Consensus Evidence-based Guidelines for In-patient Management of Hyperglycaemia in Non-critical Care Setting as per Indian Clinical Practice

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Abstract
Hyperglycaemia is an indicator of poor clinical outcome and mortality in patients with or without a history of diabetes in hospitalised patients in non-critical care condition. A consensus guideline has been developed by a panel of experts based on existing guidelines with specific attention to Indian clinical practice on the management of hyperglycaemia in patients admitted to non-critical care settings. Diagnosis for hyperglycaemia at the time of hospital admission is essential for appropriate treatment during the hospital stay and at the time of discharge. Following a consistent blood glucose target from admission to discharge is recommended for optimal glycemic management in these settings. Intervention with scheduled subcutaneous insulin therapy using basal, bolus and correctional insulin, and avoiding sliding scale insulin therapy is the key to effective management of inpatient hyperglycaemia. A safe and effective transition of therapy between home and hospital setting based on hyperglycaemic status is essential to avoid large variations in glycaemic status. The consensus guidelines will provide a basis for better clinical practice in the Indian scenario for the management of hyperglycaemia in non-critical care settings.

Introduction

Burden of diabetes

Diabetes is increasing at an alarming rate affecting more than 371 million people worldwide. Recent estimates report a 5 million increase in prevalence from 2011 to 2012, with many more undiagnosed. As a condition that persists throughout a patient’s lifespan with progressively increasing complications, diabetes decreases the quality of life, increases economic burden on the individual, their family and society. It is associated with significant morbidity and mortality with an estimated 4.8 million deaths caused due to diabetes in 2012. The increase in burden is due to the progressive nature of type 2 diabetes mellitus (T2DM) in existing patients and addition of newly diagnosed cases, which increases the number of people requiring insulin. The estimated proportion of people with diabetes (T1DM or T2DM) in US taking insulin or insulin with OADs is 12% and 14%, respectively.

Economic burden

A large component of medical expenditure on diabetes is attributed to hospital inpatient care. Out of the total estimated $176 billion spent in direct medical costs in US in 2012, the largest component of medical expenditures was hospital in-patient care (43% of the total medical cost). In India, the average annual direct costs of hospitalised patients are estimated to be more than double to those not hospitalised.

Hyperglycaemia in hospitalised patients

Approximately one in four patients admitted to a hospital has a known diagnosis of diabetes, and about 30% of patients with diabetes require two or more hospitalisations in any given year. Hyperglycaemia in in-patients can have three possible causes which include existing recognised diabetes, existing but unrecognised diabetes and hospital associated diabetes which can be iatrogenic or stress induced. Stress hyperglycaemia may occur during an acute illness and usually gets resolved with illness. The association between hyperglycaemia in hospitalized patients (with or without diabetes) and increased risk for complications and mortality is well established.

Hyperglycaemia and in-patient mortality-global

A retrospective study (July to October 1998) conducted in a community teaching hospital in US to determine the prevalence and mortality of in-hospital hyperglycaemia in patients with and without a history of diabetes, found that newly discovered hyperglycaemia was associated with higher in-hospital mortality rate (16%) than those with prior history of diabetes (3%) or normoglycaemia (1.7%; both P < 0.01) (Figure 1). Further, it was observed that new hyperglycaemic patients had a longer hospital stay, higher admission rate to an intensive care unit (ICU), and were less likely to be discharged to home, frequently requiring transfer to a transitional care unit or nursing home facility.

Hyperglycaemia and in-patient mortality-India

A retrospective analysis of patient records (during 2007) from a tertiary care hospital in India reported that diabetes...
contributed to 8.2% hospitalisations and 15.6% in-patient deaths. This corresponds to mortality rates of 48.3/1000 and 23.4/1000 admissions for patients with and without diabetes, respectively.\(^{12}\)

Control of hyperglycaemia among non-critically ill patients admitted to general medicine and surgery services is important, as it is linked to adverse clinical outcomes like infections, prolonged stay in hospital and more disability after institutional discharge and death.\(^{6,8,13}\)

**Rationale/need for India specific guidelines**

Existing guidelines on management of in-patient hyperglycaemia are provided by Society of Hospital Medicine,\(^{14}\) American Diabetes Association-American Association of Clinical Endocrinologists (ADA-AACE),\(^{15}\) Endocrine Society,\(^{16}\) Australian Diabetes Society (ADS),\(^{17}\) Association of Physicians of India (API),\(^{18}\) and Canadian Diabetes Association (CDA).\(^{19}\) These organisations provide clinical practice guidelines for management of in-patient hyperglycaemia in their respective regions.

**Existing guidelines**

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**Rationale/need for India specific guidelines**

However, due to confounding biases and non-applicability of these guidelines in Indian scenario, these cannot be widely used in Indian clinical practice. The India specific guideline formulated by the Association of Physicians of India\(^{19}\) is brief and does not provide sufficient details in the management of in-patient hyperglycaemia in specific circumstances of non-critical care conditions. Thus, there is a need for more elaborate guidelines on specific conditions of in-patient hyperglycaemia management and development of consensus for Indian clinical practice.

**Scope of the current consensus guideline**

In-hospital hyperglycaemia is observed in patients admitted to hospital in both critical and non-critical care condition. The clinical condition at the time of admission and care process in the intensive care unit (ICU) and non-ICU settings are different. The corresponding hyperglycaemic status of the subject and requirements for management procedure also differ. The scope of the current review is to frame appropriate guidelines for the management of hyperglycaemia in patients admitted to non-critical care settings, broadly divided into diagnosis and monitoring, target blood glucose, pharmacological therapy including insulin and non-insulin medications and management in special conditions. The consensus guidelines have been framed in consideration with the existing guidelines from ADA-AACE, Endocrine society, and Society of Hospital Medicine from USA, ADS from Australia, CDA from Canada and API and justified for use according to routine Indian clinical practice.

