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PRACTICAL GUIDE TO INPATIENT GLYCAEMIC CARE

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Perkhidmatan Diabetes dan Endokrinologi
Kementerian Kesihatan Malaysia

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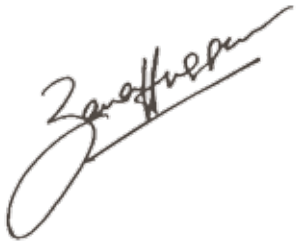
FOREWORD

Diabetes mellitus is highly prevalent in Malaysia with high rates of hospital admissions due to diabetes related acute and chronic complications. Blood glucose abnormalities are common in hospitalised patients, regardless of a prior diagnosis of diabetes. Fluctuations in glucose control may contribute to poorer patient outcomes such as an increased risk of hospital infections, compromised wound and postoperative recovery, cardiovascular complications or disturbances in acid-base, electrolyte and fluid balance.

Inpatient glucose management guidelines have an important role towards maintaining patient safety in hospitalised patients with diabetes and hyperglycaemia. Guidelines enable health care providers to apply evidence-based glycaemic targets and treatment regimens in hospitalised patients to ensure optimal glycaemic control and improved hospital – related patient outcomes. This will then prevent prolonged hospitalisation and reduce healthcare costs.

The clinical considerations of importance for inpatient glycaemic care include definitions of glucose abnormalities and glycaemic targets, blood glucose monitoring, indications for insulin therapy and options of insulin treatment regimens, role of non-insulin agents to control hyperglycaemia, management of special situations (e.g., parenteral/enteral nutrition, glucocorticoids, surgery, insulin pumps), and appropriate transitions of care. Strengthening patient education and self-management skills during hospitalisation along with careful discharge planning will likely enable improved outpatient outcomes and reduced hospital readmissions.

This practical guide aims to address these management issues related to dysglycaemia in hospitalised patients to enable improved patient safety and quality of care.



Dr Zanariah Hussein
Chairperson, Working Group on PGIGC

GUIDE OBJECTIVES

The aim of the practical guide is to assist hospital-based health care providers to recognise, diagnose and manage glycaemic abnormalities among inpatients towards improving safety and quality of glycaemic control and improved patient-related outcomes.

CLINICAL QUESTIONS

The clinical questions of these guidelines are:

1. What is the definition of glucose abnormalities and glycaemic targets in inpatients?
2. How to detect and document inpatient dysglycaemia?
3. When and how to administer insulin therapy?
4. When and how to administer non-insulin agents?
5. How to monitor glycaemia in hospitalised patients?
6. How to manage special situations and glycaemic emergencies?
7. How to practice appropriate transitions of care?

TARGET POPULATION

This practical guide is applicable to all adult inpatients.

TARGET GROUP

This practical guide is meant for all health care professionals involved in treating patients in a hospital setting which includes house officers, medical officers, specialists, nurses, assistant medical officers in medical-based and surgical-based specialties, critical and non-critical care, obstetricians and gynaecologists, pharmacists, dieticians and diabetes nurse educators.

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SUMMARY OF TREATMENT ALGORITHM

Hospital Admission

- Assess presence and type of diabetes
- Review medications: antidiabetics and others
- Assess diabetes self management knowledge and behaviours
- Review most recent HbA1c, do HbA1c test if not been performed in the prior 3 months

Check Blood Glucose

Capillary + venous blood

If DKA or HHS follow Management Protocol

Pre-existing diabetes or BG > 7.8 mmol/L Capillary BG monitoring with POCT

With BG 4 - 7.8 mmol/L may not need regular BG monitoring

ICU Admission

- If BG ≥ 10 mmol/L, initiate insulin using variable rate intravenous insulin infusion (VRIII)
- Target BG 7.8 - 10 mmol/L

General Ward (Non-ICU) Admission

- If able to eat, monitor BG pre-meals and pre-bed
- If not able to eat, monitor BG every 4 - 6 hours
- If BG ≥ 10mmol/L, initiate insulin therapy
- Prescribe basal, prandial or correctional insulin accordingly
- Consider OADs - metformin, DPPIV inhibitors in certain patients
- If BG < 4 mmol/L, initiate hypoglycaemia management
- Target BG 7.8 - 10 mmol/L
- Diabetes education and self-management

Structured Discharge Plan

- Medication adjustment and counselling If on OADs, convert 1 - 2 day before discharge
- Discharge summary
- Communication with outpatient HCP
- Outpatient follow-up within 1 month

SECTION 1
BACKGROUND

Diabetes is a serious and common public health problem. The national prevalence of diabetes continues to increase over time with the last National Health and Morbidity Survey (NHMS) 2015 reporting a prevalence of 17.5% in adults above 18 years and 22.5% in adults above 30 years. The rate of undiagnosed diabetes is generally half of the total estimated prevalence. This high rate of diabetes has a significant impact on use of health care services.

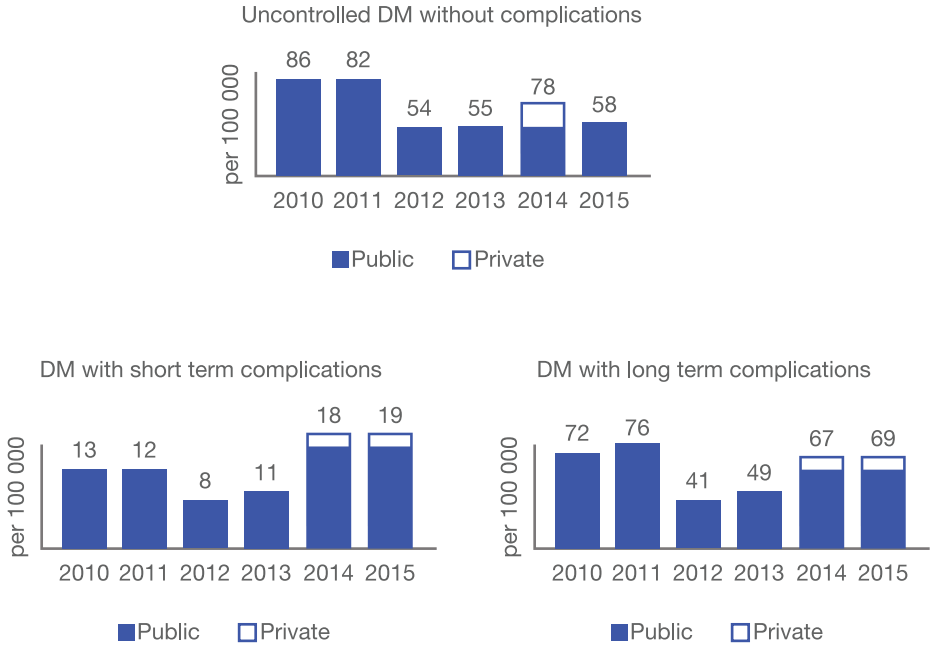
A number of studies have demonstrated that people with diabetes have hospital admission rates between 2 and 6 times higher than people without diabetes. People with diabetes also have excessive lengths of hospital stay compared to people without diabetes[1,2,3].

The Malaysian Diabetes Care Performance Report 2016 reported indicators related to hospital admission for diabetes include admission rate for uncontrolled diabetes mellitus (DM) without complications and DM with short or long term complications. The short term complications refer to complications including coma, hyperosmolarity and ketoacidosis, caused by relative shortage of insulin in the body. Long term complications include renal, eye or circulatory complications. The admission rate is calculated as a ratio between the number of hospital discharges (ICD-10 coded) and the number of population aged 15 and above[4].

Hospital admission rate for diabetes was 145 per 100,000 population in 2015. Admission rate for uncontrolled diabetes without complications was 58 per 100,000 population. Hospital admission rates for diabetes with short term complications was 19 per 100,000 population and for diabetes with long term complications was 69 per 100,000 population[4].

Trends for hospital admission rates related to diabetes are as shown in Figure 1.

Figure 1 : Hospital admission rate for uncontrolled DM with or without complications per 100,000 population, 2010-2014



Data source: *Sistem Maklumat Rawatan Perubatan (SMRP)*

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SECTION 2
INPATIENT DYSGLYCAEMIA - DEFINITIONS AND SCOPE OF THE PROBLEM

Glucose control in the hospital setting is a most important safety and quality measure that relates significantly to patient outcomes. There is a high incidence of dysglycaemia in hospitalised patients which consist of hyperglycaemia, hypoglycaemia and abnormal glycaemic variability.

2.1 Definition of inpatient hyperglycaemia and hypoglycaemia

Hyperglycaemia in hospitalised patients is defined as blood glucose (BG) > 7.8 mmol/L[1,2]. An admission HbA1c value ≥ 6.3% (48 mmol/mol) suggests pre-existing diabetes preceding hospitalisation[3].

