

INTRODUCTION

Hyperglycaemia is frequently encountered in a hospital setting. Approximately one out of four hospitalised patients has been discharged with the diagnosis of diabetes mellitus (DM). A proportion of in-patients with hyperglycaemia include patients with known diabetes, patients with previously unrecognised diabetes and those with stress-related diabetes. In-hospital, hyperglycaemia is defined as any glucose value greater than 140 mg% (7.8 mmol/L). In-hospital, hyperglycaemia is found in 32% to 40% of non-ICU patients while 41% in an ICU setting and 88% in cardiac surgery units. Among all hospitalised patients, 30% of non-ICU and 80% of ICU patients have prior history of DM.

DIAGNOSIS OF DIABETES AND HYPERGLYCAEMIA IN A HOSPITAL SETTING

It is essential to check the blood glucose either in a laboratory or by the bedside with a glucometer in all the hospitalised patients. According to American Diabetes Association (ADA) guidelines, glycated haemoglobin (HbA1c) $\geq 6.5\%$ is defined as diabetes mellitus and HbA1c between 5.7% and 6.4% is defined as pre-diabetes (at risk for development of diabetes). Measurement of HbA1c can help in differentiating undiagnosed DM from stress hyperglycaemia. The HbA1c testing should be performed in all known cases of diabetes if it is not performed within the last 2 month to 3 months.

Evidence of Beneficial Effect in Hospital Management of Hyperglycaemia

Hyperglycaemia in hospitalised patients (diabetic/non-diabetic) has a greater risk of morbidity and mortality. These patients are prone for a prolonged length of hospitalisation, increased incidence of infections, unfavourable post-discharge outcomes and, thereby, significant increase in the cost of treatment. Treatment of hyperglycaemia in critically ill settings such as cardiothoracic surgery, coronary care units, medical ICU, trauma care ICU are associated with reduction in mortality. The primary focus of this topic is regarding discussion of hyperglycaemia management in hospitalised patients.

Mechanisms of Hyperglycaemia-mediated Outcome in a Hospital Setting

Several proposed mechanisms by which hyperglycaemia can impact the outcome in hospitalised patients are given below:

1. Alternation of phagocyte function and risk of infection;
2. Increased thrombogenic activity by reduction of plasma fibrinolytic activity and increase in tissue plasminogen activator inhibitors;
3. Increased production of inflammatory mediators;
4. Endothelial dysfunction;
5. Increased production of reactive oxygen-free radicals; and
6. Impaired ischaemic preconditioning.

Hyperglycaemia and relative insulin deficiency caused by metabolic stress triggers immune dysfunction, release of fuel substrates, and other mediators such as reactive oxygen species (ROS). Tissue and organ injury occurs via the combined insults of infection, direct fuel-mediated injury, oxidative stress and other downstream mediators (**Figure 1**).

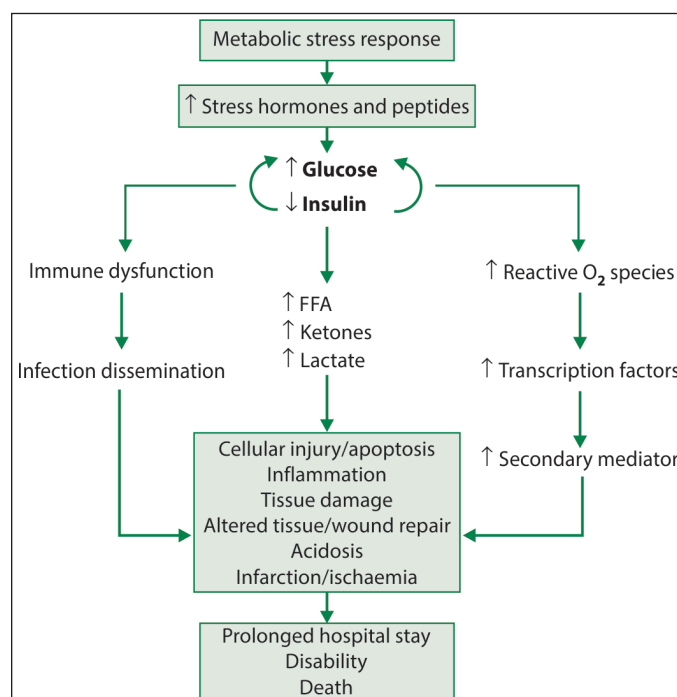


Figure 1: Link between hyperglycaemia and poor hospital outcomes
Source: Clement S, et al. Management of diabetes and hyperglycaemia in hospitals. *Diabetes Care* 2004;27:553-91.