**Methodology**

A systematic review of literature from medical databases was conducted to provide the best possible evidence base for the recommendations. Existing guidelines, meta-analyses, systematic reviews and key cited articles relating to the medical condition were reviewed by a group of doctors and recommendations relevant to Indian scenario were framed. The recommendations were discussed at the National Insulin Summit, held in August 2013 by an expert panel of physicians, endocrinologists and key opinion leaders. At this summit, recommendations for each section of the guidelines, and overall recommendations were agreed upon. Where there was little or no evidence, the committee relied on experience, judgement and consensus to make their recommendations. The consensus document was drafted and circulated for further feedback from the participants and others who could not attend.

**Grading system**

The current consensus guidelines have been developed in accordance to the AACE protocol for standardised production of clinical practice guidelines.\(^{20}\) Recommendations are organised by topic and are assigned evidence level (EL) ratings on the basis of the quality of supporting evidence all of which have also been rated for strength. Recommendations are based on clinical importance and graded as A (strongly recommend), B (intermediate), C (weak) and D (not evidence based), those are coupled by four intuitive levels of evidence: 1, 2, 3, 4. They have been positioned on the basis of available evidence to be used for grading recommendations as follows.

- “1”: Meta-analysis of randomised controlled trials, randomized controlled trials
- “2”: Meta-analysis of nonrandomised prospective or case-controlled trials, nonrandomised controlled trial, prospective cohort study, retrospective case-control study
- “3”: Cross-sectional study, surveillance study (registries, surveys, epidemiologic study, retrospective chart review, mathematical modelling of database), consecutive case series, single case reports
- “4”: No evidence (theory, opinion, consensus, review, or preclinical study)

**Management of Hyperglycaemia**

**Diagnosis of in-patient hyperglycaemia**

Hyperglycaemia is reported in approximately 33% and 80% of patient’s admitted to non-ICU and ICU settings, respectively\(^{21,22}\) and is diagnosed by measuring either fasting blood glucose (FBG) or glycated haemoglobin (HbA1c).

**Fasting blood glucose**

The ADA-AACE consensus statement on in-patient glycaemic control defines patients with FBG levels ≥ 140 mg/dL as having diabetes.\(^{15}\) This is further endorsed by other organisations\(^{15,16,18,19}\) and is recommended in the current guideline. The Endocrine society recommends that all patients be assessed for history of diabetes and determine blood glucose levels by laboratory tests, irrespective of prior diagnosis of diabetes. In in-patients with no history of diabetes and BG levels < 140 mg/dL, the point of care (POC) BG is monitored based on clinical condition, and in those with BG ≥ 140 mg/dL, the POC BG monitoring is carried out continuously with appropriate therapeutic intervention.\(^{16}\)

**Glycated haemoglobin**

Use of HbA1c for diagnosis of hyperglycaemia (> 6.5%) in patients with newly detected diabetes can help differentiate patients with previously undiagnosed diabetes and stress induced hyperglycaemia.\(^{23}\) Therefore guidelines recommend an HbA1c test in patients with known diabetes\(^{16}\) or with newly detected hyperglycaemia\(^{16,17}\) if it has not been performed in previous 2-3 months. However, currently HbA1c is not considered a suitable diagnostic test for diabetes or intermediate hyperglycaemia. The inherent limitations to the use of HbA1c test for diagnosis of diabetes in in-patients include: relatively low diagnostic sensitivity and potential altered values in the presence of haemoglobinopathies, high-dose salicylates, haemodialysis, blood transfusions, and iron deficiency anaemia.\(^{24}\)

**Recommendations**

- For patients admitted to non-ICU settings, it is recommended...
to routinely diagnose hyperglycaemia at the time of admission using laboratory blood glucose (BG) testing (Grade A; EL2).25-26

- It is recommended to diagnose in-patient hyperglycaemia as any blood glucose concentration > 140 mg/dL without the evidence of previous diabetes (Grade A; EL4).15
- All in-patients with history of diabetes or hyperglycaemia are recommended to be diagnosed for HbA1c level, if not performed in the previous 2-3 months (Grade A; EL2).27-28

Monitoring of hyperglycaemia

Timing of blood glucose monitoring

Monitoring of BG levels using POC testing in in-patients varies with the time of nutritional intake, medication pattern and therapy of choice. The ADA-AACE consensus statement on in-patient glycaemic control recommends that for patients on oral diet, POC testing is usually performed four times a day: three times before each meal and once at bedtime.8,13 This recommendation is followed by other guidelines.16-18 However, in select cases, blood glucose levels can be monitored post-prandially and overnight (predawn at 3 a.m.) when bedtime bolus/prandial insulin are administered. The API guidelines recommend glucose monitoring post-prandially and Australian Diabetes Society suggest BG monitoring post-prandially and overnight in addition to before meals and bedtime testing.17,18 Usually BG levels are monitored as close as possible to meal timings29 and at bedtime.30 More frequent POC testing is suggested in patients receiving intra venous (IV) continuous insulin infusion,31 glucogenic drugs,32 enteral or parenteral nutrition, nil per os (NPO)33 or with frequent hypoglycaemic episodes.8

Recommendations

- For patients with BG levels > 140 mg/dL it is recommended to monitor blood glucose with bedside point of care (POC) (glucose meters) testing for at least 24 to 48 hours with appropriate medication (Grade A; EL 3).33

