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# Medi Quest BRS Hospital

A monthly News letter from BRS Hospital

## Usage of Insulin in Type 2 diabetes for the Practitioner

**Dr Praveen Balachandran**
MD Int Medicine
Asst Professor SRM Medical College Hospital Kattankalathur
Visiting Consultant BRS Hospital

**Dr S Ramesh** MD DCH
Consultant Pediatrician
BRS Hospital

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Editors

Dr.B.Madhusudhan,
MS.MCh.,DNB(Plastic)

Dr.S.Ramesh,MD,DCh

28,Cathedral garden Rd,
Nungambakkam,
Chennai - 600 034.
Phone:
044 - 61434250
044 - 61434230
Email:
brsmediquest@gmail.com
Web:
www.brshospital.com

### Excerpted from

A Practical Approach to the Initiation, Titration and Intensification of Insulin Therapy in Adults with Diabetes in the Indian Context: Recommendations by Association of Clinical Endocrinologists Consensus Group -Dr Ravi Sankar Erukulapati et al Clinical Diabetology 2024, Vol 13 , No 1

### Introduction

Diabetes is a chronic diseases that affects 537 people world wide . Insulin is mandatory in Type 1 diabetes . Although Oral Anti Diabetic drugs remain the mainstay of treatment for people with type 2 diabetes in the early stages , insulin therapy becomes essential as the disease progresses to sustain life .In India four out of every 10 people with T2D use insulin, either alone or in combination with OADs

### Indications of Insulin

1.In people with Type 1D
2.Individuals with newly diagnosed T2D with HbA1c >10 % , S.Glucose more than 300 mg/dl or catabolic /osmotic symptoms
3.People with T2D who are unable to achieve glycemic control with three OADs.
4.In hospitalised patients with T2D with acute illness ,infection and sepsis
5.In pregnant patients with Type 2 diabetes

### Classification of insulins

The insulins currently in use are Human Insulins and Insulin Analogs

### Human Insulins

Recombinant DNA technology creates insulin with same amino acid sequence identical to the human form ,in a lab

Different Types of Human Insulins (Adapted from [19] and [20])

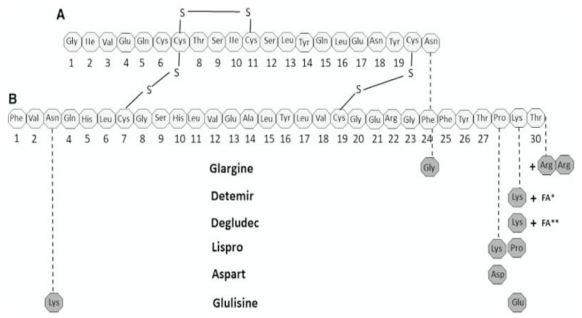
| Human insulin types | Onset | Peak | Duration | Examples |
|---|---|---|---|---|
| Short-acting (regular) [19] | 30-60 minutes | 2-4 hours | 5-8 hours | Humulin® R Insuman® R Actrapid® |
| Intermediate-acting [19] | 2-4 hours | 4-12 hours | 12-24 hours | NPH |
| Premix human insulins [20] | 30 minutes | 2-8 hours | Up to 24 hours | Mixtures of regular and NPH insulin in 25/75, 30/70, and 50/50 proportions |

NPH — neutral protamine Hagedorn

### Analog Insulins

Are same as Human Insulins , produced by same recombinant technology , but here amino acid sequence is changed or they are tagged with fatty acids. Insulin analogs are superior in management

with reduced risk of hypoglycemia. Insulin analogs are classified as rapid acting insulin (RAA), Ultra rapid acting insulin (URAA), long acting insulin analogs (LAA), Ultralong Acting insulin analogs (ULAA) and premix analog preparations




Human insulin schematic showing the amino acid sequences of the two chains (A-chain and B-chain) linked by two disulfide bridges and changes in amino acid sequences in selected insulin analogs. *FA, fatty acid; **FA, fatty acid linked to lysine through a glutamic acid linker.

