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GUIDELINES

# RSSDI clinical practice recommendations for management of In-hospital hyperglycaemia—2016

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## Process and methodology

The executive committee of the national RSSDI set up a task force to draft the 'RSSDI Clinical Practice Recommendations for management of in-hospital hyperglycaemia—2016'.

The topics were divided into six different modules and were assigned to the nominated members. All efforts were made to provide the task force with the available Indian data. Data collated was given special focus by the respective team members, analysed in-depth and referenced in accordance with the contemporary literature. The draft submitted by the task force was reviewed by all group members in a consensus meeting held at Mumbai. Thereafter, the suggestions and thoughts were translated into the recommendations which were further edited, referenced as the final draft. The final draft was circulated to all the executive committee members and KOLs across the country.

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## In-hospital management of hyperglycaemia—2016

### Need for recommendations

In-hospital hyperglycaemia is a common finding and should be considered an important marker of poor clinical outcome and increased mortality [1].

In-patients with diabetes can be a challenge for the clinician. India is a diverse and vast country with availability of medical facilities ranging from world-class facilities to just basic health care infrastructure.

The objective of these recommendations is to address the resource gaps and enhance the standards of care, while attempting to bring uniformity of care across the varied and diverse health care landscape of India, covering both the resource intense and the limited resource setting.

### Introduction

The burden of diabetes globally stands at 415 million translating to one in every 11 adults being affected with diabetes. Recent data from the International Diabetes Federation 2015 states that India has over 69.2 million adults with diabetes and it is estimated that India is housing about 97,700 children with type 1 diabetes mellitus (T1DM). By 2040, India is projected to have over a hundred million adults with diabetes [2, 3].

Acute illness results in a number of physiological changes like increase in stress hormones or therapeutic choices like steroid therapy that can exacerbate hyperglycaemia. This, in turn, causes some pathological changes that can worsen the acute illness such as decreased immune function and increased oxidative stress leading further to a vicious cycle of worsening illness and poor glycaemic control. A systematic approach to in-hospital management of hyperglycaemia has consistently demonstrated better patient outcomes and reduced burden on the health care system.

### Definition: hyperglycaemia in a hospitalised patient

Hyperglycaemia in the hospital has been defined as any blood glucose that is >140 mg/dl [4].

### The burden of hyperglycaemia in the hospital setting

In a review of medical records of roughly 2000 patients admitted in a hospital in the USA, 38% of patients had been documented to have hyperglycaemia, out of which 26% had a known history of the disease and 12% had no history of diabetes prior to admission [1]. Observational studies have reported a prevalence of hyperglycaemia ranging from 32 to 38% in community hospitals, 70–80% patients with acute coronary syndrome and CABG surgery patients [5].

In summary, the prevalence of diabetes in hospitalised adults is dependent on the criteria and the methodology utilised to define the representative patient population, which on a conservative estimate, is usually 12–25% [6].

### Classification of hyperglycaemia during hospitalisation [6]

Hyperglycaemia in a hospital setting can be classified into

1. *Previously diagnosed/known diabetes*: Diabetes has been previously diagnosed, prior to admission.
2. *Previously undiagnosed diabetes/diagnosed upon admission (HbA1c >6.5%)*: Hyperglycaemia (fasting plasma glucose (FPG) >126 mg/dl or random blood glucose (RBG) >200 mg/dl) occurring during hospitalisation and confirmed as diabetes after hospitalisation by standard diagnostic criteria.
3. *Stress hyperglycaemia (normal HbA1c)*: Hyperglycaemia (fasting PG >126 mg/dl or random BG >200 mg/dl)

occurring during the hospitalisation that reverts to normal after hospital discharge.

| Classification of hyperglycaemia during hospitalisation | |
|---|---|
| Previously diagnosed | Existing hyperglycaemia prior to hospitalisation |
| Previously undiagnosed | At admission:<br>Fasting plasma glucose (FPG) >126 m/dl<br>Random blood glucose (RBG) >200 mg/dl<br>HbA1c >6.5% |
| Stress hyperglycaemia | At admission: HbA1c <5.7%<br>During hospitalization:<br>FPG >126 mg/dl<br>RBG >200 mg/dl<br>Post discharge: normoglycaemia |

**Recognition of inpatient hyperglycaemia** [5]

- Laboratory PG (Plasma Glucose) testing should be done for all patients on admission.
- If PG >140 mg/dl in non-diabetes patients
  - Monitor with capillary blood glucose (CBG) for 1–2 days
- Monitor CBG for 1–2 days in non-diabetes patients on
  - Glucocorticoids, Octreotide, Enteral nutrition (EN) or Parenteral nutrition (PN)

***HbA1c to be tested at admission*** [5]: Every hyperglycaemic hospitalised patient should have an HbA1c test done at admission if it has not been done in the last 2–3 months. This will

1. Assist with differentiation of newly diagnosed diabetes from stress hyperglycaemia
2. Assess glycaemic control prior to admission
3. Facilitate design of an optimal regimen at the time of discharge

**Monitoring** [5]

- Bedside CBG is a preferred method.
- In which types of patients and when?
  - *In those who are eating:*
    - Test before meals (as close to meal as possible and not earlier than 1 h before meal) and at bedtime
  - *In those receiving continuous EN or NPO*: every 4–6 h
  - *More frequently in*: patients with continuous insulin infusion (CII), glucocorticoids use, abrupt stoppage of EN or PN or frequent hypoglycaemia.

**Issues with CBG monitoring**: One study from the Centers for Disease Control and Prevention (CDC) of five commonly used glucose meters showed mean differences from a central laboratory method to be as high as 32% and a coefficient of variation of 6 to 11% with a single-trained medical technologist [5].

- In the ICU, factors that can affect glucose meter readings
  - Hypotension or other perfusion problems in trauma/shock
  - Extremes of haematocrit
  - High oxygen tension (in patients receiving oxygen therapy)
  - Medications such as aspirin, paracetamol, vitamin C, dopamine and mannitol
- If CBG value does not correlate with the patient's clinical status
  - Confirm through lab testing of plasma glucose

***Clinical practice recommendations for management of in-hospital hyperglycaemia can be further classified into care of the diabetic patient in the following three categories***:

1. Critically ill (ICU)
2. Non-critically ill (non-ICU)
3. Special circumstances

- Peri-operative conditions
- Patients on enteral/parenteral nutrition
- Patients on glucocorticoid therapy
- Chronic kidney disease (CKD) patients
- Transplant patients
- Peri-partum situations

**Targets: recommendations based on the landmark trials**

The NICE-SUGAR [8] (Normoglycemia in Intensive Care Evaluation and Survival Using Glucose Algorithm Regulation) is a large multi-centre randomised control trial which demonstrated that in medical ICU, intensive glucose control targets of 81–108 mg/dl in comparison to the conventional target of <180 mg/dl led to more deaths. This concluded that the target of blood glucose in ICU should remain between 140 and 180 mg/dl [8]. The recommended targets are summarised in Table 1. The American Association of Clinical Endocrinologists (AACE) and the American Diabetes Association (ADA) [7] recommends that insulin therapy should be initiated for treatment of persistent hyperglycaemia, starting at a threshold of no greater than 180 mg/dl.

Once insulin therapy has been started, a glucose range of 140–180 mg/dl is recommended for the majority of critically ill patients.

**Table 1** Glycaemic targets in ICU and non-ICU settings

| Level of care | Glycemic target |
|---|---|
| ICU | 140–180 mg/dl |
| Non-ICU | Fasting PG 80–120 mg/dl<br>Pre-meal BG <140 mg/dl<br>Post-meal BG <180 mg/dl |
| Special circumstances | Refer to the relevant section |

Special requirement patients like those with acute myocardial infarction, patients on glucocorticoid therapy, pregnancy and labour, etc., can have individualised targets abiding with the guidelines and recommendations [4, 8, 9]. Post-transplant patient should be treated as surgical inpatients and should have the same targets [9].