Glucose monitoring sites and devices

Blood glucose BG values alter significantly depending on the site of blood drawn, finger-stick vs. alternative sites, and measurements done using POC testing device and laboratory methods.34 Therefore, consistent sampling sites and methods of measurement are recommended by all guidelines for appropriate monitoring of hyperglycaemia in in-patients.34 Use of personal glucose meters for documentation or for treatment of hyperglycaemia should be avoided.16 The accuracy of most hand-held glucose meters is not optimal.34 In a comparative study on five commonly used glucose meters, differences from central laboratory method (mean: 32%, coefficient of variation: 6-11% with single trained medical technologist) were observed.35

Recommendations

- For monitoring of glycaemic status, POC testing using glucose meters with demonstrated accuracy of use, are recommended in non-critically ill patients (Grade A; EL3).33
- In patients on oral nutrition, it is recommended that BG monitoring be carried out as close as possible before meals and at bedtime, matching the nutritional intake and medication regimen, and in those receiving enteral or parenteral nutrition or NPO every 4-6 h (Grade B; EL4).29
- In patients with stable glycaemic control on oral diet, blood glucose should be monitored post-prandially and at 3 a.m.

when bedtime bolus/prandial insulin are given (Grade A; EL 4).9,18

Glycaemic targets

Attaining target BG values in in-patients is essential to decrease the morbidity and mortality associated with hyperglycaemia. The ADA-AACE consensus statement on glycaemic targets in in-patients with hyperglycaemia recommend a pre-meal blood glucose levels of < 140 mg/dL and a random BG of < 180 mg/dL for majority of non-critically ill patients treated with insulin.33 This glycaemic target values are followed by most other organisations15,16 and are recommended in the current guideline. The API guidelines recommend a range of BG targets: pre-meal 110-130 mg/dL and RBG 140-180 mg/dL,38 whereas CDA recommends pre-meal BG between 90 and 144 mg/dL and random BG target < 180 mg/dL.39 The ADS recommends only random BG target of 180 mg/dL.9 With minor differences in target blood glucose levels and considering the general clinical practice in Indian conditions, target BG levels consistent with ADA-AACE guidelines have been recommended.

Targets in special situations and management

The ADA-AACE consensus statement further recommends reduction of total basal and prandial insulin doses if BG levels are between 70–100 mg/dL to avoid hypoglycaemia (< 70 mg/dL). In patients with terminal illness or severe comorbidities, and those in settings where frequent glucose monitoring is not possible, higher glucose ranges (BG < 200 mg/dL) are acceptable to avoid symptomatic hyperglycaemia. Relaxation of BG target in patients with terminal illness and stringent targets in patients with stable glycaemic status has been recommended by ADS and API guidelines as well.33

Recommendations

- In majority of in-patients with non-critical illness it is recommended to follow a pre-meal BG level < 140 mg/dL and random BG level < 180 mg/dL (Grade A; EL3).36
- Based on the clinical status, it is recommended to follow a lower glycaemic target in in-patients able to sustain glycaemic control without hypoglycaemia, and higher glycaemic target of 200 mg/dL in in-patients with terminal illness or high risk for hypoglycaemia or limited life expectancy (Grade A; EL4).9,15,18
- To avoid hypoglycaemia, it is recommended that glucose lowering therapy be reassessed in patients with BG levels < 100 mg/dL and modified in those with BG levels < 70 mg/dL (Grade B; EL3).37

Pharmacological Therapy

Transition from home to hospital

Although patients with type 1 diabetes mellitus (T1DM) continue to require insulin during their home-to-hospital transition, the need for patients with type 2 diabetes mellitus (T2DM) has to be reassessed upon admission. Modification of home oral and/or insulin (basal-bolus or multiple daily dosing) regimen is required to avoid hypoglycaemia or treat uncontrolled hyperglycaemia, based on the clinical condition of admission, corresponding medication and altered caloric intake.38

Non-insulin medication in in-patients

The use of oral and other non-insulin therapies pose unique challenges in hospital setting due to frequent contraindications to their use in many in-patient situations such as sepsis, NPO status, pancreatic disorders, renal failure, etc. Sulphonylureas
can cause severe and prolonged hypoglycaemia, particularly in the elderly, in patients with impaired renal function, and in those with poor nutritional intake. Metformin has to be discontinued in patients with decompensated congestive heart failure, renal insufficiency, hypoperfusion, or chronic pulmonary disease, in patients at risk of developing renal failure and lactic acidosis. Thiazolidinediones are known to take long time for exerting full hypoglycaemic effect, limiting their usefulness. Dipeptidyl peptidase IV inhibitors delay the enzymatic inactivation of glucagon-like peptide-1 that reduces postprandial glycaemic excursions, thus limiting their use in patients who are not eating or have reduced oral intake. In selected patients who are clinically stable, taking regular meals and have no contraindications to their use may be continued on OADs prescribed at home. Continuation on home-based OADs is also recommended by ADS and CDA and recommended in the current guidelines. In others, shifting to insulin therapy based on POC BG results (> 140 mg/dL) is safe and efficacious.

Recommendations

• Use of insulin therapy is recommended for optimal glycaemic control in non-critically ill in-patients (Grade A; EL 1).38,39

• In patients with T2DM admitted with acute illness, it is recommended to generally discontinue the use of oral anti-diabetic drugs and start insulin therapy (Grade B; EL 4).40,41

• To reduce the risk of hypoglycaemia and hyperglycaemia in prior insulin users, it is recommended to reassess the dose of insulin based on the clinical status of the patient (Grade B; EL 2).42

• In select patients admitted with well controlled blood glucose levels, pre-existing oral anti-diabetic drugs may be continued (Grade B; EL 4).19

Sliding scale therapy

Basal-bolus regimens have an important advantage over sliding scale regimens in that they are proactive in controlling hyperglycaemia. In a study conducted to determine the optimal management of hyperglycaemia in non-ICU patients with type 2 diabetes, patients were randomised to basal-bolus insulin regimen or sliding scale regular insulin (SSI).43 Basal bolus insulin was given at a total daily dose (TDD) of 0.4 U/kg for BG levels 140-200 mg/dL or 0.5 U/kg for BG levels 201-400 mg/dL. The TDD was divided in equal doses between basal and bolus components. The SSI component was given four times/day for BG levels > 140 mg/dL.

