UNIVERSITY of York

Insulin Management in Type 2 Diabetes

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Overview

Which insulin regimens should we be using and why ?

Insulin Initiation Pathway for People with Type 2 Diabetes

When to initiate insulin

- The aim of the treatment is to improve glycaemic control and quality of life.
- Oral hypoglycaemic agent (OHA) prescription is to the maximum tolerated dose and desired HbA1c not achieved (<59 mmol/mol)
- OHA not tolerated/contra-indicated
- Check concordance of medication (OHA)
- Symptoms related to poor glycaemic control
- Patient agrees to and understands the benefits of insulin therapy

Before insulin therapy

- Reinforce dietary advice and discuss lifestyle issues and employment i.e. smoking and physical activity
- Check ability to administer own insulin / carers district nurse involvement
- Patients should be taught home blood glucose monitoring advice to monitor blood glucose at different times.
- Refer to specialist diabetes dietitian if appropriate
- Assess for diabetes related complications

Different regimes which may be considered when initiating insulin therapy in people with type 2 diabetes

Basal Insulin with oral hypoglycaemic agents

- Overweight BMI >26
- Reluctance to start insulin
- Unable to inject themselves
- The older person with no complications but where hypoglycaemia is unacceptable

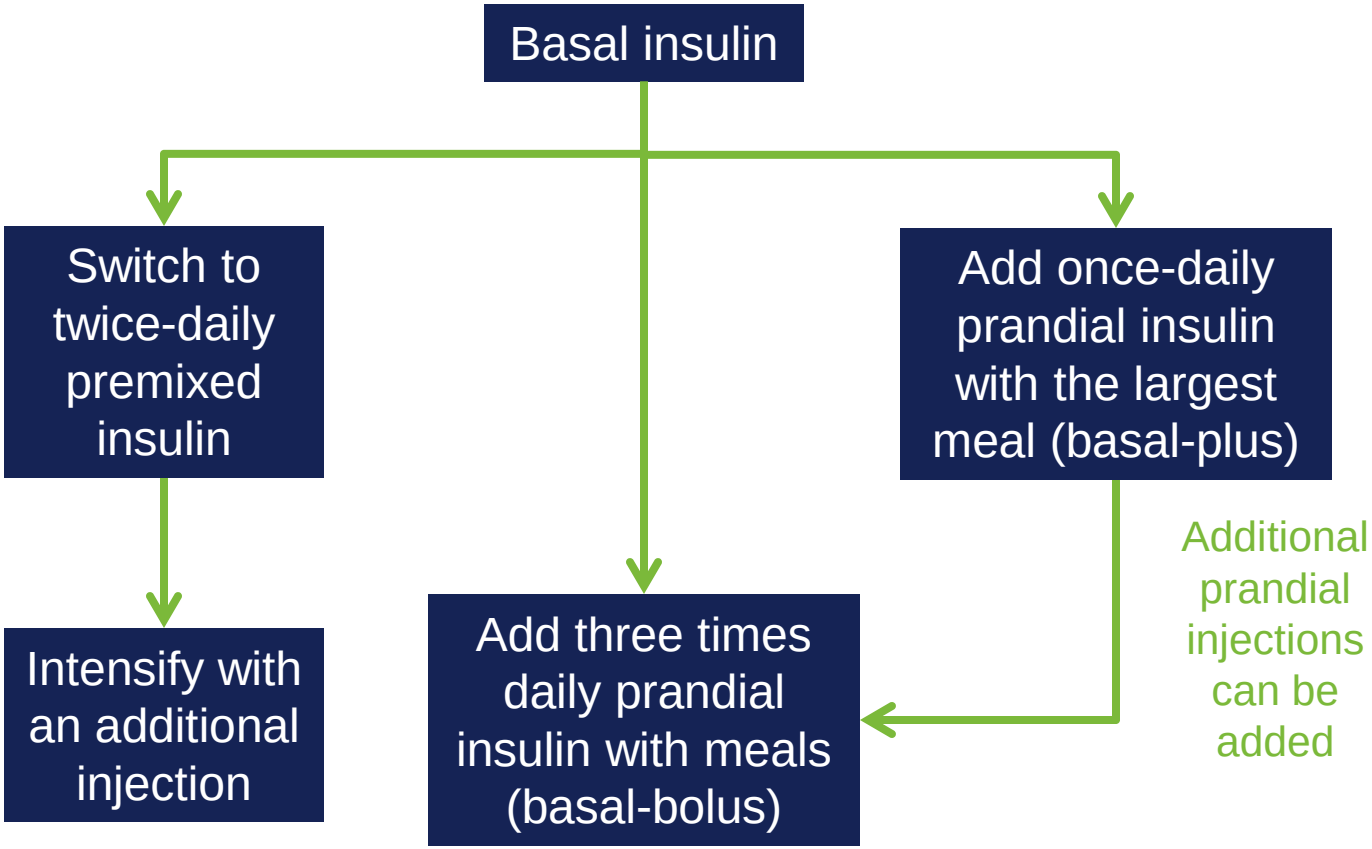
Twice daily pre-mixed insulin with oral hypoglycaemic agents

- Regular lifestyles
- Eat similar amounts at similar times of the day
- OHAs are no longer stimulating efficient insulin production leading to post prandial high blood glucose level
- Symptomatic

