Type-2 should be prioritizing the endogenous insulin secretion, while suggesting possible approaches to research further in that direction. It is known, that most types of peripherally administered insulin (PAI) have drawbacks; viz. being non-native, lacking c-peptide, not mimicking physiological insulin secretion oscillations (ISO) that reduce insulin receptor saturation, contributing to weight gain (often as visceral fat). Also, PAI is far less effective in countering gluconeogenesis, a contributor to hyperglycemia, as it doesn't mimic pancreatic release of insulin into the hepatic entrance of the portal vein as triggered by feeding. Merely maintaining tight-glycemic control may not necessarily reduce endothelial dysfunction. Hence, it may be more beneficial to steer away from PAI as well as exogenous insulin. Although, recent research demonstrates the merits of portally administered insulin, access to the portal vein is not practical. Clearly, stem cells are the right approach and deserves high priority.

While dpp4-i/glp-1, even with concomitant glitazones, are good therapeutic approaches, they remain insufficient to achieve tight glycemic control. They, also, fail to mimic the iso and feeding correlated hepatic portal secretion. Meanwhile it may be beneficial to revisit insulin secretagogues (is) and modify traditional therapy, while improving approaches to endogenous secretion and concomitantly minimizing side effects. Dosage of sulfonylureas should be reduced to maintain a very basal secretion. This should be co-administered with a short acting is (e.g. Meglitinides) prior to feeding. This approach can be titrated to mimic native secretion. Effort should be made to find new molecules that enhance secretion efficiency while minimizing side effects. While β -cellion channels have been exploited, more effort is needed to exploit the glycolysis/ glucokinase aspect. (Poster/presentation will have references)

Article Information

Conference Proceedings: Online Congress on Diabetes & Endocrinology

Conference date: September 23-24, 2020

Inovineconferences.com

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Citation: Muppurala R (2020) Endogenous Insulin Secretion should be priority in Type-2 Therapy. J Clin Res Diabetes Med

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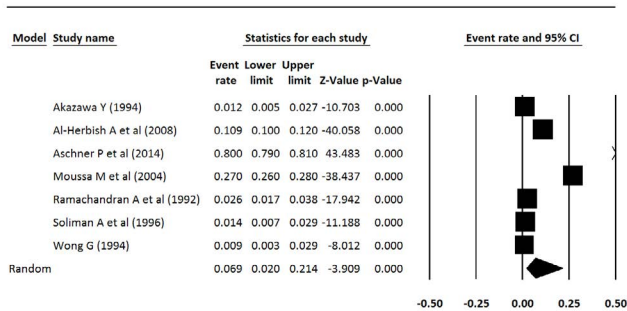


Figure 1. Prevalence of type 1 diabetes in Asia