Demystifying Insulin Treatment

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Presented at the University of Toronto's Primary Care Today: Educational Conference and Medical Exposition, Toronto, Ontario, May 2007.

Insulin for Type 2 diabetes

The inability of the pancreatic islet ß-cell to secrete adequate amounts of insulin to overcome insulin resistance is the cardinal abnormality causing hyperglycemia Type 2 diabetes. Patients with Type 2 diabetes in the United Kingdom Prospective Diabetes Study (UKPDS) showed a 50% loss of ß-cell function at diagnosis. As the duration of the disease increased, a further decline in ß-cell function was observed. Therefore, it is not surprising that insulin replacement therapy is frequently needed to control hyperglycemia.

Indications for insulin treatment in Type 2 diabetes

Insulin treatment is needed in Type 2 diabetes when individual treatment goals are not attained with a regimen of:

- nutrition therapy,
- physical activity and
- oral antihyperglycemic agents (mono- or combination therapy).

Insulin may be used as initial therapy especially in cases of marked hyperglycemia (A1C ≥ 9.0%).

Better glycemic control

Most oral antihyperglycemic agents reduce A1C levels by an average of 1% to 1.5% and combinations of oral agents can result in further robust reductions in A1C. The response to oral agents depends on pancreatic insulin reserve as well as the degree of insulin resistance. Optimal glycemic control occurs in most patients with the use of appropriate insulin regimens and doses.

Barriers to insulin therapy

Barriers to insulin therapy include:

1. Procrastination: by doctor and patient
2. Hypoglycemia
3. Concern over increasing macrovascular risk
4. Weight gain
5. Lack of resources to initiate insulin and educate patient
6. Cultural and employment factors

A weight gain of 5 kg to 6 kg was seen in the insulin arm over the duration of the UKPDS. In real-life, weight gain with insulin treatment is less when:

- it is combined with metformin,
- hypoglycemia is avoided and
- with nutritional counselling.

Three per cent of patients in the insulin treatment arm in the UKPDS suffered one or more severe episode of hypoglycemia yearly, compared to only 0.5% of those taking a sulfonylurea. Less severe hypoglycemia occurred in 40% of insulin-treated patients compared to 11% to 18% of those treated with a sulfonylurea.

There is no evidence that insulin treatment increases macrovascular risk.

Other barriers to insulin treatment need to be addressed and are generally related to:

- a lack of resources,
- a lack of time and
- inadequate compensation for diabetes management.

Insulin and oral antihyperglycemic agents

Metformin, secretagogues and acarbose in combination with insulin results in an increased reduction in glucose levels; thus, a reduced insulin dose is required to reach glucose targets.

The use of insulin with thiazolidinediones is not an approved indication in Canada.

Starting insulin

Insulin can be given in combination with oral antihyperglycemic agents, as this is the most acceptable regimen for many patients. If patients are on metformin and/or an insulin secretagogue, then these are usually continued and bedtime basal insulin is added. Begin by adding 10 to 15 units of basal insulin at bedtime and titrate as indicated below.

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Titration of basal insulin

Normal or near normal fasting glucose is 4 mmol/L to 6 mmol/L, or 4 mmol/L to 7 mmol/L. Titrate by one unit every night until fasting glucose levels fall between 4 mmol/L and 6 mmol/L.

Insulin may be used as initial therapy especially in cases of marked hyperglycemia (A1C ≥ 9.0%).

If hypoglycemia occurs, reduce the dose by two units or change isophane insulin human (NPH) to either glargine or detemir at the same dose. Once fasting glucose levels reach target, continue the same regimen as long as A1C is also at target.

Meal insulin

If A1C is above target while fasting glucose is controlled, direct your attention to the measurement of two-hour postprandial glucose (PPG). If PPG is above target, which is 5 mmol/L to 10 mmol/L for most (or 5 mmol/L to 8 mmol/L if it can be safely attained) add short-acting (regular) insulin or rapid-acting analogue insulin (*e.g.*, aspart or lispro) staring at five to six units prior to each meal.

Alternatively, a pre-mixed insulin regimen of the following can be administered:

- NPH 30/70, six to 10 units b.i.d.,
- insulin lispro and insulin lispro protamine 25 (*i.e.*, 25% lispro/75% human protamine lispro), six to 10 units b.i.d.,
- insulin aspart (*i.e.*, 30% aspart/70% protaminated aspart), six to 10 units b.i.d., or before each meal t.i.d.

Table 1

Insulins available in Canada

Basal insulins
- Isophane insulin human (NPH)
- Glargine
- Detemir

Meal insulins
- Regular
- Lispro
- Aspart

Pre-mixed insulins
- Regular insulin/NPH:
  - 30 regular/70 NPH
  - 40 regular/60 NPH
  - 50 regular/50 NPH
- Insulin lispro injection 25:
  - 25% insulin lispro and 75% human protamin lispro, an intermediate-acting insulin
- Insulin lispro 50:
  - Insulin 50% lispro and 50% human lispro
- Insulin aspart 30:
  - 30% aspart
  - 70% protaminated aspart (an intermediate-acting insulin)

Adjust the dose daily to attain PPG targets or according to pre- and post-meal glucose levels, if you use pre-mixed insulins. Once meal insulin is used, insulin secretagogues should be discontinued. Table 1 offers an overview of insulins available in Canada.

Teaching patients to use insulin

Take the following steps when attempting to teach a patient how to use insulin in five to seven minutes:
- Show the patient the equipment needed to inject insulin (pen or syringe)
- Have them practice insulin dialing (pen), or withdrawal from a bottle (syringe)
- Have the patient inject themselves with an injection in your office. You can use two to three units of NPH or long-acting analogue. Most patients will be pleased with how painless the injection is
- If available, refer to the Diabetes Centre for further education or see the patient in a few days to a week
- Review hypoglycemia:
  - symptoms,
  - prevention and
  - treatment Dx

Resources
1. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with Type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group. Lancet 1998; 352(9131):837-53.
2. Lebovitz HE: Insulin secretagogues: Old and News. Diabetes Rev 1999; 7:139-53.
3. Hanna A, Woo V, Dawson K, et al: Pharmacological management of Type 2 diabetes. CJD 2003; 27(Suppl 2):37-42.
4. Riddle MC, Rosenstock J, Gerich J, et al: The treat-to-target trial: Randomized addition of glargine or human NPH insulin to oral therapy of Type 2 diabetic patients. Diabetes Care 2003; 26(11):3080-6.
5. Hermansen K, Davies M, Derezinski T, et al: A 26-week, randomized, parallel, treat-to-target trial comparing insulin detemir with NPH insulin as add-on therapy to oral glucose-lowering drugs in insulin-naive people with type 2 diabetes. Diabetes Care 2006; 29(6):1269-74.