Basal Bolus consider referral to Diabetes specialist nurse to initiate this regime

- On daily/bd insulin regimes without optimal control
- Requiring flexibility due to an erratic lifestyle
- Shift work
- Regular travel across time zones
- Regular sport
- To optimise blood glucose control because of complications

Common options for intensifying basal insulin regimens



Adapted from Barnett A et al (2008) *Int J Clin Pract* **62**: 1647–53

Basal Human Insulin

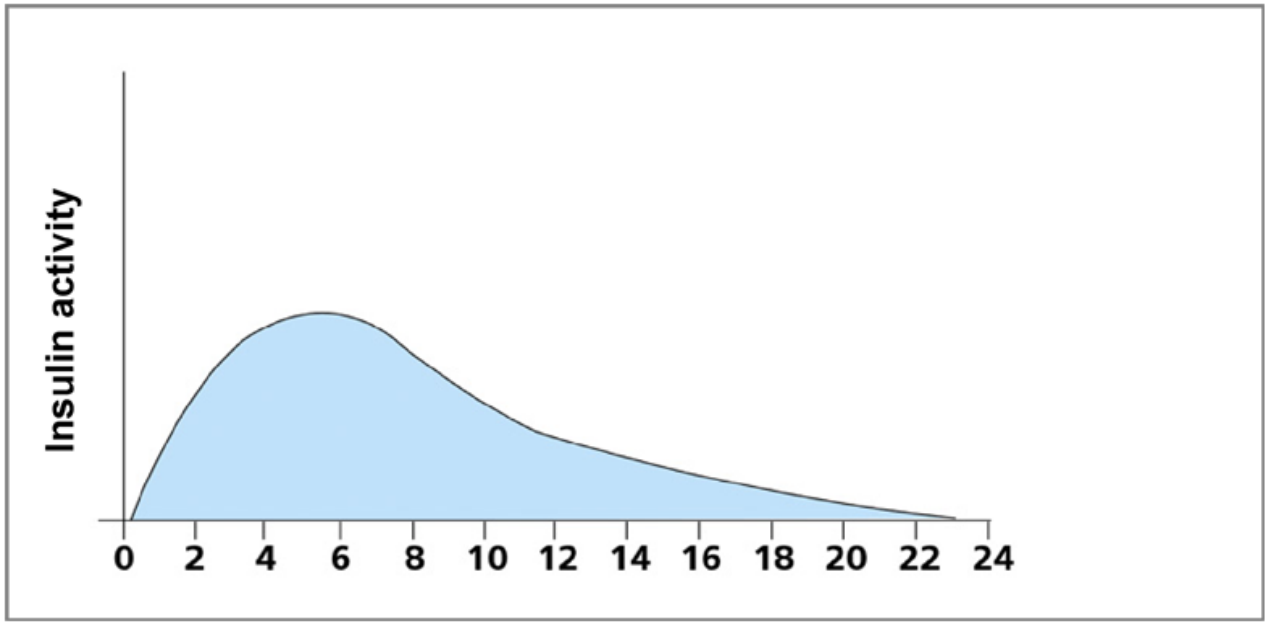
- NPH first line choice (NICE, 2009)
- Starting with a dose before bed
- Titrate in line with fasting blood glucose levels
- Continue with OHA to help control day time blood glucose levels
- May be given twice daily if blood glucose levels indicate it
- Associated with less weight gain and less hypos

Basal Human Insulin

Humulin I

Insulatard

Insuman Basal



Getting started

- Commence once daily basal insulin in the evening - 10 units start dose
- Continue Metformin if tolerated
- Consider continuing sulfonylureas
- Teach the patient to titrate insulin dose by 2 - 4 units every 3 - 5 days
- Aim for fasting blood glucose of 5 – 8 mmol/l

What are the choices?

- Humulin I -
  - Kwikpen
  - 3ml Cartridges (Savvio Pen)
- Insulatard -
  - Innolet
  - 3ml Cartridges (Novopen 4)
- Insuman Basal -
  - Solostar pen
  - 3ml Cartridges (Clikstar pen)