Hypoglycaemia in hospitalised patients has been defined as BG of 3.9 mmol/L or less. Inpatient hypoglycaemia refers to episodes that occur in hospital caused by treatment of hyperglycaemia or existing diabetes. For any persons with diabetes admitted to the hospital and found to have BG less than 4.0 mmol/L, treatment should be administered to correct hypoglycaemia regardless of presence of symptoms. It is vital to exclude hypoglycaemia in any person with diabetes who is unable to cooperate, drowsy or unconscious, acutely ill, presenting with aggressive behaviour or seizures. BG levels of 3.0 mmol/L or lower represent the threshold at which neuroglycopaenic symptoms become evident and needs immediate treatment.

Hypoglycaemia can be defined as “severe” if third party assistance is required to actively administer glucose, glucagon or take other corrective actions, irrespective of BG. Some patients may experience typical symptoms of hypoglycaemia even though BG is 4.0 mmol/L and above which is called “relative or pseudo-hypoglycaemia”.

2.2 Glycaemic variability

Glycaemic variability (GV) refers to the fluctuations of glycaemia which may occur throughout the day or for even longer periods of time. Higher GV is associated with inpatient adverse outcomes such as longer length of hospital stay, infections and increased ICU and in-hospital mortality[4]. GV is usually assessed by mean amplitude of glycaemic excursions (MAGE) which is calculated from BG profiles of continuous glucose monitoring system during hospitalisation. This is mostly done in the research setting.

2.3 Hyperglycaemia - scope of the problem

Hyperglycaemia occurs frequently in hospitalised patients. Estimated incidence of diabetes in adult hospitalised patients range from 12% to 26%[5].Hyperglycaemia in the non-diabetic patient at the time of hospital admission was 12%, which is an estimated 1 out of every 8 hospital admissions. Stress hyperglycaemia is part of the natural course of acute illness and not treated unless severe[6].

In a large review of hospital glucose data, 46% of all measured BG in the ICU setting and 31.7% of all BG in non-ICU patients were in the hyperglycaemic range (defined as a glucose >180 mg/dL or 10 mmol/L)[6].

Contributing factors to hyperglycaemia include elevations in stress-related hormones (growth hormone, catecholamines, cortisol, glucagon), pharmacologic agents (steroids, anti-psychotics, inotropes), enteral and total parenteral nutrition (TPN).

Association of hyperglycaemia to inpatient complications

Hyperglycaemia influences patient outcomes, including mortality, inpatient complications, length of hospital stay, and overall hospital costs.

Stress hyperglycaemia has been associated with longer hospital stays, higher rates of intensive care unit (ICU) admission, greater need for rehabilitation services at the time of discharge, and higher mortality rates[7].

The link between hyperglycaemia and adverse hospital outcomes is multi-factorial. Elevated BG concentrations produce a proinflammatory cytokine predominance, leading to a multitude of downstream effects, including capillary basement membrane thickening, impaired phagocytosis and immunity, oxidative stress, abnormal lipid metabolism, decreased vascular contractility, increased platelet adhesiveness, increased concentrations of coagulation factors, and increased C-reactive protein levels[7].

Tighter glucose control has been identified as a predictor of improved outcomes in a variety of patient settings, including acute myocardial infarction (AMI), stroke, community-acquired pneumonia (CAP), chronic obstructive pulmonary disease (COPD) exacerbations, and in non-ICU postsurgical settings such as renal transplantation, total joint arthroplasty, and colorectal surgery.

2.4 Hypoglycaemia – scope of the problem

In a recent large survey, it was reported that the incidence of hypoglycaemia during hospitalisation of people with diabetes was 18.4%, with 7% of inpatients experiencing severe hypoglycaemia (BG < 3.0 mmol/L) and 1.3% of patients requiring injectable rescue treatment[8]. Studies have shown that hypoglycaemia in hospitalised patients occurs most frequently overnight or in the early morning hours[9].

Association of hypoglycaemia to inpatient outcomes

Inpatient hypoglycaemia is associated with increased morbidity and mortality. It has been reported that the risk of inpatient death increased threefold for every 0.56 mmol/L decrease in the lowest BG value below 3.9 mmol/L[10]. Hypoglycaemia results in increased length of hospital stay resulting in increased cost to the healthcare system[11]. There is an increased risk of major cardiovascular event following hypoglycaemia. There is increased frequency of seizures, falls and decline in cognitive function in association with inpatient hypoglycaemia.

Predictors of inpatient hypoglycaemia include advanced age, type 1 diabetes, duration of diabetes, hypoglycaemia unawareness, use of insulin or sulphonylureas, previous hypoglycaemia, creatinine clearance and eGFR (< 60 ml/min)[12].

Recommendations

In hospitalised patients,

- Hyperglycaemia is defined as BG > 7.8mmol/L
- HbA1c ≥ 6.3% suggests pre-existing diabetes
- Hypoglycaemia is defined as BG < 4.0mmol/L

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SECTION 3
INPATIENT GLYCAEMIC TARGETS

Various degrees of glycaemic control have been studied. Treatment is recommended when glucose levels are persistently > 10.0 mmol/L.

Once insulin therapy is started, a target glucose range of 7.8–10.0 mmol/L is recommended for the majority of critically ill and non-critically ill patients.

In selected patients, such as cardiac surgery patients, and patients with acute ischaemic cardiac or neurological events, lower glycaemic targets may be recommended as long as this can be achieved without significant hypoglycaemia.

Patients with a prior history of successful tight glycaemic control in the outpatient setting who are clinically stable may be maintained with a glucose target below 7.8 mmol/L.

Higher blood glucose ranges may be acceptable in terminally ill patients, in patients with severe comorbidities, and in in-patient care settings where frequent glucose monitoring or close nursing supervision is not feasible.

The limiting factor to achieving a near euglycaemic state is hypoglycaemia. Similar to hyperglycaemia, hypoglycaemia is an independent risk factor for poor outcomes in the hospitalised patients.

Recommendations

- Inpatient glycaemic target, ICU and non-ICU is 7.8 - 10mmol/L
- Insulin should be initiated once BG persistently ≥ 10mmol/L
- In selected patients, stricter target of 6.1 - 7.8mmol/L can be considered while avoiding hypoglycaemia

References:

1. Diabetes Care in the Hospital: Standards of Medical Care in Diabetes – 2019. Diabetes Care 2019; 42 (Suppl 1): S173-S181.

SECTION 4
BLOOD GLUCOSE MONITORING

Safe insulin delivery and glucose control is dependent on regular timed BG measurements using reliable glucose meters and monitoring systems in the hospital. HbA1c should be measured in all patients with diabetes or hyperglycaemia who are admitted to the hospital in whom HbA1c has not had performed in the last 3 months.

4.1 Screening of hyperglycaemia

All adult patients should undergo screening upon hospital admission. The following circumstances define those at high risk of having hyperglycaemia during hospitalisation.

- Patients with pre-existing diabetes or prediabetes.
- Patients with features of insulin resistance and metabolic syndrome (obesity, acanthosis nigricans, PCOS, hypertension, dyslipidaemia)
- Patients with family history of diabetes
- Women with history of gestational diabetes (GDM)
- Patients receiving medications such as glucocorticoids, antipsychotics
- Patients on enteral and parenteral feeding

4.2 Bedside Blood Glucose Monitoring

Bedside capillary BG measurement using point-of-care (POC) glucose meters is currently the recommended method of glucose monitoring for inpatients. The challenge of obtaining accurate glucose POC results in acutely and critically ill patients is an important consideration as results can be compromised by medications, clinical states, and treatment.

Clinicians need to be aware of the limitations of specific POC glucose meters. Significant differences between capillary, venous and arterial plasma samples have been observed in patients with extremes of haemoglobin concentrations and with reduced perfusion. Accuracy for POC glucose meters varies with an allowable variance of 20%. Most glucose meters incorporate a correction factor of approximately 1.12 to report a “plasma adjusted” value.

Patient factors such as changes in pH, oxygen status, tissue perfusion and haemoglobin can affect measurement. Any glucose result that does not correlate with the patient’s clinical status should be confirmed through conventional laboratory sampling of plasma glucose.

