PHARMACISTS' INTERACTIVE EDUCATION CASE STUDIES

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Case 1 – Type 1 diabetes in an adolescent

AJ is a 13-year-old (weight = 35kg) male recently diagnosed with type 1 diabetes. His mother gives you a prescription for:

Glargine (Lantus®) – four units at bedtime, increase by one unit at bedtime, until morning blood glucose ~ 7 mmol/L

M: 5 x 3mL, R: 3

Aspart (NovoRapid) – four units three times a day before meals, increase as directed

M: 5 x 3mL, R: 3

AJ's mother explains she does not have a drug plan and wonders if there is a less expensive and just as effective insulin available?

Question:

What would you tell AJ's mother?

You may want to discuss the basic differences between the insulin analogues and human insulin with AJ's mother (e.g., onset of action, peak, and duration of activity) and review the costs of each product (refer to chart below).

Cost of insulin[1]:

Brand Name	Ingredients	Retail price ($)/mL*
Intermediate and long-acting insulins (Basal insulin)		
Humulin N cartridge 5 x 3mL	Insulin isophane (NPH)	2.46
Humulin N vial 10mL	Insulin isophane (NPH)	1.89
Novolin NPH penfill 5 x 3mL	Insulin isophane (NPH)	2.53
Novolin NPH vial 10mL	Insulin isophane (NPH)	1.94
Levemir penfill 5 x 3mL	Insulin detemir	7.32†
Lantus 100 units/mL vial, 10mL	Insulin glargine	5.68
Lantus 100 units/mL cartridge 5 x 3mL	Insulin glargine	5.68
Immediate and rapid-acting insulins (Bolus insulin)		
Humulin R cartridge 5 x 3mL	Insulin regular	2.53
Humulin R vial 10mL	Insulin regular	1.89
Novolin Toronto vial 10mL	Insulin regular	1.94
Novolin Toronto penfill 5 x 3mL	Insulin regular	2.54
Humalog cartridge 5 x 3mL	Insulin lispro	3.44
Humalog vial 10mL	Insulin lispro	2.58
Novorapid vial 10mL	Insulin aspart	2.69
Novorapid penfill 5 x 3mL	Insulin aspart	3.58
Mixed insulins		
Novolin 10/90 penfill 5 x 3mL	Insulin regular/NPH	2.52
Humulin 30/70 cartridge 5 x 3mL	Insulin regular/NPH	2.53
Humulin 30/70 vial 10mL	Insulin regular/NPH	1.89
Novolin 30/70 vial 10mL	Insulin regular/NPH	1.94
Novolin 30/70 penfill 5 x 3mL	Insulin regular/NPH	2.53
Novolin 40/60 penfill 5 x 3mL	Insulin regular/NPH	2.59
Novolin 50/50 penfill 5 x 3mL	Insulin regular/NPH	2.59
Humalog Mix 25, 5 x 3mL	Insulin lispro/insulin lispro protamine	3.44
Humalog Mix 50, 5 x 3mL	Insulin lispro/insulin lispro protamine	3.44
NovoMix 30 penfills, 5 x 3mL	Insulin aspart/insulin aspart protamine crystals	3.35

*Ontario Drug Benefits Formulary/Comparative Drug Index [database on the Internet]; 2008 Dec 3.
†Danielle Groleau, NovoNordisk Canada, Mississauga, ON: personal communication, 2008 Dec 9.

Question :

AJ's mother asks that you call the prescribing physician to change the prescription. What would you say to the physician?

Teaching Point #1[2]

When a basal insulin is required, insulin NPH is suggested over the long-acting insulin analogues (i.e., insulin glargine or insulin detemir) in most children with type 1 diabetes (CERC recommendation 1.1.2).

The evidence shows that for most patients the incremental cost of long-acting insulin analogues over insulin NPH outweighs their modest clinical benefit.[2] Although the evidence is limited and inconsistent, the long-acting insulin analogues had lower risk and rates of hypoglycaemia in both adults and children, especially nocturnal events.[3] Patients experiencing significant hypoglycaemia while taking insulin NPH, may benefit from long-acting insulin analogues.[4]

Unlike insulin NPH given twice daily, children treated with long-acting insulin analogues require an injection of bolus insulin at lunchtime. This may be impractical during school hours for young children (<14 years of age), since teachers usually cannot administer, or supervise the administration of insulin.[2]