Basal Analogue

- Lantus or Levemir

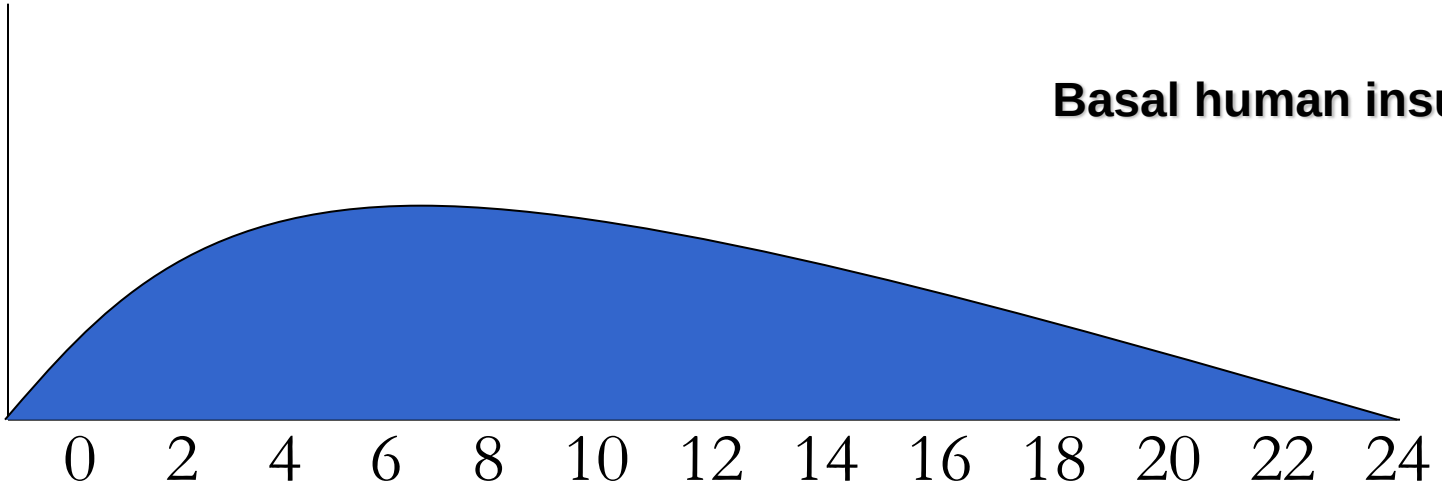
Consider:

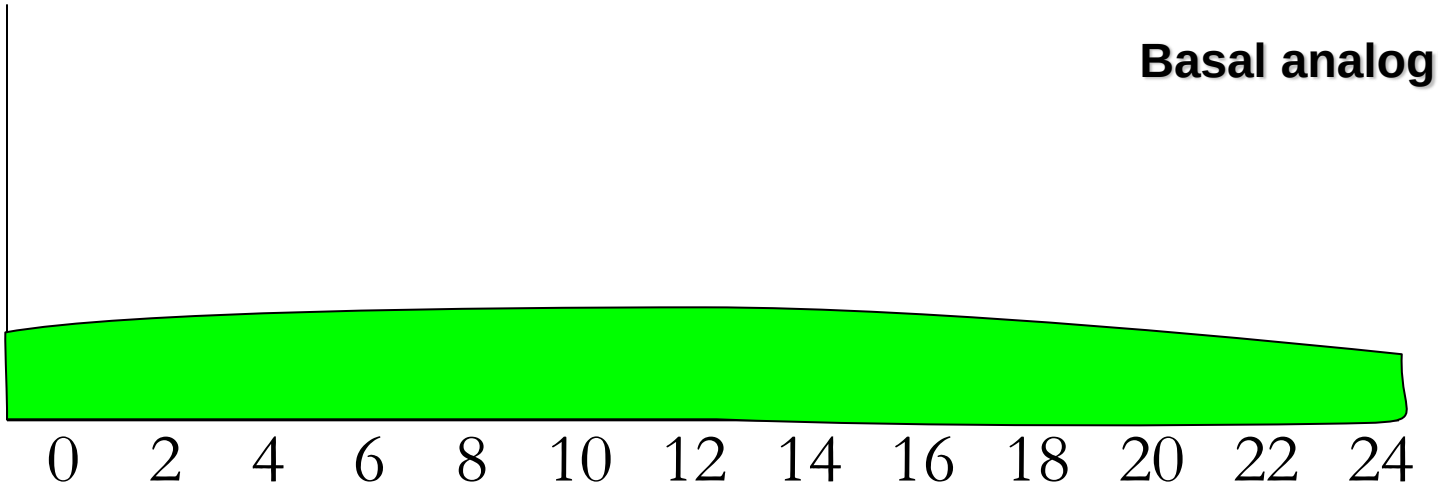
- If person needs assistance from a carer or healthcare professional to inject insulin and therefore reduce the frequency of injections
- If hypoglycaemia is a problem with NPH

What are the choices?

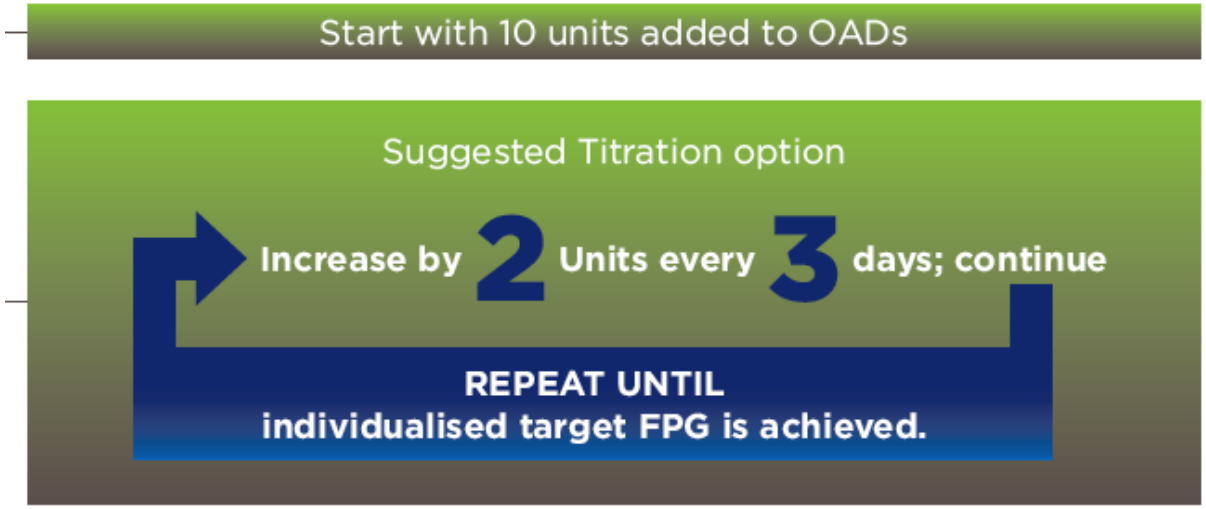
- Lantus
  - Solostar
  - 3ml Cartridges (Clikstar pen)
- Levemir
  - Flexpen
  - Innolet
  - 3ml Cartridge (Novopen 4)