Which Patient Requires Hospitalisation?

Some special situations where patients require hospitalisation are:

1. Life-threatening acute metabolic complications of diabetes;
2. Newly diagnosed diabetes in children—for dose adjustment and monitoring and if 'brittle diabetes' sets in;
3. Chronic poor glycaemic control: close monitoring; identify causes of poor control and modification of treatment;
4. Severe chronic complications requiring intensive treatment or any other conditions unrelated to diabetes that significantly affect its control particularly where ambulation may be a problem;
5. Uncontrolled or newly diagnosed insulin requiring diabetes during pregnancy for rapid control, and
6. Institution of insulin pump therapy or other intensive insulin regimens.

In-patient Diabetes Management Team

Each hospital should set a specialised hospital team for educating staff, implementing specific diabetic management protocol and monitoring the quality of glycaemic management. The primary goal of the management team is to overcome the barriers of hyperglycaemia management, patient's safety, prevention of hypoglycaemia and to provide cost-effective treatment.

Patients

The patients form the core of the team. They are encouraged to participate in the formulation and conduct of their own care plan while admitted in the hospital.

Consultant Physician/Diabetologist/Endocrinologist

The consultants are the main resource who lead the team and work closely with other members to provide the best care, innovation of new ideas towards improving the patient care.

Diabetes Educator or Diabetes Specialist Nurse

They play a key role in the patient and staff education and also for the implementation of glycaemic control strategies and are able to facilitate a smooth patient pathway from hospital to home. The diabetes educator can also be the leader of the team.

Diabetes Specialist Dietician

They play a pivotal role in those of with complex nutritional needs—those who are unable to swallow, those with renal failure, pregnancy, cystic fibrosis and the elderly.

AIMS AND TARGETS OF GLYCAEMIC CONTROL

Clinicians should interrogate all the hospitalised patients regarding previous diabetic status and it should be clearly mentioned in the individual hospital record. Initial blood glucose estimation should be performed in all patients irrespective of prior diabetic status. Regular monitoring of blood glucose is essential in the patients who are at high risk for hyperglycaemia such as patients on corticosteroids or octreotide therapy and in patients who are either on parental or enteral nutrition therapy. If any patient's blood glucose level is greater than 140 mg%, then daily bedside monitoring of blood glucose should be performed and if it is persistently higher, then it should be treated accordingly.

GLYCAEMIC TARGET IN HOSPITALISED PATIENTS

Glycaemic target should be adjusted according to the clinical status, and is based upon the individual risk for the development of hypoglycaemia.

Glycaemic Control in Non-critical Patients

Current recommendations in non-critical patients are primarily based on clinical experiences and judgement. The pre-food level of blood glucose should be less than 140 mg/dL (7.8 mmol/L) and random blood glucose level less than 180 mg/dL (10.0 mmol/L), provided these targets should be safely achieved. In patients with terminal illness and with limited life expectancy, a higher target of <200 mg/dL (11.1 mmol/L) is recommended.

Glucose Control in a Critical Care (ICU) Setting

Initiate insulin therapy for the treatment of persistent hyperglycaemia at a threshold of 180 mg/dL (10 mmol/L). Once insulin therapy is started, a glucose range of 140 mg/dL to 180 mg/dL (7.8 mmol/L to 10 mmol/L) is recommended for the majority of critically ill patients.

Blood Glucose Monitoring

Bedsides, capillary glucose testing is the preferred method for monitoring and adjusting the treatment of glycaemia in patients to achieve optimal sugar control. Glucose testing should be performed before each meal and at bedtime when the patient is eating, every 4 hours to 6 hours when the patient on enteral (nasogastric tube) and parental feeding. Matching the time of glucose testing, nutritional intake and medication are essential in a hospital setting. Accuracy and reliability of the glucometer are essential. In an acute care setting, continuous glucose monitoring by continuous glucose monitoring system (CGMS) is not found to be superior

to point glucose checking. The common errors in self-monitoring of blood glucose (SMBG) monitoring have to be kept in mind and taken care of (**Table 1**).