The basal-bolus regimen achieved better glycaemic control over the SSI regimen. Patients in the basal bolus group achieved mean BG levels of < 180 mg/dL by day 2 and < 160 mg/dL by day 4 with no increase in hypoglycaemia. A BG target of 140 mg/dL was achieved in 66% of patients in basal bolus group and in 38% of those in the SSI group. The basal-bolus regimen was associated with lower mean fasting glucose (147 vs. 165 mg/dL, P < .01), lower mean random glucose (164 vs. 189 mg/dL, P < .001), and lower mean glucose during hospital stay (166 vs. 193 mg/dL, P < .001).45

Sliding scale insulin is discontinued in clinical practice due to its non-physiologic strategy with retrospective reaction to BG levels and its association with increased rate of hyperglycaemic episodes.44 Further, sliding scale insulin promotes glucose ‘roller coaster’ and cannot predict insulin dosage requirements.41 Avoidance of SSI regimen as sole therapy in in-patients for the management of hyperglycaemia is recommended consistently across all guidelines.15-19

Recommendation

• Clinical practice of sliding scale insulin should be discontinued as the sole therapy for management of hyperglycaemia in patients with diabetes, admitted to non-critical care conditions (Grade A; EL 1).45,44

Insulin therapy

In most patients admitted to non-ICU hospital settings, scheduled subcutaneous basal insulin regimen is recommended for management of hyperglycaemia to prevent both hyperglycaemia and hypoglycaemia.15

Basal-bolus therapy

There are three components to a basal bolus regimen: basal insulin, bolus or meal or nutritional insulin and correction insulin. Intermediate- or long-acting insulin is administered once or twice daily as basal component and short- or rapid-acting insulin is administered in co-ordination with food intake for bolus or prandial component. Correction insulin (short- or rapid-acting) is administered together with the usual dose of bolus insulin for patients with higher BG levels. Correction insulin is customised to match the insulin sensitivity for each patient.

Patients who are taking oral diet with BG levels > 140 mg/dL are suitable to take basal bolus insulin therapy initiated at a total daily dose based on body weight. For patients who are not taking oral diet, basal insulin is continued once daily (glargine or detemir) or twice daily [neutral protamine Hagedorn (NPH)]. bolus insulin is held and correction doses of rapid insulin analogue (aspart, lispro, glulisine) or regular insulin (RI) every 4- to 6-h interval are added as needed.

In select patients with controlled diabetes on premix insulin therapy prior to admission and in in-patients with stable glycaemic control, continuation of premix insulin should be considered. Continuation of home insulin therapy,19 specifically premix insulin therapy in select in-patients is recommended by other organisations as well.16

Recommendations

• For in-patients with diabetes receiving insulin therapy prior to admission, a scheduled subcutaneous (SC) insulin regimen is recommended in hospital settings (Grade A; EL 1).38,39

• In in-patients taking oral diet it is recommended that scheduled SC insulin should include once or twice daily injections of basal or intermediate-acting (degludec/detemir/glargine) insulin and prandial doses of short-acting (regular insulin) or rapid (aspart/lispro/glulisine) insulin (Grade A; EL 1).38

• For patients with diabetes controlled on premix insulin therapy prior to admission, same regimen may be continued (Grade A; EL 4).

• When glucose control is stabilised; selected patients can be shifted to premix insulin therapy (Grade A; EL 4).

• In in-patients who are NPO and fulfil caloric requirement through enteral or parenteral nutrition it is recommended to initiate basal insulin alone in combination with correction doses of rapid acting insulin analogues every 4 hours or regular insulin every 6 hours (Grade A; EL 1).38,39

Determining total daily dose of insulin

For patients admitted to non-critical care setting and required
Table 1: Estimation of Total daily dose of insulin in insulin-naïve patients

<table>
<thead>
<tr>
<th>TDD estimation (units/kg body weight)</th>
<th>Patient characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.3</td>
<td>Underweight, older age, haemodialysis</td>
</tr>
<tr>
<td>0.4</td>
<td>Normal weight</td>
</tr>
<tr>
<td>0.5</td>
<td>Overweight</td>
</tr>
<tr>
<td>≥ 0.6</td>
<td>Obese, insulin resistant, glucocorticoids</td>
</tr>
</tbody>
</table>

to take insulin, the first step in ordering insulin is to estimate the patients’ total daily dose (TDD) of insulin requirement. The TDD of insulin is calculated based on the body weight, divided equally between basal (50%) and bolus (50%) insulin. Bolus insulin (adjusted daily based on patients’ anticipated caloric intake) is divided into 3 parts for each meal. In insulin naïve patients, insulin can safely be initiated at a TDD of 0.3-0.6 units/kg body weight, based on lean or overweight body, renal insufficiency, obesity, insulin resistance and concomitant medication that can affect the glycaemic status (glucocorticoids) (Table 1).

Starting insulin at different TDD has been recommended by Endocrine Society and Society of Hospital Medicine and API. Although slight variations in TDD of insulin is presented in Bajwa et al (0.25 units/kg body weight in older age and haemodialysis patients, 0.5 units/kg body weight in ordinary patients and 1.0 units/kg body weight in obese and insulin resistant patients), the consensus guidelines recommend the dosing range presented by well accepted guidelines from Endocrine Society and Society of Hospital Medicine. However, in select individual patients, the TDD of insulin can vary based on the clinical condition and treating physician’s discretion.