Human Basal V Basal Analogue





Example algorithm for titrating human basal insulin from a randomised controlled trial



Exceptions to algorithm:

1. No increase in dose if fasting plasma glucose ≤4 mmol/L at any time in the preceding week
2. Small insulin dose decreases (2-4 unit/day per adjustment) are allowed if severe hypoglycaemia (requiring assistance) or a fasting plasma glucose of 3.1 mmol/L is documented in the preceding week

Yki-Jarvinen H et al (2006) *Diabetologia* **49**: 442–51

Titration guidelines

Fasting blood Glucose mmol/l	Action
>10	Increase by 4 units
8 – 10	Increase by 2 units
5 - 7	No change
3 - 5	Reduce by 2 units
<3	Reduce by 4 units

Example 1

Breakfast	Lunch	Tea	Bed
6.5		12.9	
7.2	13.2		
8.5		14	
6.8			12
7.8	16.2		

50 year old man, doesn't want to inject more than once

- Humulin I – 56 units before bed
- Metformin 1g BD

Example 1

- FBG stable
- Elevated levels during the day
- Patient doesn't want another injection
- Consider adding in Gliclazide, titrate inline with day time blood glucose levels.
- Re-iterate hypo/ driving advice
- Consider adding GLP-1

Example 2

- 80 year old lady, able to give own insulin
- Humulin I – 40 units before bed
- Metformin 1g BD
- Gliclazide 160mg BD

Breakfast	Lunch	Tea	Bed
6.5	8.5	12	12.6
7.5	8.0	12.5	15
7.6	7.9	11	10.5
8.2	8.2	12.3	13.0

Example 2

FBG satisfactory

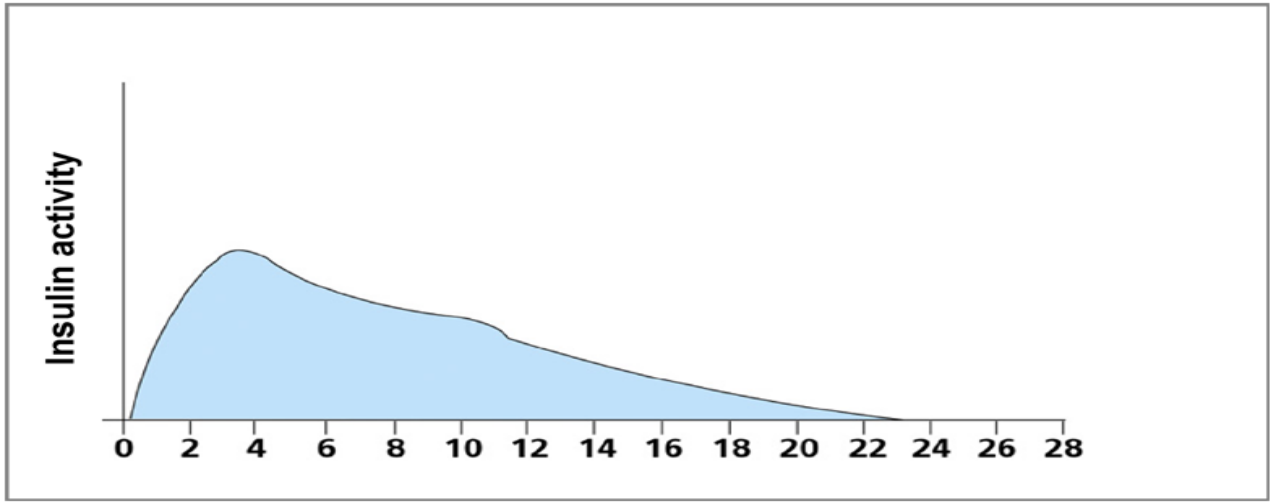
Main problem is slight elevation of levels during the day