Patients on parenteral mode of nutrition can be maintained on blood glucose targets in accordance with their condition [8].

All these targets have been derived through numerous trials and studies with expert opinions and extensive patient experience.

The management of hyperglycaemia in hospitalised patients is relatively easier as compared to an outpatient setup provided there is interdisciplinary coordination within the hospital. The correct use of insulin and insulin analogues, using intravenous (IV) or subcutaneous (SC) regimes that are required to achieve normoglycaemia, ensures better therapeutic outcomes. Training of health care providers; education of the support staff; using simple, uniform guidelines; and a good feedback system are essential for the successful management of diabetes in hospital setting.

**Summary**

- A systematic approach to the in-hospital management of diabetic patients has been associated with better outcome for the patient and reduced disease burden on the health care system as a whole.
- Hyperglycemia in the hospital has been defined as '*any blood glucose*'>140 mg/dl.
- Every hospitalised patient should have an HbA1c test done at admission, if it has not been done in the last 2-3 months, this will assist in differentiating between known, unknown and stress diabetes and facilitate planning of the treatment at discharge.
- Target of blood glucose recommended in ICU setting is between 140-180 mg/dl.

**Table 2** Preparation for insulin infusion in intensive care unit [9]

| | |
|---|---|
| Preparation | 50 U of regular insulin dissolved in 50 ml normal saline (NS) in a 50-ml disposable syringe |
| Mode of administration | Intravenous infusion with an electronic pump/infusion pump |
| The choice of IV insulin | Short-acting regular human insulin |
| Primary target | To maintain blood glucose level between 140 and 180 mg/dl |
| Control methodology | Blood glucose to be controlled gradually in case of severe hyperglycaemia by titrating the dose of intravenous insulin |
| Prerequisites | Initially, 15–20 ml of solution should be flushed through plastic tubing to saturate the insulin binding sites in the tubing |
| Targets | Dose should be adjusted as per the levels of the blood glucose |
| Monitoring | • Either by CBG or from the venous site/central line, every 1 h until BG stability has been demonstrated<br>• Monitor serum potassium levels<br>• Check regularly for blockage/disconnection/infusion pump malfunctioning |

## Managing diabetes in critically ill patients in the ICU

Hyperglycaemia is significantly associated with increased mortality and morbidity in critically ill individuals, independent of the severity of illness, diabetes diagnosis or length of stay in the ICU. Hyperglycaemia is a correctable abnormality and thus is a therapeutic target to improve outcomes in hospitalised patients [1, 9].

***In-hospital management of hyperglycaemia aims to***:

- Restore stable glycaemia
- Minimise disruption of the metabolic state
- Minimise adverse outcomes

## Insulin in critical care

- Based on the available evidence, for the majority of critically ill patients in the ICU setting, insulin infusion should be used to control hyperglycaemia, and BG >180 mg/dl should trigger insulin initiation.
- Once intravenous insulin is started, the glucose level should be maintained between 140 and 180 mg/dl.

***Recommended glycaemic targets in the ICU setting are***

- 140–180 mg/dl in majority
- 110–140 mg/dl in select few
  - Well-experienced and staffed centre
  - Cardiac surgery
  - Patient with stable glycaemic control—if can be achieved without hypoglycaemia
- *Glucose level of < 110 or > 180 mg/dl is not recommended*

## IV insulin infusion protocol

Several published insulin infusion protocols appear to be both safe and effective, with low rates of hypoglycaemia. Some examples are the Portland Protocol [10], Yale Protocol [11], Markovitz Protocol [12], Medanta [13, 14], Mayo [15], Smart Phone Protocol [16], etc. The exact protocol is probably less important, what is important is its presence in an institution and adaptation to the individual hospital needs.

For the sake of ease and simplicity, the following insulin protocol is suggested as an example (Table 2).

## Starting an IV insulin infusion

- Give a priming bolus of regular insulin 0.1 U/kg body wt. if the initial BG >300 mg/dl.

***Infusion initiation (U/h)***: Initial rate of infusion = current BG divided by 100 [11, 17]

*Example*

• Patient's BG = 200 mg/dl, then initial infusion rate = 200 / 100 = 2 units/h. (Since each ml of insulin infusion consists of 1 U of insulin, the rate will be 2 ml/h).

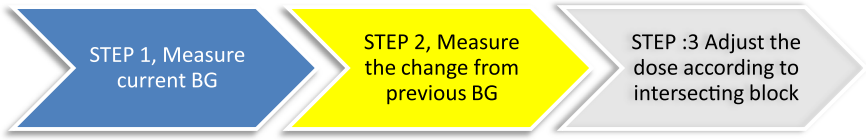


Chart adapted from Marie E. McDonnell and Guillermo E. Umpierrez [17].

**Table 3** Adjusting the insulin infusion rate

| BG (mg/dl) | ↑BG from prior BG | BG ↓ <30mg/dl | BG ↓ >30mg/dl from prior BG |
|---|---|---|---|
| ≥241 | ↑rate 3U/h | ↑rate 3U/h | No Change |
| 211-240 | ↑rate 2U/h | ↑rate 2U/h | No Change |
| 181-210 | ↑rate 1U/h | ↑rate 1U/h | No Change |
| 141-180 (target) | if BG ↑ by >30 mg/dl, ↑ rate by 25% | if BG ↓ by 10-30mg/dl, ↓ rate by 25% | if BG ↓ 30-50mg/dl , ↓ rate by 25% |
| | If previously in target range, continue the same | If previously in target range, continue the same | If previously in target range, continue the same |
| | if BG ↑ by < 30mg/dl, continue same and recheck in 1 h | if BG ↓ by < 10mg/dl, continue same | if BG ↓ by>50mg/dl, ↓ rate by 50% |
| 110-140 | No Change | ↓rate by 50% | ↓ rate by 50% |
| 91-109 | No Change | Suspend Insulin[a] | Suspend Insulin[a] |
| 71-90 | Suspend Insulin[b] | | |
| ≤ 70 | Suspend Insulin , give 25% dextrose; dose (ml)=( 100-BG) x 0.8[c] | | |

[a] Check BG q 1 h. Restart infusion at 50% of the previous rate when BG increases >140 mg/dl

[b] Check BG q 30 min till BG >90 mg/dl and then check BG q 1 h. Restart infusion at 50% of the previous rate when BG increases >140 mg/dl

[c] Example: BG = 40 mg/dl, give (100 − 40) × 0.8 = 60 × 0.8 = 48 ml of 25% dextrose IV and check BG after 15 min [17]

- If BG <70 mg%, give the calculated dose of 25% dextrose and then check BG q 15 min.
- If BG >70 mg%, check BG q 30 min till BG >90 mg%.
- If BG >90 mg%, check BG q 1 h.
- If BG >140 mg/dl, restart infusion at 50% of previous rate.

In patients with chronic kidney disease with elevated creatinine or needing dialysis, caution is advised as chances of hypoglycaemia may be more.

*The choice of IV insulin should be regular human insulin. Short-acting analogues have no advantage over regular insulin when given intravenously but have been found to be safe if preferred.*

***In adjusting the insulin infusion rate***, refer to Table 3

Monitor Capillary blood glucose (CBG) hourly.

1. Rate adjustment considers the rate of change (or lack of change) between the current and previous glucose values and the current rate of insulin infusion.
   a. If the BG decreases >30 mg/dl, continue the same dose as shown in the table.
   b. If the BG decreases <30 mg/dl, increase the dose of insulin appropriately as shown in the table.
   c. If the BG increases above the initial BG, increase the dose of insulin appropriately as shown in the table.