Table 2. Different Types of Analog Insulins Available in India (Adapted from [19], [20] and [21])

| Analog insulin type | Onset | Peak | Duration |
|---|---|---|---|
| Ultra-rapid-acting insulin (faster aspart) [19] | 10–20 minutes | 1–3 hours | 3–5 hours |
| Ultra-rapid-acting insulin lispro [21] | 15–18 minutes | 1–2 hours | ~ 4 hours |
| Rapid-acting analog (RAA) insulin (Insulin aspart, insulin glulisine, insulin lispro) [19] | 15–35 minutes | 1–3 hours | 3–5 hours |
| Long-acting analogs (LAA) | | | |
| Glargine [19] | 2–4 hours | 8–12 hours | 22–24 hours |
| Detemir [19] | 1–2 hours | 4–7 hours | 20–24 hours |
| Ultra-long-acting analogs (ULAA) | | | |
| Glargine U300 [19] | 2–6 hours | Minimal peak | 30–36 hours |
| Degludec [19] | 30–90 minutes | Minimal peak | > 42 hours |
| Pre-mix analog preparations | | | |
| Biphasic IAsp [21] | 10–20 minutes | 1–4 hours | Up to 24 hours |
| 70% aspart protamine, 30% aspart | | | |
| 50% aspart protamine, 50% aspart | | | |
| Biphasic lispro [21] | 15–30 minutes | 1–3 hours | 12–24 hours |
| 75% lispro protamine, 25% lispro | | | |
| 50% lispro protamine, 50% lispro | | | |
| IDegAsp co-formulation [21] | 10–20 minutes | 1–2 hours | > 24 hours |
| 70% degludec, 30% aspart | | | |

## Initiating insulins in people with T2D

The initial regimen can be basal insulin or premix insulin in patients with T2D.
When FPG is high consider initiating insulin therapy with basal insulin . When both FPG and PPG are high,one may consider initiating insulin therapy with premix insulin

BBR is the initial insulin regimen in acutely unwell and hospitalised people with T2D, women with T2D planning pregnancy when other regimens have not achieved optimal glucose control

Metformin, GLP1-RA, SGLT2i, DPP4i and alpha glucosidase inhibitors can be continued upon insulin initiation unless not tolerated or contraindicated .
Sulphonyl ureas are usually discontinued after insulin initiation, except with basal insulin regimens.

Pioglitazone can be used with insulin therapy with extreme caution considering the weight gain and water retention side effects

**Titrating insulins in people with T2D**

Insulin doses should be titrated regularly at least once a week , but more frequently if required . FPG levels and PPG levels should be aimed at 80-130 mg /dl and 140-180 mg /dl respectively

Initially titration should be done to control FPG , followed by PPG for prandial insulin with the highest glycemic fluctuation in a sequential order

## Basal Insulin available in India include

Intermediate Acting Insulin
NPH
Long Acting Analogs
Glargine U100 (Lantus)
Determir (Levemir)
Ultra Long Acting Analogs
Degludec (Tresiba)

## Initiation of basal insulins

Starting dose of basal insulin is 6-8 units/day or 0.1 to 0.2 units/kg/day if HbA1c is < 8%, 2/3rd does is given before breakfast and 1/3rd before dinner.
And 8-10 units/day or 0.2 to 0.3units /kg/day if HbA1c is more than 8%

## Titration

The active titration period is defined as the time period when the physician adjusts the basal insulin
Dose. This period usually lasts up to 12 weeks after starting insulin therapy .

The recommended target for titration is FPG of 80-130 mg/dl . Titrate once a week but more frequently if needed . The dose can be modified based on the lowest/mean value of three most recent FPG values. The dose may be reduced by at least 20% for individuals reporting hypoglycemia (<70mg/dl) unless there is a identifiable one off cause of hypoglycemia.

Uptitration
Insulin dose can be up titrated by 2 units every three days
Upon titration if FPG is 80-130 mg/dl no dosage change, 131-160 mg/dl increase by 2 units , 161-200mg/dl increase by 4 units and if more than 201mg/dl by 6 units.
Review other OADs during titration

If glycemic goals are not met add 1 prandial insulin before the largest meal at 4 units or 0.1unit/kg whichever is less
If glycemic targets are still not met change to premix insulins/co formulation insulin or basal bolus regimen

**Premix regimen**
Premix insulin therapy is appropriate for people who are

- Have constant eating patterns
- Unable to calculate CHOs
- Have a predictable life style

## Once a day Premix regimen

**A.Initiation when HbA1c is ≤ 8**
If HbA1c is ≤ 8, premix insulin can be initiated at 6-8 units with the largest meal of the day

**B.Titration**
The recommended target for titration is a premeal value of 80-130 mg/dl

Breakfast dose adjustments are titrated based on predinner values . If predinner values are 80-130 mg/dl no dosage change, 131-160 mg/dl increase by 2 units , 161-200mg/dl increase by 4 units and if more than 201mg/dl by 6 units.

And dinner dose adjustments are titrated based on pre breakfast values . If prebreakfast values 80-130 mg/dl no dosage change, 131-160 mg/dl increase by 2 units , 161-200mg/dl increase by 4 units and if more than 201mg/dl by 6 units.