Table 1: Sources of Errors in Bedside Blood Glucose Results

Sources of measurement error	Sources of user error
False high	Inadequate meter calibration
Low haematocrit	Inadequate quality-control
Hyperbilirubinaemia	Poor technique in finger prick
Severe lipaemia	Poor technique of applying
False low	Blood drop on test strip
High haematocrit	Test strip with unmatched meter code number
Either false high or false low	The strips have an expiry date of use
Hypoxia	
Shock and dehydration	
Drugs: acetaminophen overdose, dopamine, mannitol, salicylate	

Hospital Barriers to Glucose Control

This may seem to be a paradox. However, hospitalisation may, in fact, hamper the efforts to achieve glycaemic control in some situations and indeed it may be more prudent to have good educational facilities on an out-patient basis to enable patient self-emancipation.

1. Many diabetic patients are admitted to the hospital for reasons other than diabetes, e.g., vascular complications. The care of blood glucose becomes secondary to the primary disease.
2. Surgical trauma, infection, fevers, glucocorticoid treatment, and general medical stress increase the blood glucose levels due to release of counter-regulatory hormones.
3. Decreased physical activity (in the previously active patients) also exacerbates hyperglycaemia.
4. Strict diet and supervised compliance with drugs may result in hypoglycaemia in patients who were not compliant earlier.

COMMON ERRORS IN MANAGEMENT

Admission Orders and Lack of Therapeutic Adjustment

The out-patient treatment regimen may be continued as such or may be withdrawn on admission. The above two methodologies may be useful in some patients but most of the patients require adjustment in their treatment for adequate glucose control. A patient may be treated with regular insulin during the entire hospital stay which will deprive the treating physician to observe the patient's response to regimens that can be transferred home.

High Glycaemic Targets

Blood glucose levels are commonly allowed to be more than 200 mg/dL. In-patient care is sometimes taken

for granted to be superior; however, infrastructural limitations and nursing staffs inadequately trained in diabetes could work contrary.

Overutilisation of the 'Sliding Scales'

A number of authorities feel that the sliding scale is not a very rational method, as this tries to correct the sugar level based on the previous 4 hours to 6 hours, rather than trying to correct the next few hours of glucose control. The sliding scale is still being used quite frequently. The concurrent use of intermediate acting insulin can lead to fluctuation of insulin supply and erratic glucose control. Sliding scale may be used in certain situations as outlined in **Table 2**.

Table 2: Situations in which Sliding Scales may be Useful

To adjust pre-prandial insulin that is based on the pre-meal capillary glucose level and the anticipated carbohydrate consumption
With basal insulin analogues, such as insulin glargine
To evaluate patient's initial response to insulin
In patients receiving parenteral nutrition in whom each 6-hour period is similar

Underutilisation of Insulin Infusions

One of the important routes of administration of insulin is the intravenous route. This route is useful in hyperglycaemic emergencies, pre-operative situation and poor glucose control with subcutaneous insulin. The advantages of this route of insulin administration are a predictable action and an early control of blood glucose. Training of nurses and paramedic staff is imperative for successful implementation.

Glucose Control

Management of hyperglycaemia in a hospital requires a multi-faceted approach. Generally insulin is the most effective and preferred treatment in hospitalised patients. Medical nutrition therapy (MNT) is one of the essential parts of management that provides adequate calories to meet the metabolic demands, to prevent hypoglycaemia and to facilitate good glycaemic control. The management of hyperglycaemia should be started early and should be maintained continuously throughout hospitalisation.

General Recommendations

Assess whether a patient has an innate capacity to produce insulin or not (**Table 3**). This is an important component for providing efficient and effective insulin therapy.

Type 1 diabetic patients are insulin dependent and require insulin at all times to prevent ketosis even when they are not eating. The insulin regimen should be revised frequently based on the values of

Table 3: Characteristics of Patients with Insulin Deficiency

Type 1 diabetic patients
History of pancreatectomy or pancreatic dysfunction
Wide fluctuations in blood glucose
Patients of diabetic ketoacidosis
Patients on insulin use for >5 years and/or diabetes for >10 years

the monitored glucose. The insulin dosage needs to be adjusted frequently based on blood glucose levels. Addition of intermediate-acting insulin one or two times daily even in small doses will stabilise the control. Sliding scale as a sole therapy should not be used for long in diabetic patients. Maintain glucose levels as near normal as possible in the post-operative, post-myocardial infarction, and intensive care settings. Conservative targets should be set in patients prone to hypoglycaemia (e.g., brittle diabetes, hypoglycaemia unawareness), in very elderly or in those with short life expectancy due to co-morbid conditions and with inadequate nursing or monitoring support.