Table 1: Frequency and timing of BG testing

Clinical considerations	Frequency and Timing of POC BG testing
Patients who are eating usual meals	4 times a day - before meals and at bedtime
Patients who are nil by mouth (NBM)	Every 4 - 6 hours
Patients on continuous enteral or parenteral feeding	Every 4 - 6 hours
Patients receiving cycled enteral or parenteral feeding	Individualised but should be frequent enough to detect hyperglycaemia during feedings and hypoglycaemia when feedings are interrupted E.g.; for enteral feeding - pre-feed (3-4 hourly) or alternate feed (6 hourly)
Patients on continuous intravenous insulin infusion	Hourly or every 2 hours if patient is stable
Situations that could alter glycaemic control: change in medications such as glucocorticoid, abrupt discontinuation of enteral or parenteral nutrition	More frequently
Patients with gestational diabetes on insulin therapy	7- or 8-point testing before meals, 2 hours after meals, pre-bed and early morning

4.3 Continuous Glucose Monitoring (CGM)

Recent studies in the hospital setting have reported that the use of CGM can provide real-time information about glucose concentration, direction and rate of change over a period of hospital stay. By providing glucose values every 5 – 10 minutes throughout 24 hours, CGM may be advantageous over POC testing to reduce rates of severe hypoglycaemia in insulin-treated patients in acute care. CGM has the potential to improve the quality of patient care and provide useful information to help health care providers learn more about glucose management. However, CGM use is limited by added costs and currently not recommended due to insufficient outcome data on safety and efficacy for inpatient use.

Recommendations

- Check BG in all adult patients upon hospital admission
- Check HbA1c in patients with pre-existing diabetes without a recent HbA1c in the recent 3 months
- POC BG testing is required every 1 - 2 hours in patient on intravenous insulin infusion
- POC BG testing is required at regular and appropriate intervals depending on feeding state while on subcutaneous insulin therapy

References:

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SECTION 5
MANAGEMENT OF HYPERGLYCAEMIA IN NON-CRITICALLY ILL

Hyperglycaemia is commonly encountered in non-critically ill patients in both medical and non-medical wards. Management strategies include medical nutrition therapy, various insulin regimens, oral anti-diabetic medications and non-insulin injectables.

5.1 Non-critical medical patient

5.1.1 Medical nutrition therapy

All hospitalised patients with hyperglycaemia should receive medical nutrition therapy (MNT). They should ideally be assessed by dietician and be provided with planned scheduled meals. These meals should have a consistent amount of carbohydrate to facilitate coordination of prandial insulin doses[1].
(Refer Section on MNT)

5.1.2 Pharmacological therapy

Insulin is the preferred choice for pharmacological therapy for hospitalised patients with diabetes or hyperglycaemia. Positive effects of insulin include correction of hyperglycaemia, anti-inflammatory, vasodilatory and anti-oxidant effects.[2]

Insulin may be administered in the following treatment regimens:

a) Variable rate intravenous insulin infusion (VRIII)
b) Scheduled subcutaneous insulin – basal bolus/prandial regimen
c) Scheduled subcutaneous insulin – basal plus regimen

Table 1: Indications, advantages and disadvantages of different insulin regimens.

Regimen	VRIII	Basal Bolus	Basal Plus
Indications	• Critically ill patients • Patients who are kept nil by mouth (NBM) • Patients who are unable to tolerate orally or having persistent vomiting • To estimate insulin dose requirements in patients	• Suitable for most patients who are not critically ill and require insulin • Patients who are tolerating orally well	• Patients who have poor oral intake • Patients who are kept NBM
Advantages	• Target driven • Avoids metabolic decompensation	• Effective in management of hyperglycaemia • Does not need hourly BG monitoring • No danger of iatrogenic hypokalaemia	• Does not need hourly BG monitoring No danger • of iatrogenic hypokalaemia
Disadvantages	• Needs hourly POC BG monitoring • Iatrogenic hypokalaemia • Requires intravenous access • Not suitable for patients who are taking orally well	• Not suitable for patients who are NBM or having poor oral intake	• Not suitable for critically ill patients

a) Variable rate intravenous insulin infusion (VRIII)
Insulin rate is commenced as per VRIII scale (See Appendix 1 for steps for insulin infusion preparation and Appendix 2 for VRIII scale). BG is checked hourly by POC testing.Serum potassium should be checked 6-8 hourly to prevent iatrogenic hypokalaemia and to keep serum potassium between 4-5 mmol/L.

Concurrent intravenous fluids is given to prevent hypoglycaemia, maintain fluid and electrolyte balance. Assessment of the volume status of the patient and baseline electrolytes (particularly potassium) is required before deciding on fluid regimen. E.g., choice of fluids regime: D5% with 40 mmol KCl/L at 125 mls/hour (6 pints D5% with 1.5g KCl each pint over 24 hours) in a patient with no concern of fluid overload.

If the patient was previously on a basal insulin injection, continuation of the previous basal insulin may be considered.

If the BG is not within target
- Ensure intravenous line is functioning at the correct rate
- Consider to change scale

Consider adjustment of scale when
- BG persistently >10mmol/L (on 2 readings) (switch to higher scale)
- The initial BG is >20mmol/L and not falling by 3-5 mmol/L/hour (switch to higher scale)
- BG control is too tight (4-6 mmol/L) or episode of hypoglycaemia, (either switch to a lower scale or increase dextrose in drip).

Indications to use customised scale
- Despite changing to highest scale, BG is still not reducing within target
- Despite using the lowest scale, BG is low or too tight

Insulin scale should be reviewed
- Within 6 hours of initiation and thereafter at least daily
- When targets are not achieved
- When there is change of medications or intravenous fluids

Conversion to subcutaneous insulin regime is considered once patient is allowed orally and tolerating well. (Refer Section 7 on diabetic emergencies on conversion method)

b) Scheduled subcutaneous insulin - basal bolus/prandial regimen (for patients tolerating orally well)
Insulin treated patients:

a) For patients who are already on insulin at home, their insulin doses should be reviewed, modified if necessary and re-initiated in the hospital. Previous insulin doses may need to be reduced to avoid hypoglycaemia depending on appetite, renal status, etc.

b) For transition from VRIII, once they are allowed orally and able to tolerate it, total daily insulin dose can either be calculated from hourly insulin infusion rate (at a stable state) or from weight based calculation (see Table 2)

Table 2: Calculation of total daily insulin doses

Total daily insulin dose (unit/ kg/ day)	Patient profile
0.2 - 0.3	Elderly, renal failure, risk of hypoglycaemia
0.4	Not meeting the above criteria, BG is 7.8 - 11.1mmol/L
0.5	Not meeting the above criteria, BG is 11.2 - 22.2mmol/L

Total daily dose (TDD) is divided into 50% basal and 50% prandial insulin. For basal insulin, long acting insulin (glargine) is given once daily and intermediate acting insulin (NPH insulin) once or twice daily.

If the BG is < 4.0mmol/L, correct the hypoglycaemia, repeat BG after 15 minutes and administer half of the insulin dose provided hypoglycaemia has been corrected and encourage patient to take the planned meal.

Correction doses can be given if pre-meal or in between meal BG is elevated/not at target. See Table 3 for correction scales.

Table 3: Correctional (top up/ supplemental) insulin dosage suggestion

BG (mmol/L)	Scale A (units)	Scale B (units)	Scale C (units)
10.1 - 13.0	1	2	3
13.1 - 16.0	2	4	6
16.1 - 20.0	3	6	9
> 20	4	8	12

Scale A: Low dose correction for insulin sensitive patients or if patient is kept NBM/taking orally minimally or TDD insulin dose ≤0.5 unit/kg/day

Scale B: Usual dose correction or TDD 0.51-1.50 unit/kg/day

Scale C: High dose correction for insulin resistant patients or TDD >1.5 unit/ kg/day

Insulin naïve patients:

For patients who are on oral glucose lowering medications or diet control prior to hospitalisation, discontinue home medications.
Calculate TDD of insulin based on body weight as in Table 2

c) Scheduled subcutaneous insulin – basal plus regimen (for patients being kept NBM/ minimal oral intake)

The basal plus regimen has been shown to be an effective alternative compared to standard basal bolus regimen in general medical and surgical patients with type 2 diabetes[4]

- Calculate TDD as in Table 2
- Administer basal insulin as above
- Give correction dose of short acting insulin 6 hourly using Scale A in Table 3
- Intravenous drip containing dextrose should be considered in all patients being kept NBM

d) Oral anti-diabetic (OAD) medications

Selected patients may be suitable for continuation of home OAD medications provided they are:

- Clinically stable
- Good glycaemic control prior to admission
- Allowed and taking orally well
- No contraindications for use of OAD medications (See table 4)

