Starting Insulin Therapy for Type-2 Diabetes

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ABSTRACT

Controlling blood glucose level for diabetic patients can be accomplished by using several methods, such as life style modification, oral medication, and insulin. Many physicians are still hesitant to administer insulin. A great deal of this hesitancy is caused by lack of knowledge on how to practically giving insulin. If administrated correctly, insulin is one of means that effectively control blood glucose level. Insulin administration is often perceived as a daunting issue not only for the patients, but also for the physicians. Comprehensive understanding on insulin is expected to eradicate this fear.

It is one of physician’s roles to choose insulin type and dose. Another role which is no less important is to properly educate the patients, thus any common doubt and mistaken assumption can be put right.

Key words: insulin therapy, type-2 diabetes, diabetic patients.

INTRODUCTION

Diabetic patients facing risk of cardiovascular diseases is not a new issue. An individual with diabetes has 7-fold higher risk of vascular disease. The risk will increase even greater when the blood glucose level is uncontrolled. It may due to several causes. The first cause is increasing Advanced Glycation Endproducts (AGE), which is a substrate developed out of protein glycation by carbohydrate. Glycated protein will loose its function; one example is protein in blood vessel endothelium, which obviously will increase the impaired endothelium function. The second cause is increasing blood glucose will increase free radical production due to exhausted mitochondria capacity to carry out cellular level of metabolism. The third cause is increasing blood glucose will enhance energy metabolism primary pathway in Krebs’ cycle, thus alternative pathway, such as sorbitol pathway, will increase further. The enhancement of such pathways will increase the amount of additional products which will not bring any benefit to endothelium. Based on those causes; good control of blood glucose is an important matter to decrease the risk of cardiovascular disease.

Controlling blood glucose level for diabetic patients can be accomplished by using several methods, such as life style modification, oral medication, and insulin. Insulin administration is often perceived as a daunting issue not only for the patients, but also for the physicians. Comprehensive understanding on insulin is expected to eradicate this fear. The description below may refresh our knowledge on insulin.
HOW DOES INSULIN WORK?

Normal Secretion of Basal Insulin

The liver releases relatively constant glucose level in glycogenolysis process, which slightly increases at night and slightly decreases at dawn. The hepatic glucose production will be followed by basal insulin secretion from pancreas to maintain the blood glucose level in normal range.\(^5\)

Normal Secretion of Pandrial Insulin (Meal-time Insulin)\(^6\)

On each meal, additional insulin is released along with basal insulin to maintain normal blood glucose level. The amount of insulin released depends on the type of carbohydrates, which is called glycemic index, and the amount of fat in the meal.

INDICATION OF INSULIN THERAPY\(^7\)

Who Can Have Insulin Therapy?\(^7\)

Strong indications: Diabetic patients who cannot be controlled using oral hypoglycemic agents, diet, and lifestyle modification, gestational diabetes, weight loss more than 10% over the last 3 months, severe metabolic stress (infection, malignancy, surgery, etc).

Probably having other indications: diabetic patients who have used oral hypoglycemic agents with increased titration dose and eventually reach a better blood glucose control, painful neuropathy, diabetic foot.\(^8\)

When Should Insulin Therapy be Started?

- As soon as possible. Subsequent to rather failed medication, the diabetes cannot be controlled using titrated dose of oral hypoglycemic agents
- After having explanation and discussion on the risk and benefit of insulin therapy.

INSULIN TYPE

Based on the methods of its production, insulin can be categorized into synthetic (analogue) insulin and human insulin, both can be further classified into rapid acting, short acting, intermediate acting (also called isophane Insulin), fixed mixtures (consists of rapid or short acting and intermediate acting insulin), long acting.

Schematically, the mechanism of action is showed on figure 1 (from www.diabetes.org.uk/products/insulin).

Figure 1. Mechanism of insulin activation. A) Short acting meal-time, B) Rapid acting meal-time, C) Intermediate acting basal insulin, D) Long acting basal insulin with peak, E) Long acting peakless basal analogues
Regimen selection is adjusted according to the type of previous medication, patients’ lifestyle, and accompanying risk factors.

Insulin can be administrated in combination with oral medication, or exclusively.

**a. Combination of Insulin and Oral Hypoglycemic Agent (OHA)**

The benefit of using the combination of insulin and Oral Hypoglycemic Agent (OHA) are:
- Reduced the risk of weight gain
- Reduced the hypoglycemia risk.
- Simpler and more convenient for several patients.

