Choosing An Insulin Analogue Regime

B Kalra, S Kalra

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Abstract

Conventional insulin therapy has been the backbone of diabetes management for the past 8 decades. However, it suffers from various lacunae (1), viz.• Slow onset of action, • Marked inter- and intra- patient variability• Mismatch between peak insulin action and peak glucose meals• Increased risk of post prandial hyperglycemia• Risk of pre pyramidal hypoglycemia.

INSULIN ANALOGUES

Insulin analogues are modified variants of insulin which overcome these short comings and create physiological insulin profiles, leading to smoother glycemic control. Insulin analogues (2,3) include

- Basal insulins detemir glargine
- Rapid-acting analogues aspart lispro
- Premixed combinations protaminated aspart 30:70 protaminated lispro 25:75; 50:50

Insulin analogues are indicated in a variety of situations. This paper will review the special situations in which analogues are being used, and focus on the premixed analogues as a means of achieving safe and simple control in the vast majority of patients.

INDICATIONS FOR ANALOGUES

1.Situations with uncertainty in lifestyle/meals:

Variable lifestyle, uncertain meal times, quantity, snacks, exercises and inability to maintain injection – meal gap, e.g.

- Children
- Elderly
- Busy working people
- Sportsmen
- Policemen/army personnel/fire-fighters

2.Situations with high/unpredictable fasting blood glucose:

High or unpredictable FBG, Somogyi phenomenon, Dawn phenomenon, nocturnal hypoglycemia, high risk of hypoglycemia, brittle diabetes.

- Renal failure
- Hepatic failure
- Malabsorption/ gastrointestinal upset
- Elderly
- Children

3.Situations with high PP blood glucose, low pre-meal BG, poor HbA1c (in spite of ‘good’ glucose values)

- Pregnancy
- ? Weight gain with conventional insulin
- ? Acanthosis nigricans.
- Steroid induced diabetes mellitus

4. Situations with ‘critical’ patients/ requiring immediate management

- ICU/ICCU patients being shifted from IV to SC insulin.
- Post transplant diabetes mellitus.
- Peri-operative patients.
- OPD management of ketonuria/ketosis with IM rapid acting analogues. (4)

ANALOGUES IN SCHOOL CHILDREN (5)

Unique problems that school children with diabetes face are :

- Uncertain moods /meal quantity.
- Long breakfast- lunch gap.
- Midday meal at school, without insulin.
- Risk of hypoglycemia in school.
- Unplanned exercise/ physical activity.
- Unplanned snacks.

A 12 week long single – centre, prospective, randomized, open-label study at Bharti Hospital, Karnal, India, compared premixed aspart before breakfast, and dinner; and regular aspart before lunch, vs. conventional four dose bolus- basal regime in school children with type 1 diabetes. There were 29 children in aspart group and 23 in conventional group (3 drop outs). Baseline age, duration of diabetes and HbA1c were similar.

Self reported concordance was higher with aspart regime (3/29 missed ≥ 1 injection in preceding 1 week) than the conventional regime (6/20). Mild hypoglycemia was less in aspart regime (0.66 episodes/pt./week). than conventional regime (2.59 episodes/pt./week). Fasting glucose was similar and postprandial glycemic control was markedly better in the premixed aspart group as compared to the conventional group .HbA1c improvement (-2.88 vs -2.05%).

CHOOSING AN APPROPRIATE REGIME

Not all insulins are alike, and neither are all insulin regimes the same.

Choosing the correct regime is important, as a wrong choice may lead to hypoglycemia or poor control.

A wrong choice can also make the patient discontinue therapy. (and the doctor as well !)

Diabetes is a dynamic disease, and the treating physician may need to change the regime as per the requirements of the illness.

One may have to upgrade the regime (increase the number of units &/or the number of doses) if control is not achieved, or the comorbid conditions worsen.

Similarly, the doctor may want to downgrade therapy (decrease the number of units and/or the number of doses) if good control is achieved, co morbid illness resolves, or the patient is unwilling for intensive treatment.(2,3)

CLASSIFICATION OF INSULIN REGIMES

Traditionally, insulin regimes have been classified as:-

- Basal
- Pre-mixed
- Intensive

With the availability of pre-mixed analogues, it has become simpler to start and intensity insulin therapy. A simpler classification that is proposed for insulin regimes is (6, 7) :-

- One – dose
- Two – dose
- Three – dose

This classification covers the multiple ways in which premixed analogues can be utilized.

ADVANTAGES OF PREMIXED ANALOGUES

Premixed analogues, usually administered as 30:70 mixtures, are efficient in

- Achieving glycemic control
    - Fasting glycemia
    - Post prandial glycemia
    - Hb A1c
- Reducing hypoglycemia (8)
    - Total
    - Nocturnal
    - Major events

These 30:70 mixtures are able to achieve successful therapeutic outcome because of the simplicity of use by both physician and patient.

One can begin with a single – dose insulin analogue regime (9, 10), which will achieve adequate HbA1c in 45% cases. In

the rest, upgrading or intensifying will achieve control in a total of 75% patients. A further intensification to three –dose regime will bring down HbA1c to target in a total of 87-90% patients.

Using the same insulin to initiate, titrate, intensify and control diabetes is beneficial because it becomes easier for all members of the health care team – the nurses, diabetes educators, chemists, physician assistants – not to mention the patients and doctors, to use.

In a setting such as northern India, where trained manpower is scarce, many patients are illiterate, and chemists located in far- flung areas find it difficult to stock multiple brands of insulins, using a single analogue in multiple regimes makes sense.

Lack of monitoring facilities for frequent blood glucose estimation and inability of most patients to carry out SMBG , means that a 'safe' insulin, i.e., one which causes less hypoglycemia, and therefore needs less monitoring, should be chosen. Premixed analogues fill this need as well.

CONCLUSION

Premixed insulin analogues are a simple, easy and effective method to use for glycemic control.

The use of premixed insulin analogues is appropriate for most clinical settings.

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Author Information

Bharti Kalra, Md (Pgims)
Bharti Hospital

Sanjay Kalra, Dm (Aiims)
Bharti Hospital