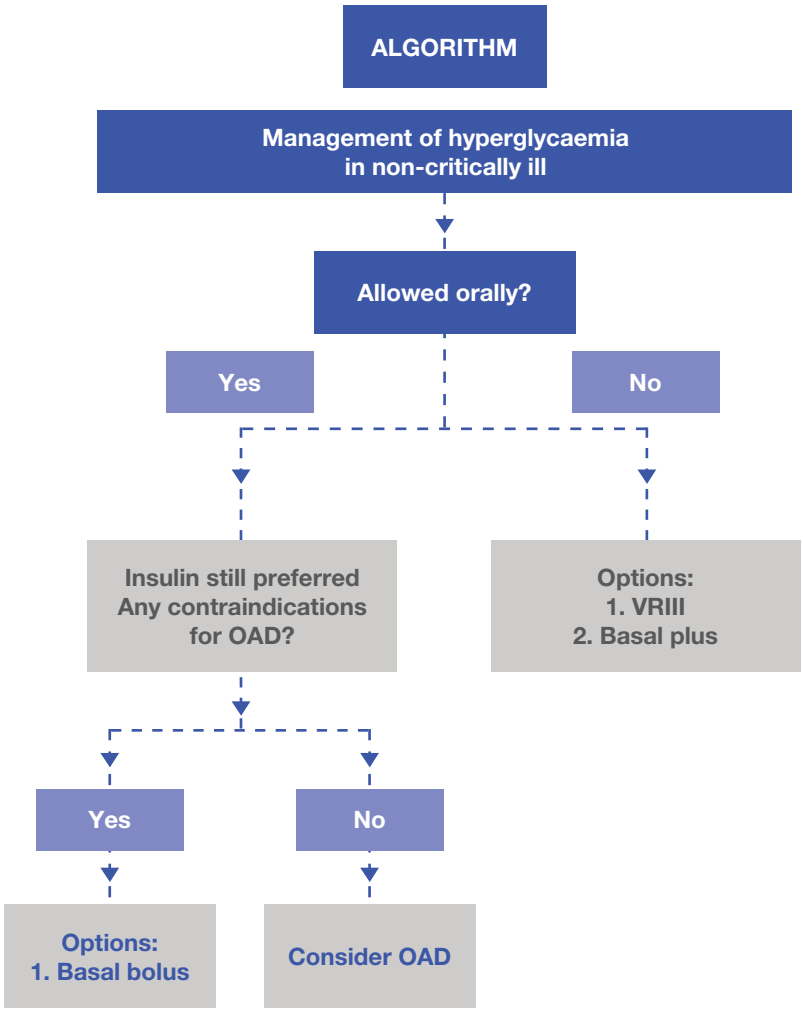
Some patients with mild diabetes requiring low dose single OAD and had good previous control may not need any therapies when hospitalised.

The use of sitagliptin plus basal bolus insulin in hospitalised patients has been shown to be as safe and effective as basal bolus insulin regimen[7]. There is no evidence yet to support the use of injectable incretin based medications such as liraglutide for hospitalised patient.

Table 4: Cautions in use of OAD medications

Oral glucose lowering medications	Potential Risks	Caution/ contraindicated in
Biguanide *Metformin*	Lactic acidosis	• Decompensated heart failure • Renal insufficiency • Hypoperfusion • Chronic pulmonary disease[5]
Sulphonylurea *Glibenclamide, Gliclazide, Glipizide, Glimepiride*	Hypoglycaemia	• Elderly • Renal insufficiency • Past hypoglycaemia • Poor oral intake
Meglitinide *Replaglinide, Nateglinide*	Hypoglycaemia	• Elderly • Renal insufficiency • Past hypoglycaemia • Poor oral intake
Thiazolidinediones *Pioglitazone*	Heart failure	• Congestive cardiac failure • Haemodynamic instability • Evidence of hepatic dysfunction
DPP-IV inhibitors *Sitagliptin, Vildagliptin Saxagliptin, Linagliptin*	Worsening in heart failure (Saxagliptin)[6]	• Less useful in patients not taking orally well • Caution in patients with heart failure
SGLT2 inhibitors *Dapagliflozin, Empagliflozin, Canagliflozin, Luseogliflozin*	DKA	• Patients with genitourinary infections • Insulin resistant patient • Presence of metabolic acidosis • Patients with risk of dehydration
Alpha-glucosidase inhibitors *Acarbose*	Gastrointestinal side effects	• Inflammatory bowel disease, bowel obstruction • Severe renal or hepatic disease

Figure 1: Algorithm for management of hyperglycaemia in non-critically ill



Recommendations

- Insulin is the preferred pharmacological therapy for most hospitalised patients with diabetes or hyperglycaemia.
- Options of insulin regimen for patient who are kept NBM or have poor oral intake are VRIII or basal plus regimes.
- Basal bolus regimen is suitable for most patients who are tolerating orally well.

5.2 Non-critical surgical patient

Surgical patients are exposed to stress during surgery and anaesthesia which result in dysregulated hepatic glucose production and glucose utilisation in peripheral tissues. As a consequent hyperglycaemia sets in even in normal patient.

There are consequential evidences that demonstrate association between perioperative hyperglycaemia and adverse clinical outcomes.[1-3] Post-operative complications correlate to both long-term glycaemic control and to the severity of hyperglycaemia on admission and during the hospital stay. Moreover, peri-operative mortality rate is up to 50% higher than that of the normal population.[2] Correction of hyperglycaemia with insulin administration has been shown to reduce hospital complications and decreases mortality in cardiac[4] and general surgery patients.[5]

Principles of Management

Glycaemic control should be maintained while minimising risk of hypoglycaemia.
Refer Table 5.5 for summary of glycaemic target.

5.2.1 Pre-Operative

Pre-admission/ pre-operation assessment

- Diabetes control needs to be evaluated and optimised. Referral to Physician/Diabetologist should be made as necessary.
- A pre-operative HbA1c target of < 8.5% (mean plasma glucose value of < 10.2mmol/L) in elective surgical patients should be aimed. Elective surgery should be deferred if HbA1c > 8.5%.
- Hypoglycaemia risk including hypoglycaemia unawareness needs to be identified and manage accordingly.
- Diabetes complication must be identified as presence of complications of diabetes might adversely influence the outcome of the proposed procedure.
- Comorbidities such as hypertension and coronary artery disease need to be optimised.
- Good nutrition must be ensured and optimised before admission.

Admission

Pre-operatively, these BG target should be aimed: 6 - 10mmol/L

Patient on diet control

- Well controlled diabetes patient may not need special intervention peri-operatively.
- Monitoring (4 points; BG pre-meals and pre-bed) should be done frequently during hospitalisation.
- Pre-operatively, if BG remains above target, scheduled subcutaneous (SC) insulin regimen basal bolus should be initiated.

Patient with OAD without Insulin

- All OAD with the exception of SGLT2 inhibitor can be continued up to the day before operation if HbA1c is controlled. (Refer Appendix 4)
- Monitoring (4 points; BG premeals and prebed) should be done frequently during hospitalisation.
- Pre-operatively, if BG remains above target despite on usual OAD, scheduled SC insulin regimen basal bolus should be commenced.
- Patients should be kept well hydrated especially those on metformin therapy.

Patient with Insulin Regimen

- Patients with good glucose control can continue their usual insulin doses and diet preoperatively.
- Those with uncontrolled glucose should have optimisation done (i.e., scheduled SC insulin regimen basal bolus regimen) before operative day.
- Fasting started from midnight and basal insulin may be continued pre-bed.
- For Type 1 diabetes patients on basal bolus regimen, whose BG is well controlled, mild reductions (between 10 and 20% if on analogue, 25 to 50% if on NPH) in the dosing of basal insulin are suggested. For those whose BG is uncontrolled [i.e., BG ≥ 10mmol/L full doses of basal insulin can be administered.
- For Type 2 diabetes, if the patient reports that the BG falls by more than 2 mmol/L overnight it would be prudent to reduce the basal (long acting) insulin. If the BG remains stable overnight the normal basal insulin dose should be maintained.

Please refer to Appendix 3 - 4 for adjustment of medication pre-operatively.

5.2.2 Operative Day

Patient on diet control & patient with stress hyperglycaemia

- On operative day, VRIII should be commenced if BG remains ≥ 10mmol/L.
- Monitoring of BG should be done hourly.

Patient with OAD without Insulin

- Some OAD can be continued on operative day (Refer Appendix 4)
- A VRIII should be commenced if BG persistently ≥ 10mmol/L.
- Monitoring of BG should be done hourly.

Patient with Insulin Regimen

- Insulin dose and regimen adjustment should be done according to the timing of surgery (Refer Appendix 3)
- A VRIII should be commenced BG persistently ≥ 10mmol/L.
- Monitoring of BG should be done hourly.