Review HbA1c, consider age and hypo risk of intensifying treatment

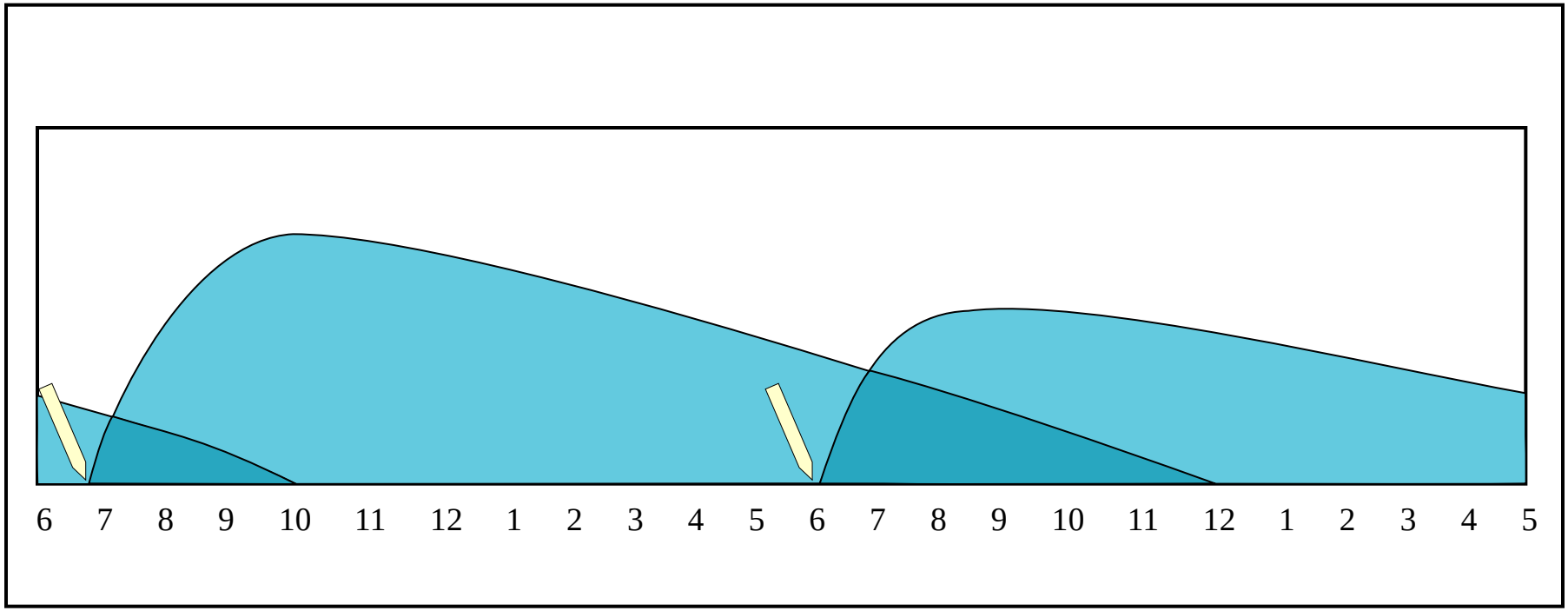
Consider adding a small dose of Humulin I with breakfast and titrate inline with blood glucose levels during the day

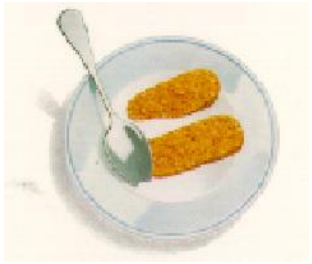
Twice Daily pre mixed human insulin

- Consider if HbA1c ≥ 75mmol/mol (9%)
- If unable to achieve control on basal insulin
- Regular lifestyle
- Increased risk of weight gain / hypoglycaemia than with basal insulin
- NICE recommend human mixtures



BD Pre Mixed Human Insulin





Breakfast

Lunch

Evening Meal

Sleep

What are the choices?

- Humulin M3
  - Kwikpens (disposable device)
  - 3ml cartridge
  - (M3 is a 30% short-acting and 70% NPH mix)
- Insuman Comb 15 / 25 / 50
  - 3ml cartridge
  - Solostar pen (disposable device) 25 mix only
  - (Insuman Comb 25 is a 25% / 75% mix)

Getting started

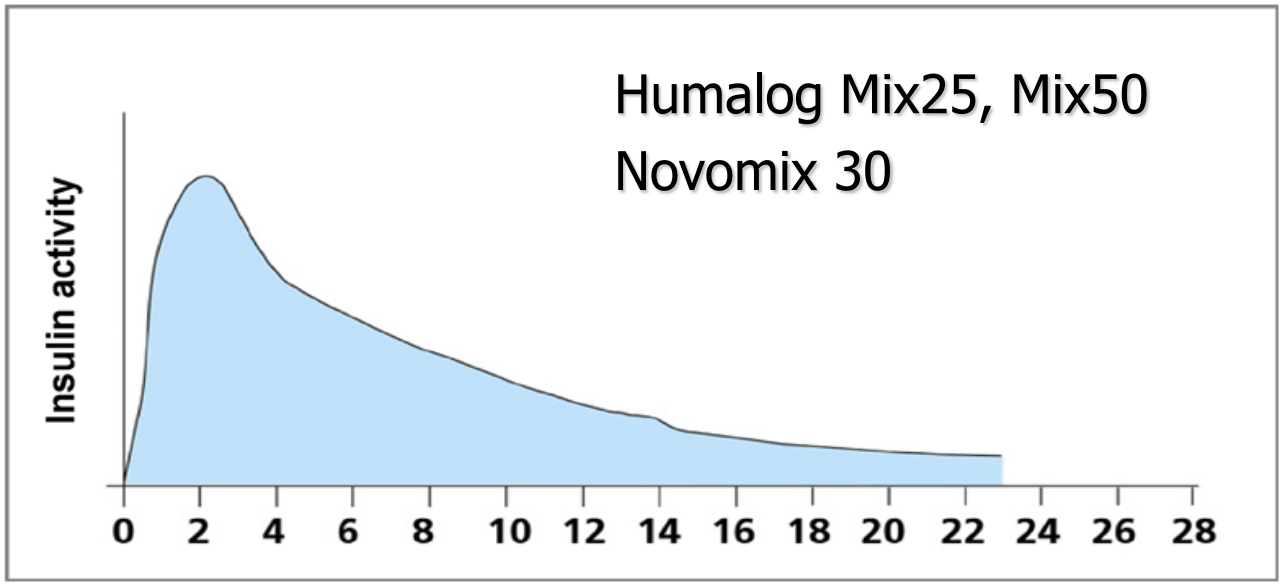
- In insulin naive patients usually start with 10 units BD
- If switching from once daily basal insulin:
  - Consider reducing dose by 10 -20%
  - Either 50 /50 spilt of dose or 2/3rds am 1/3 evening
  - Stop Sulfonylureas
  - Continue Metformin if tolerated
- Need to be injected 30 – 40 mins pre meal