**Recommendations**

- The TDD of basal bolus insulin therapy is recommended to calculate based on the body weight of the in-patient (Grade A; EL 1).
- In insulin-naïve patients who are normal in weight, initiate basal bolus insulin regimen at a TDD of 0.4 U/kg body weight (Grade A; EL 4).
- In insulin-naïve patients who are underweight or old or have renal impairment, initiate basal bolus insulin regimen at a TDD of 0.3 U/kg body weight (Grade A; EL 4).
- In insulin-naïve patients who are overweight initiate basal bolus insulin regimen at a TDD of 0.5 U/kg body weight (Grade A; EL 4).
- In insulin-naïve patients who are obese, insulin resistant or taking glucocorticoid treatment, initiate basal bolus insulin regimen at a TDD of ≥ 0.6 U/kg body weight (Grade A; EL 4).

*In select individual patients, insulin dose can vary based on the clinical condition and physician’s discretion.

**Insulin order: Basal insulin**

In general, type 1 diabetes patients typically exhibit less insulin resistance and require lower daily insulin dosage than type 2 diabetes patients, especially if they are not obese. In type 2 patients receiving insulin before admission (as outpatient regimen), insulin therapy can be initially continued with the same TDD unit for unit, administered as basal/bolus regimen. The requirement in these patients is slightly higher than insulin-naïve patients. Daily adjustments of insulin dose are required, depending on patients’ blood glucose testing results and caloric intake.

Table 2: Correctional insulin protocol

<table>
<thead>
<tr>
<th>BG (mg/dL)</th>
<th>Insulin-sensitive</th>
<th>Usual</th>
<th>Insulin-resistant</th>
</tr>
</thead>
<tbody>
<tr>
<td>100-140</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>&gt;141-180</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>181-220</td>
<td>1</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>221-260</td>
<td>2</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>261–300</td>
<td>3</td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td>301–350</td>
<td>4</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>351–400</td>
<td>5</td>
<td>12</td>
<td>14</td>
</tr>
<tr>
<td>&gt;400</td>
<td>6</td>
<td>14</td>
<td>16</td>
</tr>
</tbody>
</table>

Insulin adjustment can be carried out as below:

- if the fasting and predinner BG = 140–180 mg/dL (and absence of hypoglycaemia) increase dose of basal insulin (detemir) by 10% every day
- if the fasting and predinner BG > 180 mg/dL (and absence of hypoglycaemia) decrease dose of basal insulin (detemir) by 20% every day
- if patient develops hypoglycaemia (BG < 60 mg/dL), decrease basal insulin (detemir) dose by 20%

**Recommendations**

The TDD is distributed as ~50% intermediate acting or basal insulin and 50% bolus short- or rapid-acting insulin; insulin degludec (OD) or NPH/detemir/glargine (OD/BID, same time each day) and short/rapid acting insulin (3 divided doses before each meal) (Grade A; EL 1).

*In Indian conditions, initiating a lower basal dose may be considered.

**Insulin order: Correctional insulin**

Correctional insulin requirements depend on individuals’ insulin sensitivity. A sensitivity or correction factor is calculated by dividing 1700 by the TDD. Low, medium, and high scales are used in most hospitals to provide insulin doses when BGL > 140-150 mg/dL and increased with additional BG increments of 40-50 mg/dL. A low scale increases insulin by 1 unit for each increment of 40-50 mg/dL and corresponds to a sensitivity factor of 40-50. The low scale would be used for patients requiring a TDD of 20-42 units, moderate scale for patients requiring TDD of 43-84 units, and high-dose scale for patients requiring 85-126 units/day.

The Endocrine Society recommends that correctional insulin should be added to the scheduled insulin dose as part of bolus insulin before each meal (only half at bedtime). Correction insulin protocol for usual, insulin sensitive and insulin resistant patients is followed as per Table 2. In patients taking oral diet, correctional insulin (regular or rapid-acting) is administered following the ‘Usual’ column, before each meal (Table 2). It is administered following ‘Sensitive’ column (regular insulin every 6 h or rapid-acting insulin every 4-6 h) in patients not able to take oral diet, elderly patients, and those with impaired renal function and with ‘Resistant’ column in patients with persistent hyperglycaemia (> 140 mg/dL) of fasting and pre-meal glucose, and absence of hypoglycaemia, those receiving corticosteroids and those treated with more than 80 U/d before admission (Table 2). In patients with hypoglycaemia (< 70 mg/dL), the endocrine society recommends decreasing regular or rapid-acting insulin from the insulin-resistant to the usual column or from usual to insulin-sensitive column.

Although slight variations in correctional insulin doses is presented in Bajwa et al, the current consensus guidelines...
recommend the dosing range presented by well accepted guidelines from Endocrine Society. However, in select individual patients, the correctional insulin dose can vary based on the clinical condition and treating physician’s discretion.

Recommendations

- To treat uncontrolled hyperglycaemia in in-patients receiving basal bolus therapy, it is recommended to give regular or rapid-acting insulin as correction insulin as per the Table 2 (Grade A; EL 1).

- In patients with BG < 100 mg/dL, nutrition support given to patient should be assessed and BG levels should be monitored regularly (Grade B; EL 4).

Transition of therapy at the time of hospital discharge

Hospital discharge can be stressful to patients and their family, and insulin regimens are often complex, entailing administration of 2 different insulin preparations. Insulin regimen requires daily adjustments according to glucose readings; hence orally communicated instructions alone are often inadequate. Establishing formalised discharge instructions for patients at each hospital and educating on the same are essential. The Endocrine Society recommends that- for patients initiated on insulin therapy as a new medication as in-patient and discharged home, providing patient education and written information on the method and timing of insulin administration at prescribed doses and recognition and treatment of hypoglycaemic episodes are important. It suggests initiating insulin therapy at least one day before discharge to assess the efficacy and safety of therapy. Other guidelines are in agreement with this recommendation and suggest follow-up within 10-14 days of discharge.