Intra-operation

- BG monitoring should be done at least hourly during the intra-operative period.
- More frequent measurements may be required if the BG is changing rapidly.
- Target: 6 to 10mmol/L for all type of surgery.
- Normal electrolyte concentrations should be maintained.
- Intra-operative cardiovascular and renal functions are optimised.
- VRIII should be considered if BG cannot be kept below target.
- VRIII should be continued for at least 24 hours post-operatively and/or until patient is able to consume an adequate oral intake.

Post operation

- BG monitoring should be continued post-operatively, hourly for patient on VRIII and 4-6 hourly for those without VRIII.

- Target:
  For patient in ICU: refer critically ill patient glycaemic management
  For awake patient:
    - On VRIII - 6 to 10mmol/L
    - Not on VRIII - 4 to 12mmol/L

- Encourage an early return to normal eating/ drinking and facilitate return to their usual diabetes regimen

- For patient on VRIII -Transition from VRIII to scheduled subcutaneous insulin regimen should be considered once patient started to take orally.

- For patient not on VRIII and BG not to target – scheduled subcutaneous insulin regimen
  - NBM/ Minimal oral intake – Refer to scheduled subcutaneous insulin regimen basal plus
  - Able to tolerate orally – Refer to scheduled subcutaneous insulin regimen basal bolus

- Patients' usual diabetes regimen may be resumed once wound heals fully.

5.2.3 Transition from VRIII to scheduled subcutaneous insulin regimen or OAD post-operatively [15]

VRIII to scheduled subcutaneous insulin regimen

- Conversion to SC insulin should be delayed until the patient is able to eat and drink without nausea or vomiting.

- Patient should be restarted with the normal pre-surgical regimen.

- Be prepared to adjust the doses because the insulin requirement may change as a result of post-operative stress, infection or altered food intake.

- Consultation with diabetes specialist team may be needed if the BG are outside the acceptable range (4-12mmol/L) or if a change in diabetes management is required.

VRIII to OAD

- OAD should be started at pre-operative doses once the patient is ready to take orally
- Sulphonylureas dose should be reduced or withhold if the food intake is likely to be reduced.
- Metformin should only be recommenced if the eGFR is greater than 60ml/ min/ 1.73m^2.

5.2.4 Fluid and calorie requirement

Daily requirement of a healthy adult is 50 - 100 mmol of sodium, 40 - 80mmol of potassium, and 1.5 - 2.5 litres of water[13]. Nevertheless, changes in requirement may be necessary according to current status and progress of disease and complications.

Patients with diabetes generally require 180g glucose per day, and additional potassium is required to prevent hypokalaemia when glucose and insulin are co-administered[14]. Supplements of magnesium, calcium and phosphate may also be necessary[14]. As there is limited evidence on which to base recommendations for optimal fluid and insulin management in the adult diabetic patient undergoing surgery, recommendation are as follow:[15]

- While on VRIII, use 0.45% saline with 5% glucose (rate 83 - 125ml/h) with potassium 3 - 6 g/ day added in.
- If patient is hyponatraemic, 0.9% saline/ 5% dextrose may be considered.

Table 5: Glycaemic Target in Patients Undergoing Surgery

Timing of surgery	Target range glycaemic control	Management
Perioperative Pre-admission	Optimal HbA1c ≤ 7% Acceptable HbA1c ≤ 8.5% HbA1c > 8.5	Acceptable to proceed for elective surgery Acceptable to proceed for elective surgery Refer Physician or Diabetologist and postpone surgery.
Admission	6 to 10mmol/L	<u>Patient on diet control</u> • Well controlled may not need intervention • Uncontrolled - SSIR insulin should be initiated <u>Patient with OAD without insulin</u> • Acceptable control - Continue OAD • Uncontrolled - SSIR insulin should be initiated <u>Patient with Insulin regimen</u> • Acceptable control - Continue previous insulin regimen • Uncontrolled - Optimisation (i.e SSIR Basal bolus regimen)
Operative Day		OAD and insulin - Refer Appendix 3 and 4 Commence VRIII if BG remains above 10mmol/L
Intra-operative	6 to 10mmol/L for all type of surgery	VRIII should be considered if surgery > 4 hour and/or BG cannot be kept below target
Post-operative	Awake on VRIII - 6 to 10mmol/L Awake not on VRIII - 4 to 12mmol/L	On VRIII intra operative - transition to SSIR once started to take orally <u>Not on VRIII and BG not to target</u> NBM/ Minimal oral intake - SSIR Basal Plus Able to tolerate orally - SSIR Basal Plus

SSIR - scheduled subcutaneous insulin regimen

Recommendations

- Pre-admission glycaemic target - optimal HbA1c ≤ 7%

- If HbA1c > 8.5% - defer elective surgery & referral to Physician/ Diabetologist

- Target:
  1. Pre-operative - 6 to 10mmol/L
  2. Intra-operative - 6 to 10mmol/L
  3. Post-operative -
     - Awake - On VRIII 6 to 10mmol/L
     - Awake - Not on VRIII 4 to 12mmol/L

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SECTION 6
MANAGEMENT OF HYPERGLYCAEMIA IN CRITICALLY ILL

Introduction

Hyperglycaemia and insulin resistance are common in critically ill patients, even when glucose homeostasis has previously been normal[1]. These patients undergo a variety of metabolic changes in response to stress[2] as a result from surgery, trauma, or sepsis. This in turn causes an increased in secretion of stress hormones (cortisol and catecholamines), growth hormone and glucagon, which results in increase in gluconeogenesis, glycogenolysis, lipolysis, and proteolysis. Therefore hyperglycaemia and insulin resistance occurs even in patients with no history of diabetes mellitus.

- Despite strong association of hyperglycaemia with poor patient outcome, intervention to normalise glycaemia has had inconsistent results.

- The range of optimal glucose level is controversial. Few studies showed that intensive insulin therapy improves mortality, whereas most have shown that patients who receive intensive insulin therapy have no reduction in mortality but have significant risk for hypoglycaemia.

- The initial target of 4.4 - 6.1mmol/L (80 - 110 mg/dL) was based on 2001 Leuven Surgical Trial[3] which showed a 42% relative risk reduction in ICU mortality in critically ill surgical patients but had higher rates of hypoglycaemia.

- The largest multicentre trial for tight glucose control in ICU, the Normoglycaemia in Intensive Care Evaluation and Surviving Using Glucose Algorithm Regulation (NICE-SUGAR)[4], used intravenous insulin to achieve a blood glucose level of 4.5 to 6.0 mmol/L (81 - 108mg/dL) or a level of 8.0 - 10mmol/L (144 - 180mg/dL), respectively. However the results showed 90-day mortality was significantly higher with intensive glucose control 27.5%, vs. 24.9% with conventional control (odds ratio, 1.14; P=0.02). Severe hypoglycaemia was more in the intensive-control group than in the conventional-control group (6.8% vs. 0.5%, P<0.001)

- Due to this evidence, the American Association of Clinical Endocrinologist and American Diabetes Association[5] recommended a target blood glucose level between 7.8-10mmol/L (140-180 mg/dL) for critically ill patients in ICU setting.

6.1: VRIII protocol in ICU

This protocol is NOT for use in patients with Diabetic Ketoacidosis (DKA) or Hyperglycaemic Hyperosmolar State (HHS)

- Intravenous (IV) insulin infusion is the most effective method for achieving stable BG because of the short half life of circulating insulin, which allows rapid dosing adjustments based on individual patient requirements. The BG can be easily achieved within target, minimising the risk of hypoglycaemia and avoiding undesirable effects of hyperglycaemia.

- IV insulin infusion is initiated when BG ≥ 10mmol/L.

- Dilute 50 units of soluble short acting insulin in 49.5 ml of sodium chloride 0.9% and administer via an infusion pump

- Capillary BG should be monitored hourly.

- Clinical judgments with ongoing assessment of the patient's clinical status, severity of the illness, nutritional status, or concomitant medications that might affect glucose levels (e.g., glucocorticoids), should be taken into consideration into the day-to-day decisions regarding insulin doses.

- There are two VRIII protocol that can be used.

- Protocol 1 is adapted by Ministry Of Health Malaysia & Malaysian Society of Intensive Care ICU Protocol[6] which is currently being practiced in most ICU. (Table 1)

- Protocol 2 is an alternative to the standard practice adapted from the Joint British Diabetes Societies for Inpatient Care[7]. (Table 2)

Protocol 1: Variable rate intravenous insulin infusion (VRIII) protocol[6]

1. To start insulin infusion if BG ≥ 10mmol/L for 2 consecutive readings 1 hour apart.

2. Appropriate intravenous fluids depending on the BG. If the BG is above 15mmol/L, change to non-dextrose drip. Potassium supplementation is adjusted according to the serum potassium level.