The dose can be modified based on the lowest/ mean value of three most recent predinner/prebreakfast glucose values

For individuals reporting hypoglycemia (< 70mg/dl) reduce dose by 20% unless there is a one off cause for hypoglycemia

Human premix insulins are given 30 minutes before meals , premix analogs can be given just before a meal or after a meal

## Twice a day Premix regimen

**A. Initiation**
When BID premix /co-formulation is necessary for a insulin naïve person (HbA1c more than 8% ) it is recommended to start at 12-16 units or higher doses and divide the total daily dose as 60% at breakfast and 40% at dinner

**B. Titration**
Is similar to what has been mentioned for once a day premix insulin , titrate at least once a week and more frequently if needed.

If glycemic targets are not met and the target HbA1c is not reached even after 3 months one may intensify premix /coformulation from OD to BID and BID to TID . When intensifying from OD to BD dose increase TDD by 10 % and split 60% at breakfast and 40% at dinner.

## Thrice a day Premix regimen

**A. Initiation**
While intensifying from BID to TID , if pre dinner values are above target , one may initiate 4-6 units at lunch , while reducing the breakfast dose by 10 %. Whenever TID premix is required it is recommended to prefer 50/50 over 30/70 premix insulin

**B. Titration**
For TID Premix insulin breakfast insulin dosage is adjusted based on pre-lunch glucose values , lunch insulin dosage is adjusted based on pre dinner values and dinner insulin based on FBG.

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**Basal Plus Insulin Regimen**

A basal plus method is the addition of a single prandial insulin to the already used basal regimen before the main meal or the meal commensurate with the highest PPG .

**A.Initiation**

Can be initiated with a short acting insulin at a dose of 4 units or 0.1 unit/kg body weight with the main meal of the day in addition to the basal insulin

**B. Titration**

The recommended target for basal dose titration is FPG of 80-130 mg/dl . The prandial insulin is recommended to be titrated once a week , but more frequently if required , based on 2 hr PPG \

value .

Recommendation on titration of basal insulin

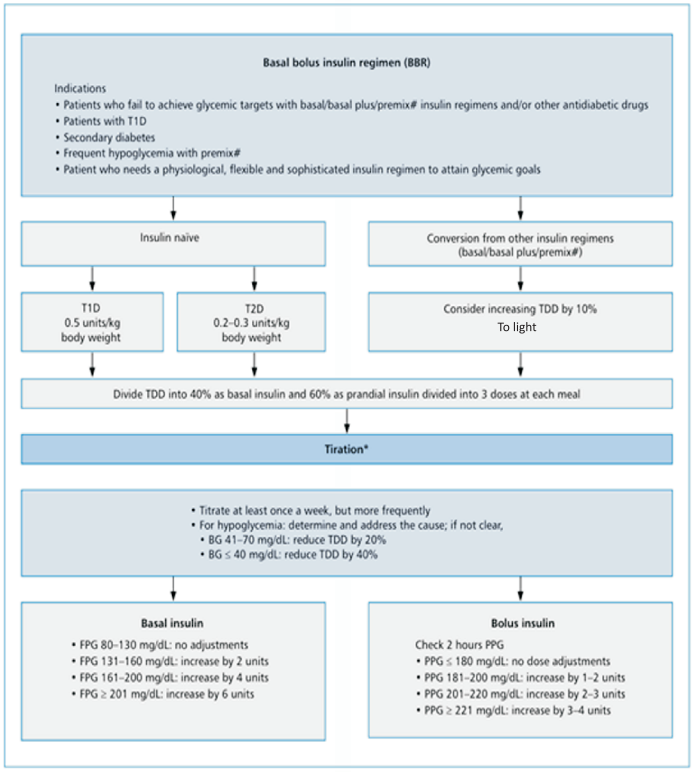
| FPG (mg/dL) | Dose adjustments (units) |
|---|---|
| 80–130 | 0 |
| 131–160 | + 2 |
| 161–200 | + 4 |
| ≥ 201 | + 6 |

Recommendation on titration of prandial insulin

| PPG (mg/dL) | Dose adjustments (units) |
|---|---|
| ≤ 180 mg/dL | 0 |
| 181–200 | + 1 to 2 |
| 201–220 | + 2 to 3 |
| ≥ 221 | + 3 to 4 |

**Basal-bolus regimen**

Basal bolus regimen is used when basal /basal plus /premixed /coformulation insulin regimens with or without OADs, does not achieve target glycemic control . It almost replicates the natural production of insulin by the pancreas. A long acting insulin is used as basal insulin to control fasting /premeal glucose and short acting insulin as bolus is administered with each meal to control PPG excursions.




To be continued

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