Proper coordination of patient care services during discharge of in-patients with hyperglycaemia from hospital to home is essential for safe transition to outpatient setting and reduced need for readmission. Measurement of HbA1c concentration in patients at the time of admission and during the hospital stay can assist in tailoring the glycemic management in these patients at the time of discharge. The Endocrine Society suggests that patients with controlled glycaemia (HbA1c < 7%) can be discharged on the same (OAD and/or insulin) outpatient regimen, intensification of outpatient regimen in patients with elevated HbA1c and continue in-patient insulin regimen in patients with severe hyperglycaemia. Due to the lack of recommendations from other organisations on use of medication at time of discharge, current consensus guidelines adapted the suggestions from Endocrine Society for clinical practice in Indian conditions. The API guidelines suggest shifting to premix insulin twice daily if possible in patients before discharge from hospital.

Recommendations

- To determine the safety and efficacy of insulin use in in-patients at the time of transition to outpatient, insulin administration should be initiated at least one day before discharge (Grade A; EL 4).

- For in-patients with good glycaemic control (HbA1c < 7%) at the time of admission and during hospital stay, restart the same oral anti-diabetics or insulin therapy at the time of discharge, if there’s no contraindication to their use (Grade A; EL 4).

- In patients with moderate glycaemic control (HbA1c 7-9%) at the time of admission and during hospital stay, restart outpatient oral anti-diabetics and basal insulin once daily at 50-80% of hospital dose (Grade A; EL 4).

- In patients with poor glycaemic control (HbA1c > 9%) at the time of admission and during hospital stay, discharge on basal bolus at same hospital dose or restart oral anti-diabetics and discharge on basal insulin once daily at 50-80% of hospital dose (Grade A; EL 4).

- For patients newly prescribed with insulin use at the time of discharge, institutions should provide patient education and formal discharge instructions on doses, methods and timing of insulin administration (Grade A; EL 3).

*Assess HbA1c in hospitals wherever possible and reassess after 3 months.

Special conditions

Switch from intravenous to subcutaneous insulin

Most in-patients recovering from a critical illness or after a surgical procedure are moved to non-ICU setting. Although intravenous (IV) insulin is administered during operative procedure, shifting to SC insulin is recommended post-operatively since many patients begin to eat by the first postoperative day. Continuing IV insulin in response to prandial hyperglycaemia in these patients has a risk of hypoglycaemia occurring after the postprandial hyperglycaemia declines. It is difficult to adequately calculate true basal insulin requirements in these patients who take oral food while receiving an insulin infusion, prompting administration of SC rapid acting insulin, dosed according to caloric intake. The transition results in significant reductions in morbidity and mortality, with lower costs and less need for nursing time.

The stress of surgery or critical illness will increase insulin
requirements, and, as stress decreases, basal insulin requirements will also decrease. During transition from IV to SC insulin, a reduction in the basal dose by 20% to 33% was observed to be safe and effective to account for decreasing requirements. A sample basal/bolus insulin dose calculation regimen for a patient started on oral diet that required 2 U/h of insulin overnight while NPO is presented in Table 3. To avoid recurrence of hyperglycaemia during the transition from IV to SC insulin, the Endocrine Society recommends initiating SC insulin, 1–2 h before discontinuation of IV insulin. Basal insulin is given before transition and continued once (detemir / glargine) or twice (detemir/NPH) daily. Guidelines from other organisations also recommend shift to SC insulin well in advance of the discontinuation of IV insulin.

**Recommendations**

- Basal bolus insulin therapy should be started in in-patients with diabetes, at least 1-2 hr before discontinuation of IV insulin (Grade A; EL 1).
- For in-patients with hyperglycaemia transitioning from IV to SC insulin and taking oral diet, initiate SC intermediate or long acting insulin (degludec/detemir/glargine) at 50% of calculated TDD as basal component along with prandial and supplemental insulin as required (Grade A; EL 2).
- For in-patients with hyperglycaemia transitioning from IV to SC insulin but not on oral diet, initiate SC intermediate or long acting insulin (degludec/detemir/glargine) at 80% of calculated TDD as basal insulin along with prandial and supplemental insulin as required (Grade A; EL 1).

**In-patients receiving enteral or parenteral nutrition**

Enteral nutrition (EN) or parenteral nutrition (PN) given to in-patients (to overcome malnutrition), is an independent risk factor for the onset or aggravation of hyperglycaemia. Hyperglycaemia in this group of patients is associated with higher risk of cardiac complications, infections, sepsis, acute renal failure, and death. Hence, it is recommended that early intervention be initiated to prevent and correct hyperglycaemia and improve clinical outcomes in patients receiving EN and PN.

Diabetes specific nutritional formulae have demonstrated a reduction of 18-29 mg/dL of BG in in-patients receiving EN or PN, suggesting early insulin intervention in this group. Achieving desired glycaemic goals in patients receiving EN poses unique challenges such as unexpected interruption of feedings that can lead to hypoglycaemia. In such case, insulin dosing should be adjusted appropriately. If interrupted for > 2 hours, all insulin dose should be withheld and patient supplemented with IV 10% dextrose, same as enteral feedings to prevent hypoglycaemia. Providing adequate water supply and monitoring of electrolytes is also important. Dehydration is a common complication of enteral feedings and a frequently overlooked cause of hyperglycaemia. A sample calculation of insulin requirements for a patient on enteral feeds is presented in Table 4.