Initial Bolus		Start insulin infusion with Scale 2
BG	IV Insulin	
10.1 - 14.9	1 unit	
> 15	2 unit	

Blood Glucose (BG)	Scale							
	1	2	3	4	5	6	7	8
mmol/L	IV Insulin (Units/hr)							
≥ 22.1	3.0	4.0	5.0	6.0	7.0	8.0	10.0	11.0
18.1-22	2.5	3.5	4.0	5.0	6.0	6.0	8.0	9.0
14.1-18	2.0	3.0	3.0	4.0	5.0	5.0	6.0	7.0
12.1-14	1.5	2.5	2.5	3.0	4.0	4.0	4.0	5.0
10.1-12	1.0	2.0	2.0	2.0	3.0	3.0	3.0	4.0
8.1-10	1.0	1.0	1.5	1.5	2.0	2.0	2.5	3.0
6.1-8	0.5	1.0	1.0	1.0	1.5	1.5	2.0	2.0
4.1-6	0.5	0.5	0.5	0.5	1.0	1.0	1.5	1.5
< 4	Cease IV insulin infusion and inform doctor. Treat BG < 4.0. (Refer to section 9 on Management of Hypoglycaemia)							

Compare the current BG range to previous BG range	• If the current BG range 1. Lower: Stay in the same column or lower infusion rate 2. Same or Higher: Move to the first right column with higher infusion rate • If BG is within target: Do not change column • If BG 4 - 6mmol/L: Move to the first left column with lower infusion rate

Inform Doctor If:	• BG < 4.0mmol/L • Serum potassium < 3.5mmol/L. Check serum potassium at least 4 hourly - 6 hourly • BG ≥ 10mmol/L for 2 consecutive measurements • Infusion rate is < 0.5 U/ h for 2 consecutive measurements or infusion rate exceeds 10 U/ h

Protocol 2: Variable rate intravenous insulin infusion (VRIII) protocol[7]

1. If BG > 12mmol/L and not falling on two or more consecutive occasions
   - Increase the insulin infusion rate to the next scale
   - Prescribe a customised insulin infusion rate if patient is already on increased rate

2. If BG 4 - 6mmol/L on two or more consecutive occasions
   - Consider a lower insulin infusion rate
   - Increase substrate to Dextrose 10% if reduced rate is already used

3. If BG < 4mmol/L, to treat for hypoglycaemia. (refer Section on "Management of Hypoglycaemia"). Restart IV insulin within 20 minutes if BG > 4mmol/L

4. In patients with renal or hepatic failure, use 'reduced rate' VRIII scale as these patients may have an increased risk of hypoglycaemia

Table 2: Variable rate intravenous insulin infusion (VRIII) protocol[7]

	Insulin Rate VRIII (units/hr) Start on standard rate unless otherwise indicated			
Blood Glucose (mmol/L)	Reduced rate - Consider in patients < 50 kg, insulin sensitive, liver or kidney failure	Standard rate	Increased rate - Consider in patients > 90 kg, insulin resistant	Customised scale
< 4	0	0	0	
4.1 - 8	0.5	1.0	2.0	
8.1 - 12	1.0	2.0	3.0	
12.1 - 16	2.0	4.0	5.0	
16.1 - 20	3.0	5.0	7.0	
20.1 - 24	4.0	6.0	8.0	
> 24.1	6.0	8.0	10.0	

Recommendations

- Variable Rate Intravenous Insulin Infusion (VRIII) is preferred with insulin protocol according to standardised regimen in ICU
- Starting insulin threshold when BG ≥ 10 mmol/L (180mg/dL) for 2 consecutive readings 1 hour apart
- Maintain BG between 7.8 - 10 mmol/L (140 - 180 mg/dL)

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SECTION 7
MANAGEMENT OF HYPERGLYCAEMIA EMERGENCIES

7.1 Diabetic Ketoacidosis

Diabetic ketoacidosis (DKA) is a biochemical triad of ketonaemia, hyperglycaemia and metabolic acidosis.

Diagnostic Criteria[1,2]

All three must be met:

- Capillary BG > 11mmol/L
- Capillary ketones > 3mmol/L or urine ketones ≥ 2+ (on standard urine sticks)
- Venous pH < 7.3 and/or bicarbonate < 15mmol/L

7.1.1 Pathophysiology

DKA usually occurs as a consequence of absolute or relative insulin deficiency that is accompanied by an increase in counter regulatory hormones (i.e., glucagon, cortisol, growth hormone, catecholamines). This enhances hepatic gluconeogenesis and glycogenolysis resulting in severe hyperglycaemia. Enhanced lipolysis increases serum free fatty acids that are then metabolised as an alternative energy source in the process of ketogenesis which results in accumulation of large quantities of ketone bodies and subsequent metabolic acidosis.

Ketones include acetone, 3-beta-hydroxybutyrate, and acetoacetate.

The predominant ketone in DKA is 3-beta-hydroxybutyrate which is best measured in serum[3].

7.1.2 Principles of management

To set 3 IV lines on admission:-

i. For maintenance fluid 125ml / hr (6 pints in 24 hrs) + potassium replacement

ii. Fluid Resuscitation line: rate of resuscitation fluid (normal saline) to be decided clinically

iii. For IV insulin infusion: Fixed Rate IV Insulin Infusion infused at 0.1u/kg/hr until ketosis resolves

1. Restoration of fluid depletion due to osmotic diuresis

a) Use 0.9% NaCl (normal saline), with strict intake output charting[4,5]. Cautious fluid replacement in patients whom are not in shock and have multiple co-morbidities. Hourly urine output, aim urine output at least 0.5ml/kg/hr.

2. Suppression of Ketosis and reversal of metabolic acidosis

a) Fixed Rate Insulin infusion (FRIII) at 0.1U/kg/hr[6,7] enables rapid blood ketone clearance until ketosis resolves. FRIII should be continued until the bedside capillary ketone levels are less than 1 mmol/L, and the pH >7.32. If BG drops <14mmol/L with persistent metabolic acidosis due to ketosis, to add concurrent dextrose 5% or dextrose 10% to NS drip to maintain capillary BG between 8-12mmol/L and avoid hypoglycaemia.

b) Priming/ bolus dose of insulin in the treatment in DKA is not necessary provided that the insulin infusion is started promptly at a dose of at least 0.1 unit/kg/hour.[6,8] Only give a bolus (stat) dose of IM/SC insulin (0.1 unit/kg) if there is a delay in setting up a FRIII[2]. May consider continuing patient's SC long-acting analogue/ human insulin while on IV insulin infusion.

c) Adequate fluid and insulin therapy will resolve the acidosis in DKA and the use of bicarbonate is not indicated.[7,9] If pH <6.9, if pH < 6.9 persistent, consider IV sodium bicarbonate.

3. Monitoring progress and resolution of ketosis

a) Use of serum 3-beta-hydroxybutyrate using bedside ketone meter for diagnosis of DKA[3]. Use of blood ketones is associated with reduced emergency department assessment, hospitalisations and a shorter time to recovery when compared to urinary ketones[3].

b) Use of venous blood gas for monitoring for resolution of acidosis. Arterial blood gas to be used if patient is hypoxic. Difference between venous and arterial pH is 0.02-0.15 pH units and the difference between arterial and venous bicarbonate is 1.88mmol/L[10] which will neither affect the diagnosis nor management of DKA. It is not necessary to use arterial blood to measure acid base status.

4. Adequate potassium replacement to avoid hypokalaemia while on insulin infusion

a) Maintain potassium level between 4 - 5mmol/L. Insulin therapy lowers serum potassium levels by promoting the movement of potassium back into the intracellular compartment. Potassium replacement should, therefore, be started when the serum concentration is < 5.5mmol/L to maintain a level of 4 - 5mmol/L.

b) Ensure monitoring 6 hourly using laboratory values or reliable blood gas analyser potassium value.

5. Identification and Management of any possible precipitating factors

7.1.3 Criteria for ICU/ HDU admission

Consider ICU/HDU admission in the following situation:

- Elderly
- Pregnancy
- Heart failure, kidney failure or other serious comorbidities
- Severe DKA by following criteria:
  - » Venous bicarbonate < 5mmol/L
  - » Blood ketones > 6mmol/L
  - » Venous pH < 7.1
  - » Hypokalaemia on admission (< 3.5mmol/L)
  - » Glasgow Coma Scale (GCS) < 12
  - » Oxygen saturation < 92% on air (arterial blood gases required)
  - » Systolic BP < 90mmHg
  - » Pulse > 100
  - » Anion gap > 16 [Anion Gap = $(Na^+ + K^+) – (Cl^- + HCO_3^-)$]

7.1.4 Metabolic treatment targets[2]:-

The following targets are recommended

- Reduction of the blood ketone concentration by 0.5mmol/ L/ hour
- Increase the venous bicarbonate by 3.0mmol/L/hour
- Reduce capillary blood glucose by 3.0mmol/L/hour
- Maintain potassium between 4.0 and 5.0mmol/L

If these rates are not achieved, then review hydration and consider increasing the FRIII rate.