Monitor BG hourly; adjust the dose of insulin infusion till target BG of 140–180 mg/dl is achieved. Once a stable BG (two consecutive readings within target) is achieved, monitoring of BG can then be done every 2–3 h.

Administer 5D/DNS at 80–120 ml/h if not receiving any nutrition; supplement $K^+$ if no contraindication.

**Recommendations for the limited care settings** [9, 17]

In the limited care and resource-constrained setting, where insulin pump facility is not available, 25 units of regular

insulin in 500 ml of normal saline is recommended to be delivered intravenously through an IV drip set as explained in Table 4. (This would give 0.05 units/ml).

To measure the rate, we must know

a. The number of drops which is equal to 1 ml, e.g. macro-drip IV set 15 drops = 1 ml
b. Time in minutes

The formula for working out flow rates is

$$\frac{\text{volume (ml)} \times \text{drop factor (gtts/ml)}}{\text{time (min)}} = \text{gtts*/min}$$

*gtts = Latin for drops

Calculation for 20 ml/h = (20 × 15) / 60 = 5 drops/min

**Transition to SC insulin is required when patient begin eating regular meals or when transferred to lower intensity care.**

- BG >180 mg/dl should trigger insulin initiation
- Continuous IV insulin infusion (CII) is the most effective method.

| Insulin infusion rate ( U/hr ) | Drip rate ( ml/hr ) | Drop rate/min By regular macro-drip IV set |
|---|---|---|
| 1 | 20 | 5 |
| 2 | 40 | 10 |
| 3 | 60 | 15 |
| 4 | 80 | 20 |
| 5 | 100 | 25 |
| 6 | 120 | 30 |
| 7 | 140 | 35 |

**For Blood Transfusion**

**Set:** 1ml = 10 drops/min

**For Regular Macro Drip**

**Set:** 1ml = 15 drops/min

**For Micro Drip Set:**

1ml = 60 drops/min

**Table 4** Insulin infusion rate and the drop rate/min

## Transition from insulin infusion to SC insulin and/or oral anti-diabetic drugs

### Introduction

The transition from IV to SC insulin is an important step in the care of a critically ill patient, usually occurring after clinical improvement has taken place. Abrupt discontinuation of IV insulin often leads to rebound hyperglycaemia. Hence, the transition orders from IV to SC insulin should be made carefully and only after it is clear that the patient exhibits stable glycaemic control.

### Safety indicators for transition from IV to SC insulin [18]

1. Stable blood glucose levels <180 mg/dl for at least 4–6 h
2. Resolution of acidosis in DKA
3. Haemodynamically stable without the use of vasopressors
4. Stable nutrition plan
5. Stable IV drip rates (low variability)

Transition is more likely to be successful if blood glucose levels are between 140 and 180 mg/dl with an insulin drip rate of <2 units/h [19]. Transition may prove challenging in elderly patients, those with high pre-admission HbA1c, those with high variability of blood glucose in the 24-h preceding transition, those on corticosteroids and subjects with fluctuating concomitant illnesses.

### Process of transition

The *total insulin dose* (TDD) should be calculated when we transition from IV to SC insulin. Subcutaneous insulin administration in hospitalised patient should include three components to be effective:

- *Basal insulin* (to inhibit hepatic gluconeogenesis)
- *Bolus* or nutritional insulin (to facilitate mealtime glucose metabolism)
- *Correctional* insulin (to provide real-time adjustment of insulin dosing based on the patient's insulin sensitivity). (Refer to Table 5)

Various factors influence insulin requirement such as post-surgical stress, pain, variable oral intake, infection and underlying insulin resistance. The safest method to calculate the TDD is to find a time interval of several hours (ideally, 4–6-h duration), during which the blood glucose values are

**Table 5** Calculation of the total daily dose (TDD) of insulin

| TDD calculation | Dose 80% of calculated TDD |
|---|---|
| **From IV to SC transition**<br>• Calculate insulin needed for stable control of BG for previous 6 h and multiply by 4<br>Or<br>• Calculate the total amount of insulin needed in previous 24 h | Use 80% of calculated TDD for starting SC insulin<br>Give<br>Basal insulin is 50%<br>Bolus insulin is 50% |

**Table 6** Calculation of basal/bolus dose including the correctional dose

| **Basal dose** | | **Correctional bolus (CB)** |
|---|---|---|
| Glargine | OD dose | BG − 100 = CB |
| Detemir | OD or BD dose | Correction factor (CF) (of regular/rapid-acting insulin) |
| NPH | BD dose | CF = 1500/TDD (regular insulin) |
| | | Or |
| | | CF = 1800/TDD (insulin analogue) |
| **For basal dose correction** | | |
| **PM basal**: check FPG every day, ↑ 2 U of basal till FPG of 80–120 mg/dl is achieved | | |
| **AM basal**: check pre-dinner glucose every day, ↑ 2 U of basal till BG <140 mg/dl (for BD dose of NPH/detemir) | | |
| **Bolus dose** | | |
| Total bolus dose ÷ 3 | With breakfast, lunch, dinner[a] | |
| For bolus: regular, aspart, glulisine or lispro can be used | | |

*CF* Correction Factor

[a] Note that if specific calorie count of each meal is available, doses may be varied according to the meal

stable and at target. The insulin requirement during this stable period can be extrapolated to a 24-h time period [18].

## Choice of insulin

On transition, regular human insulin/neutral protamine Hagedorn (NPH) or short- and long-acting insulin analogues can be used, based on affordability.

The half-life of IV insulin is less than 5 min. To prevent the recurrence of hyperglycaemia during the transition to subcutaneous insulin, the insulin infusion should be continued after the dose of SC insulin is given. For regular or rapid-acting insulin given subcutaneously, continue insulin infusion for 1–2 h and long-acting insulin 2–3 h.

## Transition basal/bolus regime examples

1. For patients who are not receiving significant amount of calories (e.g. patients who are on liquid diet alone), the basal dose can be given as a single dose of long-acting insulin (e.g. glargine, detemir) or two doses of intermediate-acting insulin (NPH) every 12 h. Correctional short-acting insulin (regular) or rapid-acting insulin (e.g. aspart, glulisine, lispro) can be added as needed depending on nutritional intake and glucose levels [20].
2. For patients who are allowed oral intake, 50% of the calculated dose of insulin is administered as the basal dose and the rest is divided evenly between the three meals as the bolus dose [20, 21] (refer to Table 6).

## Glucose monitoring after transition to SC therapy [18]

The first 24 h after the transition is crucial to assess the patient's insulin requirement as this may continue to change with clinical improvement. Hence, BG should be monitored at least five times daily for patients who are on multiple daily injections, that is

- Before each meal
- At bedtime
- At 3 a.m.

**Table 7** Maintenance of the target BG

| Level of care | Target |
|---|---|
| ICU setting | 140–180 mg/dl |
| Non-ICU setting | Fasting 80–120 mg/dl<br>Pre-meal <140 mg/dl<br>Post-meal <180 mg/dl |
| Special circumstances | Refer to the relevant section |

The target BG should be maintained as per Table 7.

In case the glucose levels are above pre-determined targets at any time, *supplemental doses* (*correction boluses*) need to be given. Correction insulin refers to the administration of supplemental doses of short- or rapid-acting insulin together with the usual dose of bolus insulin for BG above the target range.

The supplemental insulin dose is calculated using CF which is the degree of BG lowering expected from 1 unit of insulin.

## Calculating the CF and correction dose (Table 6)

Correction factor is equal to 1800 divided by the TDD if insulin analogue is used or 1500 divided by the TDD if regular insulin is used. (Refer to Tables 6 and 8).

*Correction dose* is the actual BG minus 100 divided by the CF. (Refer to Table 6).