When to consider an analogue mix?

- Analogue mixtures provide a quicker onset of action and offer some advantage in people with post prandial meals rises.
- May also help prevent hypoglycaemia in between meals, due to quicker/shorter action of rapid insulin
- If injection timing an issue

Insulin Analogue Mixtures

- Inject twice daily, within 0 to 15 minutes before or after meals.
- Useful in rapid post prandial rise as works quicker

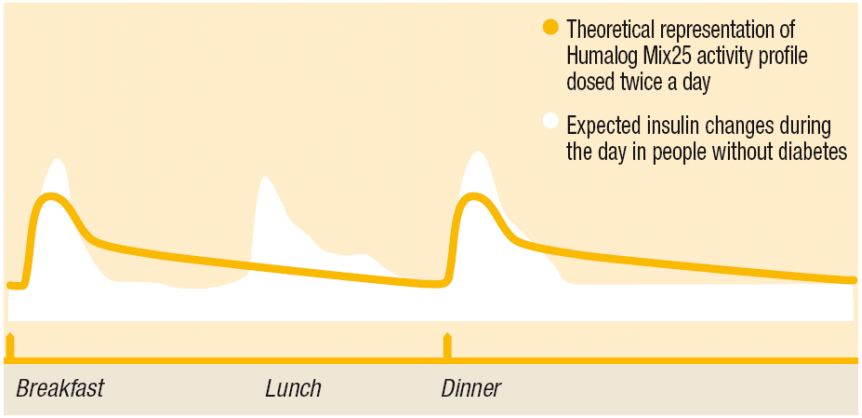


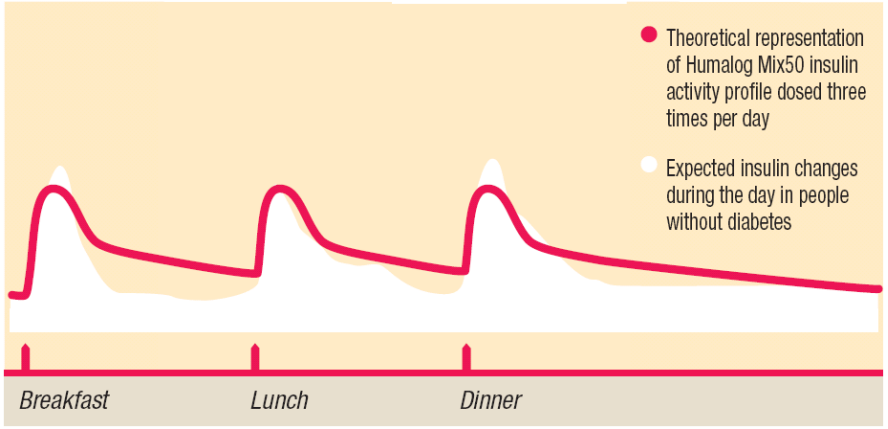
What are the choices?

- Humalog Mix 25, 50
  - Kwik pen
  - 3ml cartdriges (Savvio pen)
- Novomix 30
  - Flexpen
  - 3ml Cartridges (Novopen 4)

TDS Insulin Mixtures

- ‘Humalog Mix 50’ generally one of choice
- Higher amount of quick acting insulin per dose
- Ideal for those with a high CHO intake with meals
- Generally given 3 times a day with meals
- Don’t usually use human mixed insulin due to the concerns re stacking of insulin and increased risk of hypoglycaemia


Theoretical representation of Humalog Mix25 activity profile dosed twice a day
Expected insulin changes during the day in people without diabetes
Breakfast
Lunch
Dinner


Theoretical representation of Humalog Mix50 insulin activity profile dosed three times per day
Expected insulin changes during the day in people without diabetes
Breakfast
Lunch
Dinner