Medical Nutrition Therapy (MNT) in Hospitalised Patients

Nutritional recommendations are individualised based on treatment goals, physiologic parameters, medication usage and other comorbid conditions such as obesity, dyslipidaemia, hypertension and renal failure. A dietician skilled in diabetic MNT should serve as an in-patient team member.

Recommendations in Special Situations

Patient on Oral Agents and Consuming Food

In patients on oral agents with controlled sugars continue the same medicine but consider a dosage adjustment of 25% to 50% due to better dietary adherence. The standard contraindication for using oral agents is in elderly, renal failure cases and stages 3 and 4 heart failure patients. Metformin should be withheld in peri-operative patients (general anaesthesia), in those with standard contraindications or when dehydration is suspected or anticipated and if radicontrast studies are planned. Alpha-glucosidase inhibitors and thiazolidinediones may be continued. Insulin should be started if sugar levels are uncontrolled rather than adding new oral agents and if patient is already on sulphonylurea.

Patients on Oral Agents and Not Consuming Food

In patients on sulphonylurea or other secretagogues (Nateglinide, Repaglinide), the drugs should be withheld and a short-acting insulin sliding scale should be used temporarily. Addition of intermediate-acting insulin should be considered if insulin is needed for more than 24 hours. Metformin may be withheld owing to concerns on an altered renal function in the

acutely ill. It is necessary to avoid alpha-glucosidase inhibitors as these are effective only when taken with food. Thiazolidinediones are discontinued in patients with abnormal hepatic or cardiac function. Dipeptidyl peptidase-IV inhibitors are less helpful in this setting.

Patient on Insulin and Consuming Food

Continue insulin but consider dose reduction (10% to 50%) in well-controlled patients because of more rigid dietary control in the Hospital.

Patient on Insulin and Not Consuming Food

Intravenous insulin infusion should be strongly considered in type 1 diabetes patients. In other patients half or two-third of prior intermediate-acting or basal insulin may be given at least once or in two divided doses along with a short-acting insulin on a sliding scale. Some patients with type 2 diabetes on insulin may have improved control with diet restriction and require only short-acting insulin. A 5% dextrose solution intravenously at 75 mL to 125 mL per hour should be provided unless the blood glucose is >200 mg/dL. Basal-bolus insulin regimen is found to be more effective and safe in controlling hyperglycaemia in several clinical settings.

Perioperative Glycaemic Control

In general, patient's treatment programme is least affected if surgeries are scheduled in the early morning. Blood glucose levels should be monitored every 1 hour to 2 hours before, during and after the procedure.

Type 1 Diabetes

Insulin infusion should be given at a maintenance rate (1 to 2 units per hour) with 5% dextrose solution at 75 mL to 125 mL per hour. The dose is adjusted to maintain glucose levels between 100 mg/dL and 150 mg/dL. As an alternative, one-half to two-thirds of the usual dose of intermediate-acting insulin is given on the morning of the procedure.

Type 2 Diabetes

Patients on oral antidiabetic agents, hold the medication on the day of the procedure and start when on a normal diet. If the patient is treated with insulin, give one-half of intermediate-acting insulin on the morning of the procedure. Short-acting insulin should be given only when the blood glucose level is >200 mg/dL. Alternatively, an insulin infusion can be used.

SPECIFIC CLINICAL SITUATIONS

Insulin Pumps

Patients on continuous subcutaneous insulin infusion (CSII) therapy at home can continue using it in the hospital, provided they are mentally and physically fit to do so. The availability of hospital personnel with

expertise and experience in CSII therapy is essential. The hospital needs to lay down policies and procedural guidelines regarding continuing insulin pump.

Enteral Nutrition

For intermittent enteral feedings, intermediate-acting insulin with a small bolus of regular or rapid acting insulin may be adequate. For continuous feeding, neutral protamine Hagedon (NPH) insulin should be used twice daily while insulin glargine may be used once. Start with a small basal dose and use correction-dose insulin (short acting/rapid acting) as needed while the glargine/NPH dose is being increased.