Teaching Point #2[2]

In adolescent patients with type 1 diabetes, rapid-acting insulin analogues may be considered as first-line therapy. (Key Message #1)

The benefits seen with insulin lispro over regular human insulin outweighs the incremental cost associated with the rapid-acting analogues.[2] The evidence shows that there is reduced incidence of nocturnal and overall hypoglycemia in the adolescent population with rapid-acting insulin analogues.[2] In addition, flexibility of dosing with the rapid-acting insulin analogues also provides a better fit for those individuals with unpredictable patterns of dietary intake and physical activity.[2]

Case #2 – Type 1 diabetes in a pregnant adult

Mrs. DQ is a 30-year old pregnant female with type 1 diabetes for over 10 years. Her diabetes is controlled with insulin NPH and insulin regular before meals. She heard there is a new insulin that is more convenient.

Question:

What would you tell her?

Teaching Point #1

Review pros and cons of products with patient to provide information to assist patient with making a decision in conjunction with their health care provider. See table below.

Advantages and disadvantages of the available insulins:[5]

Insulins	Advantages	Disadvantages
BOLUS		
Short-acting human insulin -Human Regular	More long-term safety experience Low cost Safe for use during pregnancy	To give 20-30 minutes pre-meal may be impractical
Rapid-acting insulin analogues -Aspart -Lispro	Dietary flexibility (may give just before or within 5-10 minutes of starting meals[6] May experience less hypoglycemia Patient satisfaction Safe for use during pregnancy	More costly Limited long-term and safety evidence
BASAL		
Intermediate-acting human insulin -NPH	Long-term safety and outcome evidence Low cost Safe for use during pregnancy	Slightly higher risk of hypoglycemia compared to long-acting insulin analogues
Long-acting insulin analogues -Detemir -Glargine	Slightly less risk of hypoglycemia vs. NPH Possibly more convenient if given once-daily	More costly No significant difference in severe hypoglycemia Limited long-term and safety evidence Use with caution during pregnancy
Premixed	Convenient	More costly Limited flexibility with fixed dose

Teaching Point #2[2]

In patients with type 1 or type 2 diabetes requiring insulin, insulin NPH should be considered first. Although the evidence is limited and inconsistent, patients who are experiencing significant hypoglycemia while taking insulin NPH may benefit from long-acting insulin analogues. (Key Message #3)

In patients with type 1 diabetes, either regular human insulin or rapid-acting insulin analogues can be considered as first-line therapy (except in adolescent patients).
(Key Message #1).

Question:

What other information would you ask her?

Sample questions you could ask:

1) Have you experienced any signs or symptoms of hypoglycemia?
2) What are your pre- and postprandial blood glucose results?
3) Are your blood glucose levels on target?
4) How are you taking the insulin now? (Establish whether she is taking insulin regular 20-30 minutes before meals)

Question:

What would you recommend for this patient?

Teaching Point #3[7]

This would be a good opportunity to review the recommended glycemic targets.

Recommended glycemic targets preconception and during pregnancy

	Glycemic targets
Pre-pregnancy: A1C (%)	≤ 7.0 (≤ 6.0 if possible)
Once pregnant	
Fasting plasma glucose and preprandial plasma glucose (mmol/L)	3.8-5.2
1-h postprandial plasma glucose (mmol/L)	5.5-7.7
2-h postprandial plasma glucose (mmol/L)	5.0-6.6
Pre-bedtime snack plasma glucose (mmol/L)	4.0-5.9
A1C (%)	≤ 6.0 (normal)

Teaching Point #4[2]

Either regular human insulin or a rapid-acting insulin analogue (i.e., insulin aspart or insulin lispro) can be used in most pregnant women who have type 1 diabetes. (CERC recommendation 2.1.4)

Current evidence shows no significant difference in A1C, severe hypoglycemia, or overall hypoglycemia between rapid-acting insulin analogues and human insulin. The use of rapid-acting insulin analogues may be considered when flexibility of insulin administration with respect to meals is of primary importance, and in patients with unpredictable dietary patterns.[2]

Basal insulin (see Teaching Point #2)

There is a lack of evidence comparing the effectiveness between insulin NPH and long-acting insulin analogues in pregnant women with type 1 diabetes.[2] The 2008 Canadian Diabetes Association (CDA) Guidelines also recognize that there is insufficient evidence on the use of insulin detemir and insulin glargine in this population. In exceptional circumstances when a woman cannot tolerate insulin NPH because of nocturnal hypoglycemia, the CDA suggests insulin detemir be considered after discussing the risks and benefits.[7]

You may also want to include how these products are classified for use in pregnancy during your discussion on which product to recommend.