The Endocrine Society suggests SC insulin therapy in patients receiving EN with basal insulin in combination with short- or rapid-acting insulin as prandial insulin and correctional insulin as required. With slight variations in these requirements, other guidelines also recommend SC basal bolus insulin therapy. In patients receiving PN, although sparse, recommendations vary across the guidelines. Hence the current consensus guidelines have framed recommendations based on the intuitive clinical experience in Indian conditions.

**Recommendations**

- For in-patients with or without diabetes history, receiving EN and PN, it is recommended that POC testing be initiated (Grade A; EL 3).
- For in-patients without diabetes history, achieving BG levels < 140 mg/dL for one to two days with required caloric intake, and not on insulin therapy it is recommended to discontinue POC testing (Grade B; EL 4).
- For in-patients with or without diabetes history with BG levels > 140 mg/dL, and a continuing requirement of correction insulin for at least 12-24 hours it is recommended to initiate scheduled insulin therapy (Grade B; EL 4).
- For in-patients receiving continuous EN, intermediate (NPH) or long acting insulin (degludec/detemir/glargine) OD or twice daily (BID) and rapid acting insulin analogue (every 4 h) or short acting insulin (every 6 h) should be started (Grade A; EL 1).
- For in-patients receiving cycled EN, intermediate (NPH) or long acting insulin (degludec/detemir/glargine) in combination with short acting insulin at 6 hour intervals or insulin aspart at 4 hour intervals should be started during EN (Grade A; EL 1).

*In patients receiving PN, higher dose of insulin is required.

**Perioperative management of diabetes**

There is a lack of evidence from existing guidelines on management of hyperglycaemia in in-patients undergoing non-intensive surgery. In the absence of evidence, recommendations...
### Table 5: Comparison of recommendations from current consensus guidelines and existing guidelines

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Consensus guideline</th>
<th>Endocrine society</th>
<th>AACE-ADA consensus statement</th>
<th>Canadian Diabetes Association</th>
<th>Society of Hospital Medicine</th>
<th>Australian Diabetes Society</th>
<th>Association of Physicians of India</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diagnosis of hyperglycaemia</strong></td>
<td>140 mg/dL</td>
<td></td>
<td></td>
<td></td>
<td>140 mg/dL</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Monitoring of in-patient hyperglycaemia</strong></td>
<td>Same as</td>
<td>AACE-ADA;</td>
<td>More frequent in patients on NPO; Use POC glucose meters</td>
<td>More frequent in patients on NPO</td>
<td>Use POC glucose meters</td>
<td>Overnight</td>
<td>Post-prandial</td>
</tr>
<tr>
<td><strong>Glucose targets</strong></td>
<td>Pre-meal: &lt; 140 mg/dL; Random: &lt; 180 mg/dL; More and less stringent targets in stable and terminally-ill patients</td>
<td>Pre-meal: 90-110 mg/dL; Random: 140-180 mg/dL;</td>
<td></td>
<td></td>
<td></td>
<td>Pre-meal: 110-130 mg/dL Random: 140-180 mg/dL;</td>
<td>Rest same as consensus</td>
</tr>
<tr>
<td><strong>Transition from home to hospital</strong></td>
<td>Discontinue OADS, start insulin: Continue OADS in select cases</td>
<td>Continue pre-hospitalisation OADS or insulin regimens</td>
<td></td>
<td></td>
<td>Same as consensus</td>
<td>Same as AACE-ADA</td>
<td>Same as consensus</td>
</tr>
<tr>
<td><strong>Sliding scale insulin</strong></td>
<td>Avoid sliding scale insulin</td>
<td>Same as AACE-ADA. Start premix insulin in select cases</td>
<td>Start SC basal bolus insulin therapy and correction insulin as appropriate</td>
<td>Same as consensus</td>
<td>Same as AACE-ADA</td>
<td>Same as AACE-ADA</td>
<td>Same as AACE-ADA</td>
</tr>
<tr>
<td><strong>Insulin therapy</strong></td>
<td>TDD of 0.3 to 0.6 U/kg BW</td>
<td>TDD of 0.2 to 0.5 U/kg BW</td>
<td>TDD of 0.25 to 1.0 U/kg BW</td>
<td>TDD of 0.25 to 1.0 U/kg BW</td>
<td>Same as consensus</td>
<td>Same as consensus</td>
<td>Same as consensus</td>
</tr>
<tr>
<td><strong>Determining TDD in insulin-naive patients</strong></td>
<td>TDD divided as 50% basal and 50% bolus (for 3 meals); Correctional insulin as required</td>
<td>Provide formal discharge instructions on insulin use</td>
<td>Initiate insulin regimen at least 1 day before discharge; At discharge: if HbA1c &lt; 7%—start outpatient OADS/insulin *</td>
<td>Initiate insulin regimen at least 1 day before discharge;</td>
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</tr>
<tr>
<td><strong>Transition from hospital to home</strong></td>
<td>Start SC basal bolus therapy at least 1-2 hours before discontinuation of IV insulin</td>
<td>Same as consensus</td>
<td>In patients receiving EN start basal insulin in combination with short- or rapid-acting insulin and correctional insulin as required;</td>
<td>In patients receiving EN start basal insulin and multiple prandial insulin;</td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>Switch from IV to SC insulin</strong></td>
<td>In patients receiving EN start basal insulin in combination with short- or rapid-acting insulin and correctional insulin as required;</td>
<td>Discontinue OADS and non-insulin injectables; use IV or SC insulin in patients with T1DM undergoing minor or major surgery</td>
<td>Discontinue OADS and non-insulin injectables; use IV or SC insulin in patients with T1DM undergoing minor or major surgery</td>
<td>Discontinue OADS and non-insulin injectables; use IV or SC insulin in patients with T1DM undergoing minor or major surgery</td>
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</tr>
<tr>
<td><strong>In-patients taking EN</strong></td>
<td>In patients receiving EN start basal insulin in combination with short- or rapid-acting insulin and correctional insulin as required;</td>
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<tr>
<td><strong>In-patients taking PN</strong></td>
<td>In patients receiving PN, start higher dose of insulin</td>
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<tr>
<td><strong>Peri-operative management of diabetes</strong></td>
<td>Use SC insulin in patients undergoing day care surgery and IV insulin in patients undergoing major surgery</td>
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<td></td>
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<td></td>
</tr>
</tbody>
</table>