7.1.5 The management of diabetic ketoacidosis in adults

a) Immediate management in A&E: time 0 - 60 minutes

Initial Assessment

- Respiratory rate; temperature; blood pressure; pulse; oxygen saturation
- Glasgow Coma Scale
- Full clinical examination

Initial Fluid Replacement

Commence 0.9% sodium chloride solution (use large bore cannula) via infusion pump. Set 3 IV lines (IV insulin, maintenance drip with K replacement, resus fluid)

- 500ml of 0.9% normal saline over 10 - 15 minutes, repeat if necessary (hypovolaemic)
- Then 1 L 0.9% normal saline over next 60 minutes.

Potassium Replacement

To be given in maintenance drip via separate IV line
Maintenance IVD 400ml NS 4 hourly (125ml/hour)
Potassium level (mmol/L) Potassium replacement per
500ml fluid
serum K >5.5 : Nil
serum K 3.5-5.5 : 20-30 mmol/l KCl*
serum K <3.5 : additional K+ replacement required**
* 1 g KCl = 13.4 mmol K+;
** Maximum potassium replacement per hour is 40 mmol/h
Withhold K+ replacement if there is no urine output.
Maintain serum K level at 4 to 5 mmol/L, adjust in IVD accordingly
- Caution in renal impairment

Commence Fixed Rate IV Insulin Infusion

(0.1 unit/ kg/ hr based on estimate of weight) aim for drop in BG 3 - 5mmol/ L/ hour. Increase if BG doesn't drop by minimum 3mmol/hr
Reduce dose if BG drops too rapidly, > 5mmol/ hr
Add concurrent dextrose 5%/ dextrose 10% if CBG < 14mmol/L to maintain CBG between 8 - 12mmol/L while on FRIII until ketosis resolves.

Investigations

- Capillary and laboratory glucose
- VBG
- RP
- FBC
- Blood cultures (suspected infection)
- ECG
- CXR
- Urine feme

Monitoring

- Hourly capillary BG
- Venous bicarbonate and K level at 60 minutes
- Continuous pulse
- Oximetry if needed

TREATMENT OF PRECIPITATING CAUSES

b) Ward management

60 minutes - 6 hours

Reassess Patient, Monitor Vital Signs

- Hourly blood glucose (lab blood glucose if meter reading 'HI')
- 3-4 hourly blood ketones if meter available
- Venous blood gas for pH, bicarbonate and potassium at 60 minutes and 6 hourly
- Maintain if potassium around 4mmol/L - 5mmol/L, adjust potassium accordingly

Continue Fluid Replacement Via Infusion Pump:-

- 0.9% normal saline, 1pint 4 hourly with potassium chloride in each pint NS to maintain K 4-5 mmol/L. Review hydration and decide on further NS depending on hydration status and urine output
- Once BG <14 mmol/L, add concurrent 5% or 10% dextrose to NS to achieve total maintenance fluid 125ml/hr with adjustment of fluid requirement accordingly based on hydration and urine output.
- More cautious fluid replacement in elderly, pregnant, heart or renal failure. (Consider HDU and/ or central line insertion)

Assess Response To Treatment

Insulin rate may need review if

- Capillary ketones not falling by at least 0.5 mmol/L/hr
- Venous bicarbonate not rising by at least 3 mmol/L/hr
- Plasma glucose not falling by at least 3 mmol/L/hr
- Continue fixed rate IV Insulin Infusion until:-
  - Serum ketones <1 mmol/L
  - Venous pH over 7.3 and/ or venous bicarbonate over 18 mmol/L
- If ketones and glucose are not falling as expected always check the insulin infusion pump is working and connected and that the correct insulin residual volume is present (to check for pump malfunction). If equipment working but response to treatment inadequate, increase insulin infusion rate by 1 unit/hr increments hourly until targets achieved.

Monitoring

- Accurate fluid balance chart, minimum urine output 0.5ml/kg/hr
- Consider urinary catheterisation if incontinent or anuric
- Nasogastric tube with airway protection if patient obtunded or persistently vomiting.
- Measure arterial blood gases and repeat chest radiograph if oxygen saturation < 95%
- Thromboprophylaxis with low molecular weight heparin
- ECG monitoring if potassium abnormal or concerns about cardiac status

c) Ward management: Time 6 - 24 hours

If patient's parameters improve:-

- Continue IV fluid via infusion pump at reduced rate, adjust according to patient's hydration status and urine output with K supplementation in each pint NS + concurrent 5% or 10% glucose maintenance fluid total 125ml/ hr if BG falls below 14mmol/L.

If ketonaemia cleared and patient is not eating and drinking move to a variable rate IV insulin infusion (VRIII) / progressively reduce FRIII

Reassess cardiovascular status at 12 hours; further fluid may be required.
Check for fluid overload

Review biochemical and metabolic parameters

- At 6 hours check venous pH, bicarbonate, potassium, capillary ketones and glucose

If DKA is not resolving review insulin infusion, seek senior consult

7.1.6 Resolution of DKA

Resolution of DKA

Expectation:

Patient should be eating and drinking and back on normal insulin. If DKA not resolved identify and treat the reasons for failure to respond, seek senior consultant/ specialist input

Resolution of DKA is defined as:
- pH > 7.3
- Plasma ketone < 0.6mmol/L

Once DKA resolves & patient able to take orally
Convert to subcutaneous insulin regimen (Basal bolus / premix regimen)
Convert to subcutaneous regimen when biochemically stable (capillary ketones < 0.6 mmol/L, pH over 7.3) and the patient is able to take orally well

Stop intravenous insulin infusion 60 minutes after subcutaneous short acting insulin has been given.

Calculate SC insulin dose in insulin-naïve patients; Calculating a Basal Bolus (QID) Regimen once DKA resolves :-

Newly diagnosed patients or adult patients who have not previously received insulin can be started at a total daily dose (TDD) of 0.5 - 0.7 U/ kg/ day[7].

In patients previously on insulin, previous regimen may be restarted and adjusted or estimation of TDD from hourly insulin dose which maintains BG 8 - 12 mmol/L after DKA resolves - Calculate the average insulin intravenous infusion rate to obtain the mean hourly rate then multiply by 24 to get the total daily insulin requirement.

TDD is then divided into 50% TDD for basal and the remaining 50% TDD as prandial insulin divided equally by number of main meals per day.

7.2 Hyperglycaemic Hyperosmolar State (HHS)

A precise definition of HHS does not exist and would be inappropriate, but there are characteristic features that differentiate it from other hyperglycaemic states such as DKA. Defining HHS by osmolality alone is inappropriate without taking into account other clinical features.

Diagnostic Criteria[12]:

- Severe dehydration
- Marked hyperglycaemia (BG > 30 mmol/L)
- Osmolality > 320 mOsmol/ kg
- pH greater than 7.3, bicarbonate greater than 15 mmol/L
- Blood or urine ketones nil/ minimal

Calculation of effective serum osmolality

The best approximation to measured osmolality can be calculated using the formula:-

2 (Na^+)[mmol/L] + glucose[mmol/L]

Effective osmolality is calculated without taking urea into consideration as urea is an ineffective osmolyte therefore may be omitted from the equation to allow calculation of tonicity[7,12].

In HHS there is usually no significant ketosis/ketonaemia (less than 3 mmol/L), though a mild acidosis (pH greater than 7.3, bicarbonate greater than 15 mmol/L) may accompany the pre-renal failure. Some patients have severe hypertonicity and ketosis and acidosis (mixed DKA and HHS) which may reflect insulin deficiency, due to beta cell exhaustion as a result of temporary glucotoxicity. These patients may require a modification of this treatment guideline account for predominating aspect.[12]

Clinical features of dehydration in the patient with HHS can be deceptive and may not be reflective of the seriousness of the fluid depletion. This is because hypertonicity leads to preservation of intravascular volume, causing movement of water from intracellular to extracellular space.