Insulin in Pregnancy[8]

Category B = Likely safe = Regular, Toronto, insulin aspart, insulin lispro, NPH
Category C = Caution = insulin glargine, insulin detemir

B = Likely safe = Minimal risk, either no evidence of risk in animals or risk found in animal studies not reproduced in humans
C = Caution = Potential risk = Risk evident from studies in animals and/or no human studies available. Use only if benefit outweighs risk. May be more or less safe depending on trimester.

Case #3 – Gestational diabetes

Mrs. KC is 30 weeks pregnant, and has just been diagnosed with gestational diabetes. She tried dieting and light exercise; but was not successful. She comes into the pharmacy with the following prescription:

Insulin glargine – 10 units at bedtime, increase by two units every two days until fasting blood glucose is near 5 mmol/L

M: 5 x 3mL, R: 3

Insulin lispro – three units before breakfast, four units before lunch, and five units before supper or as directed. M: 5 x 3mL, R: 3

Cost is not an issue.

Question:

What other information is required from her?

Sample questions you could ask:

1) What are your current fasting plasma glucose, 1-h postprandial plasma glucose, 2-h postprandial plasma glucose, and A1C levels?
2) How often do you check your blood glucose levels?

Question:

What would you recommend to Mrs. KC?

Teaching Point #1[2]

Either regular human insulin or rapid acting insulin analogues (i.e., insulin lispro or insulin aspart) can be used in most women who develop gestational diabetes. (CERC recommendation 2.1.5)

Current evidence has shown no significant difference between human insulin and insulin lispro for A1C or overall hypoglycemia. In a comparison of human insulin and insulin aspart in women with gestational diabetes, there was no significant difference observed in A1C and none of the hypoglycemia (severe, nocturnal, and overall) measures favoured insulin aspart over human insulin.[2]

Teaching Point #2[2]

Basal Insulin (See Case #2 for insulin use in pregnancy)

- There are no comparative trials looking at insulin NPH and long-acting insulin analogues in women with gestational diabetes. Review the advantages, disadvantages, and safety of these two types of insulin products as shown in Case #2.
- You may choose to discuss the possibility of switching the prescription to insulin NPH directly with the physician.

Teaching Point #3

This may also be a good opportunity to review plasma glucose targets for women with gestational diabetes.

Target Plasma Glucose in gestational diabetes[7]

Measurements	Plasma Glucose (mmol/L)
Fasting Plasma Glucose	3.8 – 5.2
1-h postprandial plasma glucose	5.5 – 7.7
2-h postprandial plasma glucose	5.0 – 6.6

Case 4 – Type 2 diabetes in an adult

Mr. AF is a 55-year old male (weight = 85 kg, height = 5'8") with type 2 diabetes mellitus. He is currently taking metformin 1000mg twice daily, and glyburide 10mg twice daily. He comes into the pharmacy with the following prescription:

Insulin detemir (Levemir®) 10 units at bedtime, increase by two units every two days until morning blood glucose near 7 mmol/L. M: 5 x 3mL, R: 3.

Insulin aspart (NovoRapid®) three units before breakfast, four units before lunch, and five units before supper or as directed.

M: 5 x 3mL, R: 3

Question:

When is it appropriate to consider initiating insulin?

Insulin therapy should be initiated if targets cannot be achieved with lifestyle changes and oral therapy[7]

- Glycemic targets must be individualized: however, therapy in most individuals with type 1 or type 2 diabetes should be targeted to achieve an A1C ≤ 7.0% in order to reduce the risk of microvascular complications and in individuals with type 1 diabetes, macrovascular complications.[7]
- A target A1C of ≤ 6.5% may be considered in some patients with type 2 diabetes to further lower the risk of nephropathy, but this must be balanced against the risk of hypoglycemia and increased mortality in patients who are at significantly elevated risk of cardiovascular disease.[7] A higher A1C target may be appropriate in these patients. Intensive therapy in type 2 diabetes increases the risk of severe hypoglycemia by 2-to-3 fold, particularly among those using insulin.[7]

Other factors:

- Type 2 diabetes with severe infection, undergoing major surgery, or requires corticosteroid therapy
- Ketoacidosis or hyperosmolar nonketotic syndrome
- Rapid glucose reduction/control desired
- A1C ≥ 9.0% +/- symptomatic hyperglycemia with metabolic decompensation

Question:

Mr. AF is hesitant to add insulin to his current treatment regimen. What advice could you provide to get his buy-in for initiating insulin?