*If HbA1c 7-9%—start outpatient OADS and 50-80% in-hospital basal insulin; If HbA1c >9%—start in-hospital basal bolus insulin or OADS+ 50-80% in-hospital basal insulin. Abbreviations: AACE-ADA: American Association of Endocrinologists and the American Diabetes Association; POC: point of care; BW: body weight; NPO: Null per os; OADS: Oral anti-diabetic drugs; TDD: total daily dose; HbA1c: glycated haemoglobin; EN: Enteral nutrition; PN: Parenteral nutrition; T1DM: Type 1 diabetes mellitus; BW: Body weight
were based on general principles of blood glucose control in patients with diabetes, and review articles as well as clinical experience in Indian practice.

Patients with diabetes undergoing minor or major surgical procedures require CII or SC basal bolus insulin administration adjusted according to the results of BG testing. Failure to provide basal insulin to a patient with diabetes can lead to the rapid development of severe hyperglycaemia and diabetic ketoacidosis.

In patients with diabetes undergoing day care surgery, require SC insulin during perioperative period. In this procedure, on the night before surgery insulin should be initiated with 2/3rd dose of bedtime NPH/RI or 100% dose of bedtime aspart. On the morning of surgery it is suggested to administer half dose of NPH, hold RI or hold all rapid-acting insulin analogues. During the immediate preoperative conditions, start IV 5% dextrose at 100 mL/h and titrate to 140-180 mg/dL and BG levels have to be adjusted by supplemental with rapid acting insulin aspart. However, API recommends that in select patients with controlled glycaemia, undergoing relatively minor surgical procedures (cataract surgery) can be maintained on OAD therapy.

In patients with diabetes undergoing major surgery require continuous IV insulin infusion during perioperative period. In these patients, it is suggested to administer 0.1U/mL of regular insulin dose at a rate of 0.02 U/kg/h (1.4 U/h for a 70 kg individual). Alternatively, the pre-admission TDD insulin can be divided by 24 hours to determine the infusion rate. It is further suggested to start CII at least 2 hours before surgery and continue until BG levels fall in normal range. In the absence of guidelines on hyperglycaemia management in these patients, recommendations were framed from review articles as well as clinical experience of expert panel.

**Recommendations**

- **In patients with diabetes undergoing day care surgery on SC insulin (Grade A; EL 4).**
  - on the night before surgery reduce the dose of bedtime NPH/RI to two third dose or continue bedtime short or rapid acting insulin at same dose
  - on the morning of surgery modify the dose of basal insulin to half dose and hold RI or other insulin analogues
  - prior to surgery, start IV 5% dextrose at 100 mL/h and titrate to 140–180 mg/dL
  - supplement with short or rapid acting insulin as required

- **Patients with diabetes undergoing major surgery, should preferably be initiated on IV insulin (Grade A; EL 4).**
  - initiate at 0.02 U/kg/h (1.4 U/h for a 70 kg individual) or with pre-admission TDD insulin dose divided by 24 hours
  - Start at least 2 hours before surgery

**Patients receiving drugs that influences glycaemic status**

In patients with or without a history of diabetes, use of glucocorticoids results in hyperglycaemia. It alters a variety of metabolic pathways including hepatic glucose production, impaired glucose uptake in peripheral tissues with resulting hyperglycaemia. Due to inadequate quality evidence in the management of hyperglycaemia in these patients, framing appropriate guidelines is difficult. The API guidelines recommend basal bolus insulin therapy, with correctional insulin doses and sustained monitoring of BG for first 48 hours in patients receiving glucocorticoid therapy. Sustained monitoring of BG for the first 48 hours is important to adjust the TDD of insulin in patients receiving glucocorticoid therapy according to the usual, sensitive and resistant conditions.

**Recommendations**

- **In-patients receiving glucocorticoid therapy** with persistent hyperglycaemia, SC basal bolus insulin therapy should be initiated, based on a starting dosage of 0.3 to 0.6 U/kg/day (Grade A; EL 4).
- **In patients with mild hyperglycaemia oral anti-hyperglycaemic agents can be considered (Grade B; EL 4).**

*Adjust dosages based upon steroid regimen and type

**Summary**

Management of different types of hyperglycaemia in the non-critical condition involves systematic evaluation of glycaemic status, setting of glycaemic target and providing therapeutic interventions. For most patients in non-critical condition, a scheduled subcutaneous insulin regimen is the preferred therapy. However limitations exist in dispensing accurate doses of basal and bolus insulin during and after the hospital stay, based on clinical conditions. The advent of new rapid acting insulin analogues like aspart and ultra-long acting insulin degludec provide better therapeutic options for the physician to control the glycaemic excursions during the prandial and basal conditions. The current consensus guideline was developed based on the best clinical observations for hyperglycaemia management from exiting guidelines and protocols (Table 5). Further, this guideline aims to provide better management of hyperglycaemia in non-critical care setting as per Indian scenario.

**Proposed Algorithm for Hyperglycaemia Management in Non-Critical Care**

Based on the consensus guidelines developed for in-patient management of hyperglycaemia in non-critical care settings, an algorithm has been proposed (Figure 3).

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**References**

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