**Table 8** Calculation of correction factor and correction dose

| **Example** | |
|---|---|
| **Total calculated daily dose is 30 U** | **Additional correctional bolus:** |
| - Basal 15 U | Estimated pre-meal BG 250 mg/dl |
| - Bolus 15 U | CF 1500/30 = 50 U |
| Bolus 5 U-5 U-5 U before each 3 meals + additional correctional bolus for BG not at target at any meal | CB 250 − 100 = 150 = 3 U<br>CF 50 50<br>Total meal dose 5 U + 3 U = 8 units |

Unexpected hyperglycaemic excursions are common, and the use of correction insulin remains a pervasive and arguably logical practice. If correction insulin is used, it should be ordered as a separate step after considering basal and nutrition insulin needs. The doses of scheduled insulin should be adjusted regularly if correction insulin is required consistently. There is no evidence to support the routine use of continuous glucose monitoring.

### Transition in stress hyperglycaemia

If the patient requires less than 1 U/h of IV insulin, it is prudent to monitor blood glucose levels and institute SC insulin only if glucose levels are consistently >180 mg/dl.

### Safety markers for transition to oral anti-diabetic drugs [22]

It is advisable to transition patients administered IV insulin in hospital to subcutaneous insulin therapy after stabilisation.

**Transition to oral anti-diabetic agents in combination with insulin is done when**

1. Patient is on normal diet
2. Glycaemic control is stable with no ketoacidosis
3. In post-surgical patients where expected tissue damage is minimal
4. There are no serious co-morbid conditions

***Transition to oral agents alone is not preferred in hospitalised patients who have a prolonged stay because***

- Sulfonylureas and other insulin secretagogues (e.g. meglitinides) could lower glucose rapidly, increasing the risk of hypoglycaemia.
- Efficacy and side effects of Alpha-Glucosidase Inhibitors (AGI ) limit their use.
- For patients who have been on metformin, dipeptidyl peptidase (DPP)-IV inhibitors, sodium-glucose co-transporter (SGLT)-2 inhibitors or a thiazolidinedione before admission, these agents often are restarted in the post-operative period when oral intake of medications is possible and hepatic and renal function are stable.

**Summary**

- Discontinuation of IV insulin often leads to rebound hyperglycemia. Hence the transition orders from IV to SC insulin should be made carefully and only after it is clear that the patient exhibits stable glycemic control.
- Transition is more likely to be successful if blood glucose levels are between 140-180 mg/dl with insulin drip rates being constant.
- It should be ensured that there is continuity between IV insulin infusion and the first dose of SC insulin.
- The calculation of the total daily insulin requirement can be best ascertained during a time interval of 4-6 hours during which the blood glucose values are at goal and IV insulin rates are not particularly elevated or variable.
- Regular insulin or rapid acting analog should be used for the bolus/prandial insulin and the supplemental insulin. The basal insulin requirement should be met using NPH, insulin detemir or glargine.

## Glycaemic control in the non-critically ill patients

In general, insulin is the preferred treatment for hyperglycaemia in hospitalised patients with diabetes. Patients with type 1 diabetes must be maintained on insulin therapy at all times to prevent diabetic ketoacidosis (DKA).

The targets for the majority of non-critically ill patients are pre-meal BG <140 mg/dl and post-meal BG <180 mg/dl [6, 7].

## Insulin initiation in hospital

Common approaches to insulin dosing in the hospital are the sliding scale insulin (SSI) approach and the use of basal insulin dosing with prandial and correctional doses. Medical articles have questioned the effectiveness of SSI since at least in 1970. A Medline search of 52 trials from 1966 to 2003 showed no clinical trials demonstrating benefit from SSI, and most experts currently question the effectiveness and safety of traditional SSI. The largest prospective cohort study to date revealed that SSI regimens failed to adequately control hyperglycaemia, resulting in high rates of hypoglycaemia, and were associated with longer hospital stays. SSI regimens do not allow for basal or mealtime insulin requirements and grossly underestimate total daily insulin requirements. Furthermore, SSI regimens respond to hyperglycaemia after it has happened, rather than preventing it, and the sliding scale depends on the inaccurate assumption that insulin sensitivity is uniform among all patients.

- Subcutaneous (SC) insulin administration in the non-ICU hospitalised patient should include three components to be effective:
  - Basal insulin
  - Nutritional (bolus) insulin
  - Correctional insulin

## Other insulin regimes which can be followed in the hospital

The following insulin regimes can be initiated in the non-critical care settings:

- Basal/bolus therapy
  - NPH and regular insulin
  - Long-acting and rapid-acting insulin analogues
- Pre-mixed insulin analogues
- Use of incretin-based therapy with basal insulin with supplemental rapid-acting insulin as required

For most patients in the hospital, basal bolus is the preferred regime. However, if patients have been well controlled on pre-mixed insulin, they can be continued on the same regime. These patients require frequent monitoring.

Recently, there are increasing reports of the use of glucagon-like peptide-1 receptor agonist (GLP-1 RA) in hospitalised patients as they can reduce the total daily dose of insulin and minimise the risk of hypoglycaemia. They can be used if there are no contraindications to incretins.

## Estimating SC insulin dose

- Patients, who were well controlled on insulin prior to admission, can usually be maintained on their home insulin regimen with specific adjustments made for differences in meals and activity levels, the effects of illness and the effects of other concomitant medications.
- In patients who were on an insulin infusion and now transferred to non-critical care settings, the TDD of insulin can be calculated from the insulin requirement in previous 6 h of stable control of BG and multiplied by 4 to get the TDD in 24 h or the actual total insulin requirement in the last 24 h.
- For insulin-naive patients or when no IV insulin therapy has been given, the TDD of insulin can be calculated as shown in Tables 9, 10 and 11.

## Insulin dose modification in hospital

- In patients who are NPO or unable to eat, bolus insulin must be withheld until nutrition is resumed. However, doses of correction insulin can be continued to treat BG above the desired range.
- Adjustments of scheduled basal and bolus insulin can be based on total doses of correctional insulin administered in the previous 24 h.

**Table 9** Estimation of the TDD of insulin

| **TDD calculation** | | **Dose 80% of calculated TDD** |
|---|---|---|
| **For insulin naive** | **Total dose as per body weight** | Use 80% of calculated TDD for starting SC insulin |
| Ideal body weight | 0.4–0.5 U/kg | Give when |
| Obese | 0.5–0.6 U/kg | Basal insulin is 50% |
| Lean or renal compromised | 0.3–0.4 U/kg | Bolus insulin is 50% |
| **From IV to SC transition** | | |
| Calculate the insulin requirement in the previous 6 h of stable control of BG and multiply by 4 to get the TDD in 24 h or the actual total insulin requirement in the last 24 h | | |

**Table 10** Calculation of the dose with correctional factor

| **Basal dose** | | **Correctional bolus (CB)** |
|---|---|---|
| Glargine | Single dose AM/PM | BG − 100 = CB |
| Detemir | Given in 12-h split dose | CF |
| NPH | Given in 12-h split dose | CF = 1500/TDD (regular insulin) |
| | | Or |
| | | CF = 1800/TDD (insulin analogue) |
| **For basal dose correction** | | |
| **PM basal**: check FPG every day, ↑ 2 U of basal till FPG of 80–120 mg/dl is achieved | | |
| **AM basal**: check pre-dinner BG every day, ↑ 2 U of basal till BG <140 mg/dl (for BD dose of NPH/detemir) | | |
| **Bolus dose** | | |
| Total bolus dose ÷ 3 | With breakfast, lunch and dinner | |
| For bolus dose: regular, aspart, glulisine or lispro can be used | | |

- Sliding Scale Insulin (SSI) (defined as the administration of a pre-established amount of short-acting insulin in response to hyperglycaemia) as the sole regimen for the management of hyperglycaemia in the hospital setting is ineffective and, therefore, is *not recommended*.

