When to Start Basal Insulin Therapy in Type 2 Diabetes Patients

by Hermina Novida

When to Start Basal Insulin Therapy in Type 2 Diabetes Patients

Hermina Novida

Surabaya Diabetes Nutrition Center
Internal Medicine Department Universitas Airlangga-

Dr. Soetomo Teaching Hospital

Introduction

Type 2 diabetes (T2D) accounts for 90% of all cases of diabetes, however, the vast majority of patients in treatment for T2D have suboptimal glycemic control, with glycated hemoglobin (AIC) levels greater than the 7%. The number of people living with diabetes mellitus in Indonesia has continued to increase over the last decade. Indonesia is ranked 7th in the world in terms of most people with diabetes. There were over 10,700,000 cases of diabetes in adults in Indonesia in 2019 (IDF Atlas, 2019). Data at the Dr. Soetomo Hospital in 2007 showed that the prevalence of DM who underwent hospitalization reached 16.4% with a range of complications and mortality reached 28.8%. As the prevalence of DM is increasing. it is very important to improve glycemic control to delay microangiopathy, neuropathy and other complications of diabetes (Pranoto A et al. 2015).

Traditional oral antidiabetic drugs (OADs) such as sulfonylureas (SUs), thiazolidinediones (TZDs), and metformin, have limited durability with respect to glycemic control. A 6-year survey determined that 53% of patients allocated to treatment with an SU required insulin therapy for the first time by the end of the study period. T2D is a progressive disease, characterized by gradual deterioration in pancreatic beta-cell function, decreasing insulin levels, and increasing insulin resistance, ultimately leading to chronic hyperglycemia. At diagnosis, most patients with T2D have already lost 50% of their remaining beta-cell function, which reduces rapidly over a period of just a few years. This rapid beta-cell decline means that insulin replacement quickly becomes necessary in order to achieve and maintain glycemic control, because other available therapies rely on the body's ability to produce insulin. As such, insulin replacement is the most effective treatment for long-term control of hyperglycemia, and significant improvements in glycemic control can be achieved with this therapy in a short time.

There are 3 stages to insulin therapy: initiation, optimization, and intensification. This review focuses on basal insulin initiation and optimization. The right time to initiate insulin therapy will be considered, as will suggestions for overcoming patient and physician barriers to initiating insulin therapy. Practical formula for patients Starting insulin therapy will be discussed, including the initial optimization of dose titration to achieve target A1c levels (Philis-Tsimikas, 2013).

Management T2D in Indonesia

The Indonesian Society of Endocrinology (Perkeni) is responsible for developing diabetes treatment guidelines in Indonesia. Guidelines for diabetes mellitus type 2 are periodically reviewed and the newest version was last published in 2019. We can initiate using insulin for the naive patients (HbA1c > 9% with symptoms) and also for patients with failed to achieve treatment goal with one or more others antihyperglycemic agents (Perkeni, 2019).

When to Start Basal Insulin Therapy

When glycemic control cannot be achieved using the maximum-tolerated dose of metformin (or another OAD), insulin initiation must be considered as a next step. The new ADA/ EASD joint position statement recommends the introduction of basal insulin as one of 5 treatment options for dual therapy in combination with metforcnin, each being equally preferred, although the higher the baseline HbA1c, the more likely insulin will be required; other options include SUs, TZDs, dipeptidyl peptidase-4 (DPP-4) inhibitors. or glucagon-like peptide-I receptor agonists (GLP-1RAs).

Basal insulin is favored in a triple combination therapy over the other treatment options, as it is likely to be more effective than most other agents, especially when Alc is very high. The main factor affecting the decision to initiate insulin should be the current level of glycemic control, as determined by frequent HbA1c monitoring. However, in practice, other barriers such as clinical inertia, lack of physician time, and the presence or absence of patient insurance prevent insulin initiation taking place (Philis-Tsimikas, 2013).

How to Initiate insulin

Insulin therapy has the powerful advantage of improving the glycemic control better than other OADs, but it may be associated with risks of hypoglycemia and weight gain. Therefore, healthcare professionals need to provide comprehensive self-care education including insulin injection skills, self-monitoring of blood glucose, hypoglycemia management, and simple dosage adjustment before patients begin insulin therapy (Choi et al., 2017).

Basal insulin remains the single most effective medication to reduce hyperglycemia and is a recommended option that can be combined with almost ail other T2D therapies at any time in the course of disease management. Patients for whom basal insulin should be considered include those with complicated noninsulin regimens that may contribute to poor adherence and failure to achieve AIC goals, and patients with T2D who have not attained Al C goals despite multiple treatments cver time (Philis-Tsimikas, 2013).

Basal insulin therapy is designed to replace endogenous basal insulin in patients who lack insulin either completely, as in type 1 diabetes, or partially, as is the case in T2D. The ADA/EASD and the American Association of Clinical Endocrinologists/ American College of Endocrinology state that the goals of insulin therapy are to

replicate, as closely as possible, a normal glycemic profile without unacceptable weight gain or hypoglycemia. These guidelines, and those from the International Diabetes Federation, recommend initiation of insulin with basal insulin followed by titration to a FPG target. Each organization further states a preference for basal insulins over NPH insulin because of their relatively flat action profile over 24 hours, which reduce glycemic variability, and lower hypoglycemia risk.

For patients not previously taking Insulin. the recommended dose of basal insulin is 0.2 U/kg once daily, or 10 U once dally (Perreautt et al , 2019)

Basal Insulin Titration

Targeted titration of basal insulin is an essential part of the process of initiating basal insulin therapy. Regular glucose monitoring is necessary for accurate titration, and patients must be trained in SMBG using commercially available glucose meters and test strips. For most patients initiating basal insulin, SMBG can be done once a day to assess FPG with the dose adjusted upward or downward at regular intervalls based on the results. Adjusting every 2 to 3 days is typically recommended with basal insulin (Perreault et al. , 2019).