Titration guidelines

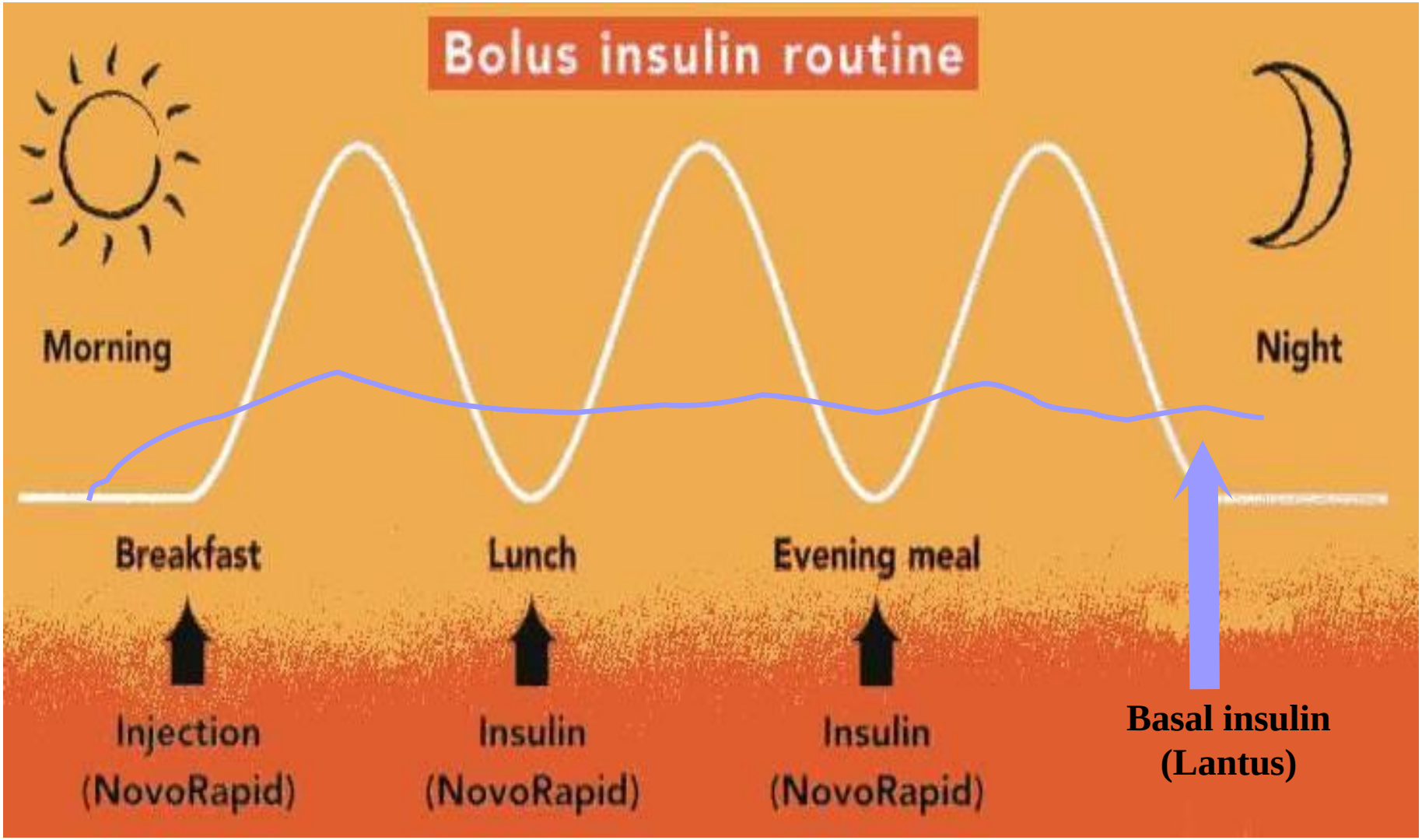
Increase insulin every three - five days and review until individual targets are achieved

BD mix

- Morning dose titrated against pre lunch, pre evening meal blood glucose
- Evening dose titrated against pre bed and pre breakfast blood glucose

TDS mix

- Morning dose titrated against pre lunch, blood glucose
- Lunch dose titrated with pre evening meal blood glucose
- Evening dose titrated against pre bed and pre breakfast blood glucose


Bolus insulin routine
Morning
Night
Breakfast
Lunch
Evening meal
Injection
(NovoRapid)
Insulin
(NovoRapid)
Insulin
(NovoRapid)
Basal insulin
(Lantus)

Basal plus

- Addition of prandial rapid acting insulin to basal insulin (Humulin I, Insuman basal, Insulatard)
  - Monitor 2hr -post meal blood glucose,
  - Give rapid dose with main meal or highest post meal blood glucose level
  - Stepwise approach leading to injection with each meal
  - Usual starting dose 6 units
    - NovoRapid / Humalog / Apidra
- Continue on basal insulin

Example 3

- 50 year old lady
- Humulin M3 50 units BD
- Metformin 1g BD

Breakfast	Lunch	Tea	Bed
6.5	7.5	15	8.2
7.5	8.1	12.5	9.5
6.9	6.5	14.3	8.5
8.0	6.9	15.5	10

Example 3

- Elevated levels before evening meal
- Lunch appears to be elevating levels
- Review diet ???
- Consider giving TDS mix 50 so lunch is covered with the quick acting component of the Mix 50