## Role of oral anti-diabetic drugs/non-insulin injectables in non-critically ill patients

The use of oral and other non-insulin therapies presents unique challenges in the hospital settings, because there are frequent contraindications to their use in many inpatient situations (sepsis, NPO status, IV contrast dye, pancreatic disorders, renal failure, etc.)

Selected patients may be candidates for continuation of previously prescribed oral anti-diabetic drug (OAD) therapy in the hospital, those who are clinically stable and eating regular meals and who have no contraindications to the use of these agents.

Conversion to basal bolus insulin therapy based on BG values results to a better management of hyperglycaemia.

*Common problems encountered with OADs*

- Sulfonylureas
  - May cause severe and prolonged hypoglycaemia, particularly in elderly, renal-impaired patients and patients with poor oral intake
  - For long-acting SUs, dose adjustments may be difficult.
  - Skipping a meal poses a severe risk of hypoglycaemia.
- Metformin
  - Must be discontinued in patients with decompensated congestive heart failure, severe renal insufficiency, hypoperfusion or chronic pulmonary disease and in patients who are at risk of developing renal failure and lactic acidosis, as such may occur with the administration of IV contrast dye or surgery
  - Discontinue temporarily before major surgery or IV contrast use; restart after 48 h if kidney function is normal.
- Thiazolidinediones (TZDs)
  - May take several weeks to be effective, thus limiting the usefulness of these agents for achieving glycaemic control in the hospital.
  - They are contraindicated in patients with congestive heart failure, hemodynamic instability or evidence of hepatic dysfunction.
  - If the patient is previously taking TZDs, they may be continued in the absence of any contraindications.
- DPP-IV inhibitors/GLP-1 RA
  - Contraindicated in patients with pancreatic illness, medullary thyroid carcinoma and gastroparesis

**Table 11**

| **Example** | **Additional correctional bolus** |
|---|---|
| ***Total calculated daily dose: 30 U*** | |
| - Basal 15 U | Estimated BG 250 |
| - Bolus 15 U | CF 1500/30 = 50 U |
| Bolus 5U - 5U - 5U before each 3 meals + additional correctional bolus for BG not at target at any meal | CB 250 − 100 = 150 = 3 U |
| | CF 50 50 |
| | Total meal dose 5 U + 3 U = 8 units |

- SGLT-2 inhibitors
  - Higher incidence of genitourinary infections
  - Possible risk of diabetic ketoacidosis
  - Contraindicated prior to major surgery
  - Insufficient data in hospitalised patients

**For limited care settings**: Human insulin rather than analogues may be used.

### Management in special circumstances

### Minor procedures

The management of in-hospital hyperglycaemia includes special circumstances like minor day-care procedure including dental interventions and cataract surgery. All procedures which do not require patients to be in the hospital overnight and are anticipated to miss not more than one meal are considered minor procedures, e.g. cataract surgery, some therapeutic or diagnostic procedures requiring overnight fasting for more than 8–10 h.

### Targets for therapy are categorised as pre, intra and post procedure [23]

There are no pre-requisites for emergency life-saving procedures. A stable glycaemic control prior to the elective procedure with HbA1c target of <8% (corresponding to mean plasma glucose of 180 mg/dl) is acceptable. If the HbA1c is >9% or blood glucose >200 mg/dl and the surgery cannot be postponed, it is advised to first achieve blood glucose control prior to the procedure (Tables 12) [23].

### Glycaemic management in regard to the timing of the surgery [23–28]

Ideally, patients with diabetes should be posted in the morning, preferably as the first case. Considering the prevalence of diabetes, it may not always be feasible to finish all procedures on patients with diabetes in the morning, especially in a high turnover centre or diabetes specialty hospital. Hence, the protocol for patients posted in the morning and afternoon is provided.

**Table 12** Pre-procedure glycaemic control

| | Ideal | Acceptable | For intensification |
|---|---|---|---|
| FPG (mg/dl) | 80–120 | <140 | >140 |
| PPBG (mg/dl) | <160 | <180 | >200 |
| HbA1c (%) | <7 | <8 | >9 |

BG targets during the procedure are 140–180 mg/dl with avoidance of hypoglycaemia.

### For morning procedures

On the day prior to procedure, patients should be advised to take full dose of anti-diabetes medications including insulin and OADs at dinner. The patient will remain NPO till the procedure is complete in the morning. Patient should take their usual dose of insulin and/or OADs when they have breakfast by mid-morning.

If the procedure is delayed unexpectedly and the blood glucose levels are above the target (>180 mg/dl), insulin infusion can be started. If the facility for infusion is not available, subcutaneous correction dose of short-acting insulin may be given followed by a close monitoring to avoid hypoglycaemia.

### For patients who are not on insulin (on OADs or GLP-1 RA)

All OADs and GLP-1 RA can be continued as usual on the day prior to procedure but should be omitted on the morning of procedure. OADs and GLP-1 RA can be restarted once the patients resume their diet. Metformin may not be discontinued for minor procedures unless there is renal, cardiac or hepatic impairment. For procedures requiring IV radio-contrast administration, it is recommended to discontinue metformin 24 h prior to the procedure. Metformin can be restarted after confirming normal renal function after 48 h.

Patients with long-duration type 2 diabetes and those receiving more than two OADs are likely to deteriorate after discontinuation of anti-diabetes medications. Similarly, dysglycaemia is more likely in patients with poor pre-procedural glycaemic control and if the procedure is unexpectedly prolonged or complicated. These patients should be treated with insulin infusion during procedure and may require subcutaneous insulin for a short duration after the procedure (Tables 13 and 14).

### Insulin regimes for hyperglycaemia management in post-op period

A. *Immediate post-op period:*
   IV insulin protocol
B. *Enteral feeding:*
   Basal plus or basal bolus with correction bolus
C. *Tube feeding:*
   Low-dose basal with short-acting insulin every 6 h or rapid-acting insulin every 4 h as correction bolus
   OR
   NPH with short-acting regular insulin every 8 or 12 h
D. *Parenteral nutrition:*
   Add 0.1 U of regular insulin per gram of dextrose in non-diabetic patients and 0.15 U of regular insulin per gram of dextrose in diabetic patients to the parenteral solution as IV infusion
   OR
   Basal with short-acting insulin every 6 h if BG >180 mg/dl

**Table 13** Recommendation for peri-operative adjustment of insulin (short starvation period—no more than *one* missed meal)

| Insulin | Day prior to admission | Day of surgery | |
|---|---|---|---|
| | | Morning surgery | Afternoon surgery |
| Once daily (evening)<br>Basal insulin | No dose change | No dose change<br>Check BG 6 h | No dose change<br>Check BG 6 h |
| Once daily (morning)<br>Basal insulin | No dose change | No dose change<br>Check BG 6 h | No dose change<br>Check BG 6 h |
| Twice daily<br>Pre-mixed | No dose change | Halve the usual morning dose.<br>Check BG 6 h.<br>Leave evening dose unchanged | Halve the usual morning and evening dose.<br>Check BG 6 h |
| Twice daily<br>Separate short- + intermediate-acting insulin | No dose change | Calculate the total dose of both morning insulin and give half as intermediate acting only in the morning.<br>Check BG 6 h.<br>Leave evening dose unchanged.<br>Supplement correction doses with short-acting insulin as required | Calculate total dose of both morning insulin and give half as intermediate acting only in the morning.<br>Check BG 6 h and post-op and supplement correction doses with short-acting insulin as required |
| 3, 4 or 5 injections daily | No dose change | **Basal bolus regimens:**<br>Omit the morning and lunchtime short-acting insulin.<br>Keep the basal unchanged based on BG values.<br>**Pre-mixed insulin (morning dose):**<br>Halve the morning dose and omit lunchtime dose (if any).<br>Check BG 6 h | Take the usual morning insulin doses.<br>Omit lunchtime dose.<br>Check BG 6 h and supplement correction doses with short-acting insulin as required |

## Evaluation for emergency surgery

### *Pre-op assessment*

A. *Metabolic status:*
   Measure plasma glucose, pH, urea, Sr. creatinine, Sr. Na and K and urine ketones
B. *Volume status:*
   Check for orthostatic hypotension, elevated BUN and/or creatinine, urine output, osmolality and adequacy of peripheral circulation
C. *Cardio-respiratory status:*
   ECG, chest X-ray, 2D ECHO

### *Preoperative treatment*

- Delay surgery if possible until metabolic control and volume status are stabilised.
- Optimise blood glucose, electrolytes and acid–base status.