Biosimilar Insulin

Biosimilar insulins (hereafter called biosimilars or followon biologics) are designed to be highly similar to the original, or reference, insulin product described in a patent. They are analogous to generic versions of small-molecule drugs and are developed by companies other than the reference product's patent holder Producers of biosimilars use manufacturing techniques that are similar, but likely not identical to, those used by the original patent holder. Thus, although a biosimilar and its reference insulin product will have the same amino acid sequence, they may differ slightly in their more subtle molecular characteristics and clinical profiles. Insulin glargine is expected to be the primary target for biosimilars producers (Rotenstetn et al., 2012).

The growth of biosimilar insulins has generated considerable scientific and clinical interest, partly because in contrast to a typical small molecule product, insulin has well-defined primary, secondary and tertiary structures that are crucial for Its biologic action. Biosimilar insulins glargine are expected to cost less than ther reference products, saving the health care system as much as $44 billion through 2024 (Heinemann L & Hompesch M, 2016). Several studies have published that the biosimilars glargine have comparable safety and clinical efficacy as its reference product (Tieu et al., 2018).

CARDIOMETABOLIC HEALTH TOWARD - 2020
CHALLENGES in PREVFMION and TREATMENT of
DM OBESITY Mets. CMR, and the CMDs   125

Conclusion

The majority of patients in treatment for T2D have suboptimal glycemic control, with glycated hemoglobin (A1c) levels greater than the 7%, When glycemic control cannot be achieved using the maximum-tolerated dose of metformin (or another OAD), insulin initiation must be considered as a next step. Basal insulin remains the single most etfective medication to reduce hyperglycemia and is a recommended option that can be combined with almost all other T2D therapies. Biosimilar insulin glargine are expected less cost with comparable safety and clinical efficacy. These biosimilars may be considered as alternative options for non-basal and basal insulin therapy in patients with type 1 and type 2 diabetes.

REFERENCES

Heinemann L. Hompesch M (2016). Biosimilar Insulins: Basic Considerations. *J Diabetes Sci Technol* 8 (1):6-13. Pmid:24876530

IDF (2019). International Diabetes Federation Atlas 2019.

Perkeni (2019). Pedoman Pengelolaan DM Tipe 2 Dewasa di Indonesia.

Perreautt L, Vincent L, Neumiller JJ, Santos-Cavaiola T (2019). Initiation and Titration of Basal insulin in Primary Care: Barriers and Practical Solutions. *J Am Board Fam Med* 32:431-447

Philis-Tsimikas A (2013). initiating Basal Insulin Therapy in Type 2 Diabetes: Practical Steps to Optimize Glycemic Control. *The American Journal of Medicine* 126, S21-S27

Pranoto A. Novida H, Prajitno JH. Tiokroprawiro A (2015). Safety and Efficacy in Early Insulin Initiation as Comprehensive Therapy for Patients with Type 2 Diabetes in Primary Health Care Centers. *Acta Medica Indonesiana* 47, 104-110

Rotenstein LS. Ran N, Shivers JR Yarchoan M. and Close KL (201 2), Opportunities and Challenges for Blosimilars: What's on the Horizon in the Global Insulin Market? Climcal Diabetes 30(4): 138-150.

Tieu Ca. Lucas EJ. DePaola M, Rosman L, Alexander GC (2018). Efficacy and safety of bjosnar insulins compared to their reference products: A systematic review. PlosOne. https://doi.org/10.1371/journal.pone.0195012

When to Start Basal Insulin Therapy in Type 2 Diabetes Patients

1. Carolyn Tieu, Eleanor J. Lucas, Mindi DePaola, Lori Rosman, G. Caleb Alexander. "Efficacy and safety of biosimilar insulins compared to their reference products: A systematic review", PLOS ONE, 2018
Publication

7%

2. Byung-Wan Lee, Jin Hwa Kim, Seung-Hyun Ko, Kyu-Yeon Hur et al. "Insulin Therapy for Adult Patients with Type 2 Diabetes Mellitus: A Position Statement of the Korean Diabetes Association, 2017", Diabetes & Metabolism Journal, 2017
Publication

4%

3. Sarita Bajaj. "RSSDI clinical practice recommendations for the management of type 2 diabetes mellitus 2017", International Journal of Diabetes in Developing Countries, 2018
Publication

2%

4 R. Chawla, B. M. Makkar, S. Aggarwal, S. Bajaj et al. "RSSDI consensus recommendations on insulin therapy in the management of diabetes", International Journal of Diabetes in Developing Countries, 2019
Publication

1 %

5 T. Ligita, K. Wicking, N. Harvey, J. Mills. "The profile of diabetes healthcare professionals in Indonesia: a scoping review", International Nursing Review, 2018
Publication

1 %

6 Seung-Hyun Ko, Kyu-Yeon Hur, Sang Youl Rhee, Nan-Hee Kim et al. "Antihyperglycemic Agent Therapy for Adult Patients with Type 2 Diabetes Mellitus 2017: A Position Statement of the Korean Diabetes Association", Diabetes & Metabolism Journal, 2017
Publication

1 %

7 Shah, Viral N., Emily G. Moser, Aaron Blau, Megha Dhingra, and Satish K. Garg. "The Future of Basal Insulin", Diabetes Technology & Therapeutics, 2013.
Publication

1 %

Exclude quotes   Off
Exclude bibliography   On

Exclude matches   < 10 words