Consider the following points in your discussion:

- benefits of insulin therapy
- use of newer insulin devices (ie., insulin pens)
- provide training for patient in administration of insulin injections
- refer patient to community support programs involving a Certified Diabetes Educator

What other factors are important to discuss with a patient initiating insulin? (Optional)

You may want to include the following items in your discussion:

- Incorporating insulin into current treatment regimen
- How the optimal insulin dose is calculated (0.1-0.2 units/kg)
- Establishing a time to follow-up with the patient
- Review treatment targets
    - Timely adjustments to and/or addition of antihyperglycemic agents should be made to attain target A1C within 6 to 12 months.[7]

It is also a good time to review the importance of proper nutrition and physical activity in diabetes management and insulin therapy.

Mr. AF does not have a private drug plan and cannot afford insulin detemir or insulin aspart. What would you recommend to him and his physician?

Teaching Point #1[2]

When a basal insulin is required, insulin NPH is recommended over the long-acting insulin analogues (i.e., insulin glargine and insulin detemir) in most adults with type 2 diabetes taking oral antidiabetes drugs (CERC recommendation 1.1.3). If a long-acting insulin analogue is used, there is no preference between the available agents (CERC recommendation 1.2.2).

The long-acting insulin analogues have no advantage in reducing A1C and in some cases appear to be slightly worse. The advantage appears to be a reduction in hypoglycemia, especially nocturnal hypoglycemia, although the evidence is limited and inconsistent.[2]

Teaching Point #2[2]

When a bolus insulin is required, regular human insulin is suggested over the rapid-acting insulin analogues for most adults with type 2 diabetes (CERC recommendation 2.1.7). If a rapid-acting insulin analogue is used, there is no preference between the available agents.

The evidence shows small improvements in A1C (although not clinically significant) with the use of rapid acting insulin analogues. The small impact on rates of hypoglycemia that are seen with these agents may be important in certain populations.[2]

Ask the group how they would discuss the following issue with the patient (optional).

If Mr. AF was willing to pay for insulin detemir or insulin aspart, would you call the physician to discuss the possibility of changing the prescription?

Question:

Mr. AF experienced nocturnal hypoglycemia on insulin NPH – 30 units at bedtime (at 0400, blood glucose = 3.2 mmol/L) once last week. He treated the nocturnal hypoglycemia episode with ¾ cup of orange juice and a peanut butter sandwich. The morning of nocturnal hypoglycemia, fasting blood glucose = 15.5 mmol/L. What additional information would you ask Mr. AF? What would you recommend?

Sample questions you could ask:

1) What are your pre- and postprandial blood glucose measurements?
2) What is your most recent A1C level?
3) How often do you experience hypoglycemia (blood glucose < 4.0mmol/L) during the day?
4) How often has nocturnal hypoglycemia (blood glucose <4.0mmol/L) occurred in the past month?
5) Do you have symptoms consistent with nocturnal hypoglycemia, such as waking up with a wet pillow case or bed sheets, waking up with a headache, or feeling hungry?
6) What were your fasting blood glucose results with lower doses of insulin NPH at bedtime?
7) How often do you check your blood glucose level at 0300-0400?

Recommendations[9]

Decrease insulin NPH 30 units at bedtime to 28 units at bedtime and recheck blood glucose at 0300-0400 at least once weekly. Decrease insulin NPH by two units at bedtime until blood glucose at 0300-0400 is within normal range (ideally 4-8 mmol/L)

- Nocturnal hypoglycemia prevention is a priority and should include the insulin which does not "peak" between 2100 and 0300. The addition of a bedtime carbohydrate snack may be necessary if bedtime blood glucose levels warrants it (<6-8 mmol/L) or there has been sustained exercise that day.
- Ideally, it is better to lower the insulin NPH dose at bedtime to prevent nocturnal hypoglycemia.
- If hypoglycemia persists despite the decrease in NPH or fasting blood glucose is not well controlled, then consider switching to insulin glargine or insulin detemir.

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