## Steroid-induced diabetes

### Introduction

The use of steroids in clinical practice is a common practice.

The relationship between steroids and diabetes can be in the form of

**Table 14** Recommendation for peri-operative adjustment of non-insulin medications (short starvation period—no more than *one* missed meal)

| Tablets | Day prior to admission | Day of surgery | |
|---|---|---|---|
| | | Morning surgery | Afternoon surgery |
| Acarbose | Take as normal | Omit morning dose if NPO | Give morning dose if eating |
| Meglitinide | Take as normal | Omit morning dose if NPO | Give morning dose if eating |
| Metformin | Take as normal | Take as normal | Take as normal |
| Sulfonylureas | Take as normal | For once daily: omit AM dose<br>For twice daily: omit AM dose | For once daily: omit AM dose and give PM dose<br>For twice daily: half AM dose and give PM dose |
| DPP-IV inhibitors | Take as normal | Take as normal | Take as normal |
| GLP-1 RA | | Omit on the day of surgery | Omit on the day of surgery |

1. Chronic use of steroids leading to diabetes
2. Use of steroids in a patient with pre-existing diabetes
3. Increased endogenous secretion of glucocorticoids

In either of the situations, it is important to achieve good glycaemic control to improve outcomes and prevent adverse events. Commercial preparations of steroids are available as mentioned in Table 15.

## Management of steroid-induced diabetes

### Monitoring of blood glucose

A. ***In patients with no history of diabetes***

- In patients perceived to be at high risk (family history, obesity, other ADA risk factors) or with symptoms suggestive of *hyperglycaemia*, check HbA1c prior to starting steroids.
- After starting steroid, recommend BG once daily, pre or post meal.
- If the CBG is <200 mg/dl, consider the patient to be at low risk and record the CBG daily post meal.
- If CBG consistently <180 mg/dl, consider cessation of CBG testing.
- If CBG is found to be >200 mg/dl, the frequency of testing should be increased to a minimum of three times a day and treatment should be initiated accordingly.

B. ***In a known case of diabetes***

- If a CBG is found to be >200 mg/dl, the frequency of testing should be increased to a minimum of three times a day and treatment should be initiated accordingly.

**Table 15** Steroid dose equivalents [29]

| Steroids | Steroid potency (equivalent doses), mg | Duration of action (half-life in hours) [40] |
|---|---|---|
| Hydrocortisone | 20 | 8 |
| Prednisolone | 5 | 16–36 |
| Methylprednisolone | 4 | 18–40 |
| Dexamethasone | 0.75 | 36–54 |
| Betamethasone | 0.75 | 26–54 |

N.B. potency relates to anti-inflammatory action, which may not equate to hyperglycaemic effect

### Treatment protocols

A. *Single-dose prednisolone in morning*

- BG rise within 4–8 h after administration of oral steroids and earlier with IV steroids. The most commonly prescribed steroid is prednisolone in the morning, resulting in the rise of blood glucose levels by late morning.
- Hence, the anti-hyperglycaemic management should be tailored to combat daytime hyperglycaemia and to avoid nocturnal hypoglycaemia.

### Insulin therapy

- Intermediate-acting insulin (NPH or detemir) administered at the same time of steroid ingestion may best manage hyperglycaemia with a once daily oral steroid.
- The starting dose of NPH can be calculated as per steroid equivalent dose by the formula given in Table 16 [30].
- Increase the daily dose of insulin by 10–20% based on blood glucose level.
- For patients on non-insulin therapy, a single dose of short-acting sulfonylurea such as gliclazide 40 mg for every 5 mg of prednisolone (or equivalent steroid) (max one-time dose 240 mg) taken before breakfast may best manage hyperglycaemia from a once-daily oral steroid treatment. If not controlled by OADs, intermediate-acting insulin (NPH or detemir) may be added in the morning. If the hyperglycaemia is continued late in the evening or overnight, an additional dose of gliclazide or intermediate-acting insulin can be given in the evening [29].
- Current evidence does not support the use of DPP-IV inhibitors, GLP-1 RA or SGLT-2 inhibitors in the management of steroid-induced diabetes.

B. **Patient taking multiple hydrocortisone injections or dexamethasone or methylprednisolone pulse therapy**

a. Hyperglycaemia is observed throughout the 24-h period.
b. Insulin therapy is usually recommended. Subcutaneous insulin using a basal or multiple-dose daily injection regimen is the choice of treatment.

**Table 16** Calculation of NPH dose

| Glucocorticoids | Frequency | Insulin dosing |
|---|---|---|
| Prednisolone or methylprednisolone | Every day | NPH 0.5 U/mg glucocorticoid (range 0.25–1 U) |
| | | Administered at the time of the glucocorticoid dose |
| Prednisolone or methylprednisolone | ≥2 times a day | NPH 0.5 U/mg glucocorticoid (range 0.25–1 U) in divided doses twice daily |
| | | Or |
| | | Use 130–140% of basal and bolus insulin doses |
| Dexamethasone | | NPH 3 U/mg glucocorticoid equivalent (range 2–5 U) in divided doses twice daily |
| | | Or |
| | | Use 140–150% of basal and bolus insulin doses |
| Hydrocortisone | Once a day | NPH 0.125 U/mg administered at the time of the glucocorticoid dose |
| Hydrocortisone | Twice a day | NPH 0.125 U/mg administered twice a day at the time of the glucocorticoid dose |

c. Insulin can be given as twice daily pre-mixed (with an increase in the morning insulin dose), basal bolus or individualised regimen having OADs and insulin both.
d. If on basal insulin, consider switching to morning administration and increase dose in 2–4-unit increments (or by 10–20%) every 24–48 h.
e. In acutely unwell patients, IV insulin infusion may be required for a short duration.
f. Intravenous insulin infusion may be used for the estimation of TDD of insulin requirement with steroids, which can be used from the next day as basal/bolus injections.

- **Tapering and discontinuation**

  Conversely, glucose levels drop to normal in previously non-diabetic individuals within 24 h after discontinuation of IV steroids. This may take several weeks in a dose-dependent manner if oral steroids are weaned over several weeks. The dose of anti-hyperglycaemic agents needs tapering accordingly. A weekly reduction of 5 mg of prednisolone (or equivalent steroid) roughly requires reduction in the total daily dose of insulin by 20–25% or reduction in the dose of gliclazide by 40 mg.

**Management of hyperglycaemia during obstetric procedures, caesarean section and vaginal delivery** [31, 32]

Most obstetric procedures (e.g. cervical cerclage, amniocentesis, D&C) are day-care procedures and do not require more than 6–8 h of overnight fasting. The aim is to maintain blood glucose levels between 70 and 140 mg/dl during and immediately after the procedure.