Parenteral Nutrition

The high glucose loads in standard parenteral nutrition frequently results in hyperglycaemia. Continuous insulin infusion is always preferred. Initial use of an insulin infusion pump can help in determining the total daily dose of insulin. Mixing of insulin with parental nutrition and use of subcutaneous correction dose of insulin is preferred to control hyperglycaemia.

Glucocorticoid Induced Hyperglycaemia

Glucocorticoid induced hyperglycaemia is seen between 20% and 50% of patients without prior history of diabetes. Glucocorticoid-induced diabetes is seen commonly in patients with a family history of diabetes, increasing age and glucocorticoid dose and duration. For patients receiving high-dose intravenous glucocorticoids, an intravenous insulin infusion may be appropriate. During steroid tapering, insulin dosing and oral antidiabetic drugs should be proactively adjusted to avoid hypoglycaemia.

Transition from Intravenous to Subcutaneous Insulin

It is important to start rapid-acting insulin subcutaneously 1 hour to 2 hours before the discontinuation of the intravenous insulin infusion. Intermediate or long-acting insulin must be injected 2 hours to 3 hours before discontinuing the insulin infusion. Total daily dose of insulin should be based on insulin requirement within last 6 hours to 8 hours that can be done by extrapolating to 24 hours. About 60% to 80% of total dose can be administered as the basal or intermediate insulin and the rest as short-acting or rapid-acting insulin.

Safety Issues in the Management of Hypoglycaemia

Hypoglycaemia is the most important barrier in the management of diabetes, more so in the patients on insulin. Institutions have protocols for the

treatment of hypoglycaemia than for its prevention. Tracking such episodes and analysing their causes are important quality improvement activities. It is essential to implement standardised hospital-wide, a nurse initiated protocol for the early recognition and treatment of hypoglycaemia.

The causes of hypoglycaemia are given in **Table 4**.

Table 4: Causes of Hypoglycaemia in Patients on Insulin

Sudden reduction in oral intake or nil per oral status
Discontinuation of nutritional therapy
Pre-meal insulin given and meal not taken
Transfer from one nursing unit to other after rapid-acting insulin is administered
Reduction/omission of corticosteroid dose

DISCHARGE PLANNING

It is also important to guide the patients and their relatives regarding how to control the blood glucose after discharge. Patients (and their families) should be familiar with their glucose targets and drug regimens after discharge. This can improve the long-term outcome and avoid repeated visits or hospitalisation (**Table 5**).

Table 5: Important Guidelines before Discharge from Hospital

Educate regarding diagnosis of diabetes
Self-monitoring of blood glucose and set home blood glucose level goals
Recognition, treatment and prevention of hyperglycaemia and hypoglycaemia
Patients should know the healthcare provider who will take care of his diabetes after discharge
Information on consistent eating patterns
When and how to take oral medications and insulin administration
Sick-day management
Proper use and disposal of needles/lancets/syringes

SUGGESTED READING

1. Hammersley MS, JJ. In-hospital treatment and surgery in patients with diabetes. In: Holt RIG, Cockram C, Flyvbjerg A, Goldstein BJ, ed. *Textbook of Diabetes*; 4th ed. West Sussex: Wiley-Blackwell; 2010:pp.514-27.
2. Lansang MC, Umpierrez GE. Management of in-patient hyperglycaemia in non-critically ill patients. *Diabetes Spectrum* 2008;21:248-55.
3. McDonnell ME, Umpierrez GE. Insulin therapy for the management of hyperglycemia in hospitalized patients. *Endocrinol Metab Clin North Am* 2012;41:175-201.
4. Robyn Houlden, Sara Capes, Maureen Clement, et al. Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Clinical Practice Guidelines In-hospital Management of Diabetes. *Can J Diabetes* 2013;37:S77-S81.
5. Thomas N, Jeyaraman K, Velavan J, et al. *A Practical Guide to Diabetes Mellitus*; 5th ed. New Delhi: Academia; 2010:178-347.
6. Umpierrez GE, Hellman R, Korytkowski MT, et al. Management of hyperglycemia in hospitalized patients in non-critical care setting: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab* 2012;97:16-38.