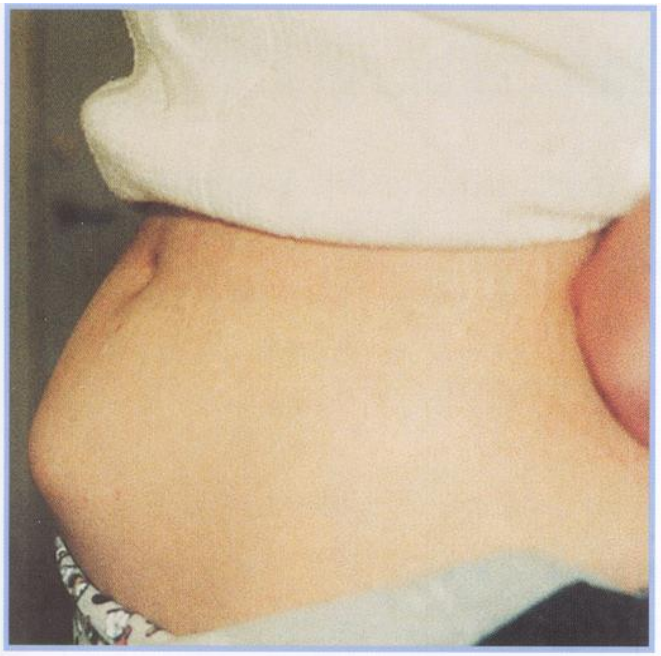
What else do we need to know?

- Blood glucose monitoring
- Hypoglycaemia management
- Illness management / sick day rules
- Injection rotation & sharps disposal
- Driving
- Identification / insulin passport
- INSULIN TITRATION guidelines.

Needle size

Needle length	Injection technique recommendation
5mm 	
8mm 	
12,7mm 	

Lipohypertrophy



Treatment of hypoglycaemia

- Blood glucose below 4 mmol/l
  - 4- 5 glucotabs
  - 100mls lucozade
  - 3-4 jelly babies
  - 1x mini can of coca cola.
- RECOVERY 10 – 15 MINS
  - Longer acting Carbohydrate
  - 1 portion fruit / 2 plain biscuits / 1 slice of bread.

Blood glucose testing -

- Individual assessment based on
  - Number of injections
  - Occupation / driving
  - Treatment

- Consider post meal in patients who you suspect of post prandial hyperglycaemia.

DVLA requirements

- Specific to insulin treated – treated patients with group 1 entitlement
  - Must have awareness of hypoglycaemia
  - Must not have had more than one episode of hypoglycaemia requiring assistance of another person in the preceding 12 months
  - There must be appropriate blood glucose monitoring
  - Must not be regarded as a likely source of danger to the public while driving
  - The visual standards for acuity and visual field must be met.

Costs

- Consider human basal and mix initially

- Analogue basal and mix insulin to be considered when clinically indicated

- Take care when considering change for people taking animal insulins – they are most probably on these for a reason !!!

- Analogues are routinely used in the management of type 1 diabetes due to their predictability.

Cost comparison

based on prefilled disposable pens x5

	Basal	Biphasic
Lilly	**Humulin I -** £21.70	**Humulin M3** - £21.70 **Humalog Mix 25 / 50 -** £30.98
Novo Nordisk	**Insulatard -** £20.40 **Levemir -** £42.00 **Degludec -** £72.00	**Novomix 30 -** £29.89
Sanofi Aventis	**Insuman Basal -** £19.80 **Lantus -** £41.50	**Insuman Comb 25 -** £19.80

Insulin regimens for type 2 diabetes compared

Basal

- 1 insulin
- 1-2 injections

Pros
- Simplicity
- Once daily blood testing

Cons
- Controls background blood glucose only

BD Human Mixtures (30/70)

- 1 insulin
- 2 injections

Pros
- Simplicity
- Covers breakfast and evening meal

Cons
- Lack of flexibility
- Regular meal patterns
- Inject about 30 mins prior to meals
- Regular snacks

BD Analogue Mixtures

- 1 insulin
- 2 injections

Pros
- Simplicity
- Inject and eat
- Covers breakfast and evening meal
- Maybe used where hypoglycaemia is a problem with human mixtures

Cons
- Lack of flexibility
- Regular meal patterns

TDS Analogue Mixtures

- 1 insulin
- 3 injections

Pros
- Inject and eat
- Covers breakfast, lunch and evening meal
- Simple fixed mixture

Cons
- Lack of flexibility
- Regular meal patterns

Basal +,++,+++*

- 2 insulins
- 2,3,4 injections

Pros
- Flexibility to have irregular meal times
- Inject and eat

Cons
- Requires self titration and carbohydrate counting

* + indicates the addition of a bolus insulin

Basal Bolus

- 2 insulins
- 4/5 injections

Pros
- Flexibility to have irregular meal times Inject and eat

Cons
- Requires self titration and carbohydrate counting
- Frequent blood glucose monitoring

LOW — Patient Skills and Capabilities — HIGH

Summary

- Stepwise approach to insulin regimens
- Newer non-insulin therapies should be considered first, especially if weight / hypoglycaemia risk is an issue
- No one insulin regimen fits all
- Intensification necessary in majority of patients over time
- Individual assessment on most appropriate regimen is required

Case Studies

- In groups – you will given one case study to look at - brainstorm ideas for five minutes and feed back