**Intra-partum glucose management**

Insulin requirements significantly reduce during active labour due to reduced hepatic gluconeogenesis and increased calorie requirement. Uncontrolled maternal hyperglycaemia during the labour can lead to foetal hyperinsulinism, consequently resulting in neonatal hypoglycaemia. Feasible target levels of maternal blood glucose levels during delivery for prevention of neonatal hypoglycaemia are 70–140 mg/dl.

**Glycaemic management during vaginal delivery** [31]

Maintenance of target blood glucose levels during labour requires a balanced administration of insulin and glucose preferably in the form of separate infusions. Depending on the glycaemic status, insulin infusion can be started at the rate of 0.5 to 1 units/h. Glucose-containing fluid (in the form of 5% dextrose or dextrose normal saline (DNS)) can be started to provide glucose at the rate of 80–125 ml/h. Glucose infusion can be started either simultaneously with insulin infusion or when blood glucose levels fall below 70 mg/dl. Where facility of infusion is not available, subcutaneous short-acting insulin every 4–6 h may be given.

**Glycaemia management during caesarean section and induction of labour**

A planned caesarean section should be posted early in the morning. Patient should take usual dose of night-time insulin (short as well as intermediate or long acting) and OADs on the day prior to surgery. The

morning dose of insulin as well as OADs should be withheld on the day of surgery, and blood glucose levels should be monitored closely. A similar protocol should be followed for induction of labour which again should be planned early in the morning. If the procedure is expected to get delayed (may take 8–12 h for induction of labour especially in primigravida) and a light breakfast is allowed by obstetrician, half the usual dose of insulin can be administered subcutaneously in the form of intermediate-acting insulin. Insulin and glucose infusions may be administered as required to maintain blood glucose levels between 70 and 140 mg/dl, if prolonged fasting is anticipated. In the post-partum phase, blood glucose levels may normalise in patients with gestational diabetes while the insulin requirement may drastically come down for patients with type 1 and type 2 diabetes. If appropriate, the insulin regimen and doses can be deescalated.

### Insulin in renal-compromised patients

Insulin requirements show a biphasic course in patients with diabetes and renal disease (Table 17). In the beginning, glucose control deteriorates because of insulin resistance; therefore, more insulin is needed to achieve glycaemic control. In advanced renal failure with creatinine clearance below 50 ml/min, the need for insulin is lower or even the cessation of insulin may be necessary. The need for insulin is decreased because of less caloric intake in uremic patients. With the institution of haemodialysis, the need for insulin changes because the insulin sensitivity and liver metabolism improve.

Most patients who are renal compromised need a lower total daily dose of insulin and have less stringent glycaemic targets. In non-critical care situation, the preferred insulin is short-acting insulin analogue over regular insulin. Patients with normal GFR with albuminuria or post-transplant patients may need tighter control albeit without the risk of hypoglycaemia [36].

### Insulin therapy

Multiple doses of rapid-acting insulin analogues are best suited for patients with estimated glomerular filtration rate (eGFR) <30 ml/min to deal with poor and unpredictable food intake, nausea and vomiting. Most patients with advanced CKD (eGFR <30 ml/min) do not require basal insulin. Multiple-dose insulin injection therapy with two to three rapid-acting insulin (preferably analogues) and one to two basal insulin injections may be required for patients with eGFR between 30 and 60 ml/min.

### Oral anti-diabetic agents

The use of oral insulin-sensitising agents in addition to insulin may improve glycaemic control in patients with CKD (Table 18). Occasionally, few patients with milder hyperglycaemia may get controlled with only OADs. Most OADs require dose adjustment with declining renal function. Insulin therapy remains the mainstay of treatment in diabetic patients on hemodialysis. On the day of dialysis, the usual dose of short- or rapid-acting insulin should be administered after the session of dialysis.

### Peri-operative management of transplant patient [31, 33, 34]

Care of glycaemic status during a pre-transplant period involves patients with pre-existing diabetes as well as new-onset diabetes after solid organ transplantation (NODAT). For a planned transplant in patients with pre-existing diabetes, it is advisable to achieve optimal blood glucose control prior to a procedure. Glycaemic control in the peri-procedural period is achieved with insulin infusion which may be continued till the patients resume solid diet.

**Table 17** Glycaemic targets for renal patients [36]

| | HbA1c (%) | FPG (mg/dl) | 2 h PPBG (mg/dl) |
|---|---|---|---|
| Normal GFR, microalbuminuria + | 6.5–7 | 80–120 | <180 |
| Pre-dialysis (CrCl <10) | <7.5 | 100–120 | <180 |
| Dialysis | 7.5–8 | 100–140 | <200 |
| Post renal transplant | 6.5–7 | 80–120 | <180 |

**Table 18** Safety of anti-hyperglycaemic medications in patients with diabetes and CKD [36]

| eGFR (ml/min/1.73 $m^2$) | Safe without dose adjustment | Can be used in reduced dose | Contraindicated |
|---|---|---|---|
| More than 60 | Insulin<br>Almost all OADs<br>Liraglutide | | |
| 30–59 | Insulin (caution for longer-acting preparations)<br>Acarbose<br>Linagliptin<br>Gliclazide<br>Nateglinide<br>Repaglinide<br>Pioglitazone[a]<br>Liraglutide | Metformin (max 1 g/day)<br>Saxagliptin (2.5 mg)<br>Sitagliptin (50 mg)<br>Exenatide (5 mcg BD) | Glibenclamide<br>GLP-1 RA<br>SGLT-2 inhibitors |
| 15–29 | Insulin (caution for longer-acting preparations)<br>Linagliptin<br>Nateglinide<br>Repaglinide<br>Pioglitazone[a] | Sitagliptin (25 mg)<br>Saxagliptin (2.5 mg)<br>Gliclazide | Acarbose<br>Voglibose<br>Metformin<br>Glibenclamide<br>GLP-1 RA<br>SGLT-2 inhibitors |
| Less than 15 or dialysis | Insulin (avoid longer-acting preparations)<br>Linagliptin<br>Nateglinide<br>Repaglinide<br>Pioglitazone[a] | Sitagliptin (25 mg)<br>Gliclazide | Acarbose<br>Voglibose<br>Metformin<br>Glibenclamide<br>Saxagliptin<br>GLP-1 RA<br>SGLT-2 inhibitors |

[a] Risk of volume overload

Care of glycaemic status during a post-transplant period additionally involves patients with NODAT. Hence, blood glucose monitoring should be done regularly in all individuals with or without pre-existing diabetes. The threshold for the diagnosis of NODAT is the same as described by the American Diabetes Association using fasting plasma glucose (FPG) >125 mg/dl and post-meal blood glucose >200 mg/dl. Treatment of post-transplant diabetes is the same as that of type 2 diabetes.

**Management of CKD patient on hemodialysis** [35, 36]

Insulin is generally the choice of treatment for uncontrolled diabetes with CKD, but few OADs can be used safely after dose adjustment for milder hyperglycaemia. The target as well as threshold to start anti-hyperglycaemic agents in patients with CKD is HbA1c >7%. A less stringent target may be chosen in individuals with chronic co-morbidities or limited life expectancy with acute co-morbidities and risk of hypoglycaemia.

**Management in special feeding** [37]

- Total parenteral nutrition (TPN)
- Enteral feeding via Ryle's tube/jejunostomy feeds

Usually, insulin is added along with the nutrition in patients receiving TPN. Initially, a separate IV infusion of regular insulin may be required to estimate the TDD of insulin. Subsequently, the separate insulin infusion can be stopped, and 80% of the 24-h infusion insulin dose can be placed in the TPN bag as regular insulin. Correctional dose may be given subcutaneously for unusual hyperglycaemia (as discussed in earlier sections). Long-acting insulin should never be added to TPN bag.