Below are several examples of insulin and OHA combination:
- Once-daily intermediate insulin before sleep and OHA is an effective treatment for those with high insulin resistance, such as patients with obesity. Usually, the group of patients selected for this therapy is those with high night and fasting blood glucose, but with a tendency decreased blood glucose level after doing activity.
- Twice-daily pre-mixed insulin and OHA will be effective for those with a tendency of hyperglycemia after meal, but improved on fasting blood glucose test.
- Long acting peakless insulin in day or night, and OHA is usually administrated for those with persistent high blood glucose in daytime and night time.

Other benefit of insulin and OHA combination is the occurrence of ‘flexible compromise’ in patients who need lifestyle modification, with fear of using insulin and need to accept their diabetes condition which already needs insulin.

**b. Twice-daily pre-mixed insulin**

By using mixed insulin, the amount of active insulin in blood is a mixture of insulin inside as seen on Figure 2.

There are 2 types of mixed insulin available in Indonesia, which are: 30/70 composition (30% short acting and 70% intermediate acting); and 25/75 (25% rapid acting and 75% intermediate acting).

**c. Multiple injection therapy (basal-bolus)**

This regimen is the most similar regimen to physiological insulin secretion. Principally, the patients will receive a quantity of ‘basal’ long acting insulin and ‘bolus’ of short acting or rapid acting insulin.

Schematically, this can be explained as follows:
- Short acting insulin and human long acting insulin.

**SELECTING INSULIN REGIMEN FOR PATIENTS**

Principals:
- For every patient, actually there is more than one regimen to be selected
- No best regimen is suitable for every patient.
- In selecting regimen, we have to pay attention not only on how insulin works, but also on adjusting it with meal time, activity, and lifestyle of the patients.

**These are Several Things to Consider**

We can select basal insulin and OHA for this type of patients.
- Overweight.
• Those who are afraid of needle, thus the simplest insulin therapy is being used.
• Those who need other person to give them a shot, thus the patients do not need to be too dependent to other people.

We can select twice-daily pre-mixed insulin for this type of patients:
• Those who can watch over the quantity of their own meal, maintaining them on more or less similar quantity each day.
• Those who are very busy, thus there is a big chance that they do not get their shot if insulin is administrated on day time.

We highly recommend multiple injection therapy for this type of patients:
• Those who have excessive physical activity, such as athletes, people traveling regularly over time zone, work on shift, constantly changing from each shift (day and night).
• Those whose blood glucose is strictly controlled, such as hospitalized patients.

A STEP BY STEP GUIDE TO START INSULIN TREATMENT

These are practical measures which can be a step by step guide to starting insulin treatment.

The main reason of delaying insulin treatment for patients includes physician with lack of confidence. Once the patients are not controlled by oral medication, the physician goes straight for referral.

Steps that can be taken by the physician on insulin treatment are:
• Patients are identified to have indication for insulin treatment.
• Select the most accurate regimen. If there is any doubt, select mixed insulin and OHA regimen.
• Explain the risk and benefit of insulin treatment to the patients.
• If the patient has agreed and after redeeming prescription, at that very time, both physician and patients should perform the first injection together (first agreement, first injection). By injecting the insulin together, it will put confidence in physician and the patients increase.
• Teach the patients on how to properly inject the insulin.
  o Inject using 31G needle.
  o Explain the best shot location (on the abdomen, 4 fingers from the navel; thigh; shoulder; buttoc).

o The location of the shot should be constantly moved, rotation wise, on one area (in example: only on the abdomen).

o There is no need for alcohol.

o The needle should be injected perpendicularly against the skin.

o After injection, leave it for more or less 10 seconds.

o If minor bleeding occurs, do not panic. Just simply press it until the bleeding stops. Mark the location and the patients should not perform any further injection on that bleeding location.

o Mixed insulin and intermediate acting insulin are cloudy as it contains protamine sulphate, thus they should be shaken thoroughly so the agents are mixed and become homogenous.

• The information that needs to be explained to the patients includes clinical signs of hypoglycemia and how to handle it.

• Insulin storage:
  • Once opened, an insulin vial can be kept at room temperature for more or less 1 month.
  • Stock of intact insulin needs to be stored in the refrigerator of 4-8°C

It is expected that by the practical step by step guide as mentioned above, it will lessen any doubt on using insulin for patients who do need insulin.

REFERENCES