If continuous feeds are given through Ryle's tube or jejunostomy, insulin can be administered as a basal bolus regimen with multiple daily subcutaneous injections. Fifty percent of TDD (determined by IV infusion initially) is given as long-acting insulin and 50% as short-acting insulin. Regular insulin at an interval of 6 h is preferred over rapid-acting analogues for their longer duration of action. Patients receiving bolus enteral feeds

are typically treated with basal bolus regimen the same as patients who are eating regular meals, taking care to match the timing of short-acting insulin with the enteral feeds.

**Planning discharge from hospital**

The discharge plan of a patient with diabetes should begin well before the discharge to ensure smooth transition of care between hospital and home. Different factors to incorporate into discharge plan include educational status, affordability, patient and family competence, psychological state, social and religious beliefs, co-morbidities and accessibility to health care [38, 39].

**Recommended care (Table 19)**

The following aspects can be integrated [7, 30, 40–42]

1. Diabetes self-management must be reviewed.
2. The discharge summary must include information on the type of diabetes, individualised targets, hypo- and hyperglycaemic emergencies, sick day rules, lifestyle modifications with medical nutrition therapy and exercise.
3. A detailed medication summary must be given to all patients in clear writing which should include the medications, formulations, dosage, instructions for use and duration of therapy.
4. Those on insulin should be sufficiently adept with insulin injection rotation technique, site rotation, frequency of self-monitoring of blood glucose, insulin dosage adjustments to achieve glycaemic targets and hypoglycaemia management.
5. Patients must be encouraged to take their insulin themselves during hospital stay especially in those for whom insulin has been recently initiated.

**Table 19** On-discharge recommendations

| |
|---|
| Review *self-management* with the patient |
| Issue *discharge summary* with clear instructions |
| *Discuss about prescribed drugs*—description, dosages, possible adverse events |
| Instruct on *SMBG* and keeping of proper record of measured BG |
| Clear instructions regarding *insulin treatment*—dose, technique, frequency, various formulations |
| Instruct regarding *hypoglycaemia* and its treatment and measure to avoid it |
| Discuss regarding *BG targets* required for good control |
| Importance of regular *follow-up* |

6. Medications at discharge

A. In a patient *previously diagnosed to have diabetes*, the medications at discharge can be based on the HbA1c at admission or the pre-admission HbA1c [42].

- HbA1c <8%—The patient's baseline medications may be continued. HbA1c >8%—Changes include the addition of an oral anti-diabetic medication, intensification of the doses of pre-existing medications (or insulin) and/or initiation of basal insulin for patients not on insulin.
- In cases where HbA1c is not available and the patient has fair glycaemic control, the pre-admission anti-diabetic medication may be continued. In those with poor glycaemic control, the pre-admission medications may be up-titrated.

B. In a patient with *previously undiagnosed diabetes*, a similar approach may be followed. [43, 44]

- HbA1c 6.5–7%—Lifestyle modification and follow-up are recommended. Monotherapy with an oral glucose-lowering agent may be considered.
- HbA1c >7%—Use of oral anti-diabetic and/or insulin where indicated

C. Patient with *stress hyperglycaemia*

- HbA1c <5.7%—Follow-up is recommended.
- HbA1c 5.7–6.4%—Must be treated as per recommendations for pre-diabetes.

**Table 20** Protocol for discharge management

| HbA1c | Action to take |
|---|---|
| **Previously diagnosed** | |
| <8% | Pre-discharge medications to be continued |
| >8% | Intensify treatments with OADs, insulin |
| No A1c available | |
| Good glycaemic control | Re-introduce pre-admission treatments |
| Poor glycaemic control | Intensify pre-admission treatment |
| **Previously undiagnosed** | |
| 6.5–7% | Lifestyle modification, metformin, follow-up |
| >7% | Continue treatment with OADs/insulin as per guidelines |
| **Stress hyperglycaemia** | |
| <5.7% | Maintain follow-up |
| 5.7–6.4% | Treatment as recommended for pre-diabetes |

7. A follow-up appointment must be scheduled within 15 days of discharge with the specialist and/or primary care physician (Table 20).

SUMMARY

- Different factors to incorporate into discharge plan include educational status, affordability, family support, co-morbidities and accessibility to health care.
- Integrated care is important; diabetes self-management must be reviewed, with a follow-up appointment scheduled within 15 days of discharge, with the medications summary at discharge.
- HbA1c levels of 8% should be cut-off to determine the future course of medications at discharge in most cases.
- Limited care settings determine a customized approach with emphasis on the education on insulin technique and blood glucose monitoring.

***Hypoglycaemia management***

**Definition**: The American Diabetes Association (ADA) defines hypoglycaemia as BG <70 mg/dl. This could present as symptomatic or asymptomatic hypoglycaemia.

*Severe hypoglycaemia* requires assistance of another person to actively administer carbohydrates, glucagon, or take other corrective actions.

**Treatment of hypoglycaemia**

Adults who are experiencing hypoglycaemia symptoms but have a blood glucose level >70 mg/dl should be treated with a small carbohydrate snack only, e.g. one medium banana, a slice of bread or normal meal, if due.

All adults with a BG <70 mg/dl with or without symptoms of hypoglycaemia should be treated as outlined below.

A. *Adults who are conscious, oriented and able to swallow*

1. Give 15–20 g quick-acting carbohydrate of the patient's choice where possible. Some examples are
   - Commercially available glucose tablets or liquids
   - 150–200 ml pure fruit juice, e.g. orange (not applicable for patients with CKD)
   - Three to four heaped teaspoons of sugar dissolved in water (for patients on alpha-glucosidase inhibitors, glucose is recommended since they cannot breakdown complex carbohydrates)
2. Repeat CBG measurement 10–15 min later. If it is still <70 mg/dl, repeat dose
3. If CBG remains <70 after 30–45 min or 3 cycles, then give 25% dextrose, as described below.

B. *Severe hypoglycaemia: unconscious/unable to eat*/requires assistance of another person for treatment

1. Check airway (and give oxygen), breathing, circulation and blood glucose.
   If the patient is on an insulin infusion, stop it immediately.
2. If IV access is available, give 25% dextrose IV [5].

Amount of 25% dextrose to be infused (ml) = (100 − current BG) × 0.8

Repeat capillary blood glucose measurement 15 min later and recalculate the dose of second bolus 25% dextrose if BG is <100 mg/dl.

- Following the bolus of 25% dextrose, infusion of 10% dextrose in water (D/W) may be needed.
- *For ICU patients on insulin infusion*: After reaching the target blood glucose, resume insulin infusion at half the previous rate [5].
- *Patients on subcutaneous insulin and NPO*: After reaching the target blood glucose, resume insulin regimen after appropriate insulin adjustment if needed.

3. Once blood glucose is >70 mg/dl and the patient has recovered, give a long-acting carbohydrate of the patient's choice where possible.

   Some examples are

   - Two biscuits
   - One slice of bread/toast
   - 200–300 ml glass of milk
   - Normal meal if due

4. *Do not omit insulin injection if due*. However, revision of insulin dose may be required.
5. Document event in patient's notes.
6. Ensure regular capillary blood glucose monitoring is continued for 24 to 48 h.
7. Give hypoglycaemia management education to the patient and family
8. Find the cause

**SUMMARY**

- The treatment of hypoglycemia is guided by the ADA definition of hypoglycemia with a cut off plasma glucose concentration of 70 mg/dl.
- If the patient is conscious, oriented and able to swallow, initial15-20 gm quick acting carbohydrate would suffice, with the monitoring and the step-up approach depending on the response for the increase in the plasma glucose.
- If the patient is unconscious, IV access or an infusion pump is preferred to provide 100-200 ml of 10% glucose over 15 minutes (e.g. 400-500 ml/hr), with monitoring to repeat till the plasma glucose is 70mg/dl.

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