Precipitating factors for HHS are:

a) Infections and sepsis
b) Thrombotic stroke
c) Intracranial haemorrhage
d) Silent myocardial infarction
e) Pulmonary embolism

Management goals: Identify and treat the underlying cause as well as to gradually and safely:

1. Replace fluid and electrolyte losses
2. Normalise the osmolality
3. Normalise blood glucose
4. Prevention of potential complications e.g. electrolyte imbalance, cerebral oedema/ central pontine myelinolysis
5. Prevention of arterial or venous thrombosis

Principles of Management

1. Replacement of fluid and electrolyte losses

a) If hyponatraemia is present, there is a need to exclude pseudohyponatraemia in the presence of severe hyperglycaemia. Recognition of pseudohyponatraemia is important to avoid the use of hypertonic saline during fluid management.

b) As the majority of electrolyte losses are sodium, chloride and potassium, the base fluid that should be used is 0.9% sodium chloride solution with potassium added as required with strict intake output charting[12].

c) Fluid replacement alone (without insulin) will lower BG which will reduce osmolality causing a shift of water into the intracellular space. This may result in an initial rise in serum sodium (a fall in blood glucose of 5.5 mmol/L will result in a 2.4 mmol/L rise in sodium). This is not necessarily an indication to give hypotonic solutions.

d) If the osmolality is no longer declining despite adequate fluid replacement with 0.9% sodium chloride solution AND serum sodium is >145 mmol/L then 0.45% sodium chloride solution should be substitute[7,12]

e) Cautious fluid replacement in patients whom are not in shock and have multiple co-morbidities. Hourly urine output, aim for urine output at least 0.5ml/kg/hr.

2. Replacement of fluid and electrolyte losses

a) Aim for gradual decline in serum osmolality at rate of 3 mOsm/kg to 8 mOsm/kg per hour (normal plasma osmolality ranges between 275-295 mOsm/kg).

b) An initial rise in sodium is expected and is not in itself an indication for hypotonic fluids. Thereafter, the rate of fall of plasma sodium should not exceed 10 mmol/L in 24 hours.

3. Normalise the blood glucose

a) Establish fluid replacement first. Aim for a fall in blood glucose of 4-6 mmol/L/hr. Patients with HHS are insulin sensitive, therefore there is a risk of lowering the osmolality precipitously. Low dose IV insulin (0.05 units/kg/hr) should be commenced[12]. FRIII is preferred[7,12].

b) Once insulin infusion is already in place, the infusion rate can be increased by 1 unit/ hr if BG is not falling by minimum 3 mmol/L /hr in the first 2 - 3 hours despite adequate hydration.

c) If BG drops < 14mmol/L to add concurrent dextrose 5% or dextrose 10% to NS drip to prevent rapid drop in blood glucose level.

4. Prevention of complications and electrolyte imbalance

a) Maintain potassium level between 4 - 5mmol/L. Potassium replacement to be started in separate maintenance drip once insulin infusion has been commenced if the serum concentration is < 5.5mmol/L to maintain a level of 4 - 5mmol/L. Ensure monitoring 6 hourly using laboratory values or reliable blood gas analyser potassium value[7].

b) Na level to be repeated and reviewed within first 2 hours on presentation in HHS patient with deranged sodium levels on admission and monitored 4 to 6 hourly thereafter.

5. Prevention of Arterial / Venous thrombosis

a) All patients should receive prophylactic low molecular weight heparin (LMWH) for the full duration of admission unless contraindicated. Patients in HHS have an increased risk of arterial and venous thromboembolism.

6. Identify and treat precipitating Factors – Stroke / MI / Acute coronary syndrome / infection / missed medication

The management of Hyperglycaemic Hyperosmolar State (HHS) in adults

Diagnostic criteria:

- Severe dehydration
- Marked hyperglycaemia BG > 30mmol/L
  pH > 7.3, bicarbonate > 15mmol/L with Urine or Serum ketones nil /minimal
- Serum osmolality > 320 mOsm/kg (normal serum osmolality: 275 - 295 mOsm/kg)

Immediate management in A&E

0 - 60 minutes

Initial Assessment

- Respiratory rate; temperature; blood pressure; pulse; oxygen saturation, Glasgow Coma Scale
- Full clinical examination + investigations

Initial Fluid Replacement

Commence 0.9% sodium chloride solution (use large bore cannula) via Set 3 IV lines (IV insulin, resuscitation fluid, maintenance fluid + K replacement) infusion pump. Strict I/O charting - CBD insertion. Full clinical examination + investigations

- 500ml of 0.9% normal saline over 10-15 minutes, repeat if necessary (hypovolaemic). Then 1000ml 0.9% normal saline over next 60 minutes. Subsequent resuscitation fluid (NS) based on urine output & hydration status.
- 1 L over next 1-2 hours then 1 L over 2 hours followed by 1 L over 4 hours, reassess hydration every 4-6 hrs thereafter to decide on subsequent need of additional saline.

Monitoring Serum NA Level And Osmolality

- Initial fluid to be given NS over the first 1-2 hours
- If Initial Na > 145mmol/L, then repeat BUSE and review within first 2 hours of fluid resuscitation. Continue hydration to aim for decline in serum osmolality at 3-8 mOsm/kg per hour.
- IV 0.45% saline solution is used if serum sodium is >145 mmol/l or the serum osmolality is not declining (<3mOsm/kg) despite adequate hydration.

Investigations

- Capillary and laboratory glucose
- VBG
- RP
- FBC
- Blood cultures (suspected infection)
- ECG
- CXR / CT Brain if poor GCS / fitting
- Urine feme

Immediate management in A&E

0 - 60 minutes

Potassium Replacement

- To be given in maintenance drip via separate IV line (0.9% or 0.45% NaCl solution)
- Maintenance IVD 500ml NS 4 hourly (125ml / hour)
- Potassium level (mmol/L) Potassium replacement per 500ml fluid
  serum K >5.5 : Nil
  serum K 3.5-5.5 : 20-30 mmol/L KCl*
  serum K <3.5 : 20-40 mmol/L KCl (additional K^+ replacement required**)

  * 1 g KCl = 13.4 mmol K^+;
  ** Maximum potassium replacement per hour is 40 mmol/L
- Maintain serum K^+ 4-5mmol/L, monitor K levels 6 hourly

Commence fixed Rate IV Insulin Infusion (FRIII)

- (0.05 unit/kg/hr based on estimate of weight), aim for drop in BG of 4-6 mmol/L/hr
- Adjust infusion rate accordingly, consider increasing infusion if BG doesn't drop by 3 mmol/L in the first 2 - 3 hours despite adequate fluid replacement.
- Add concurrent dextrose 5% or dextrose 10% to maintenance NS if BG < 14 mmol/L. FRIII can be reduced or maintain at 0.05U/kg/ hr

Monitoring

- Hourly capillary blood glucose
- Venous bicarbonate, Na & potassium at 60 mins
- Continuous pulse oximetry if needed
- 4-6 hourly calculated / lab osmolality

Treatment Of Precipitating Causes

Ward management

60 minutes - 6 hours

DVT Prophylaxis with low molecular weight heparin/ heparin if no contraindications Reassess Patient, Monitor vital signs

- Hourly blood glucose (lab blood glucose if meter reading 'Hi')
- 2-4 hourly calculated / laboratory osmolality
- ABG/VBG for pH, bicarbonate as needed
- BUSE for Na, potassium at 60 minutes. K monitoring 6 hourly while on FRIII
- Maintain if potassium around 4 mmol/L - 5 mmol/L, adjust potassium accordingly in IVD
- Accurate fluid balance chart, minimum urine output 0.5ml/kg/hr
- Nasogastic tube with airway protection of patient obtunded or persistently vomiting
- Cardiac monitoring / GCS charting, hourly CVP monitoring

Continue Fluid Replacement Via Infusion Pump:-

- 0.9% / 0.45% NaCl solution, 1pint 4 hourly with potassium chloride in each pint NS to maintain serum K 4-5 mmol/L. Review hydration, urine output hourly, serum osmolality and serum Na and decide on further fluid replacement.

Switch to 0.45% NaCl solution after initial fluid resuscitation if:-
Decline in serum osmolality < 3 mOsm/kg with Na persistently > 145 mmol/L, despite adequate fluid hydration

- Once BG < 14 mmol/L, add concurrent 5% or 10% dextrose to NaCl infusion to achieve total maintenance fluid 125 ml/hr with adjustment of fluid requirement accordingly based on hydration status and urine output.
  More cautious fluid replacement in elderly, pregnant, heart or renal failure.
  (Consider HDU and/ or central line insertion)

Assess Response To Treatment

Insulin infusion rate and adequacy of fluid replacement may need review if

- Serum Osmolality not falling by at least 3 mOsm/kg - 8 mOsm/kg per hour
- Plasma glucose not falling between 4-6 mmol/L/hr
- Continue fixed rate IV Insulin Infusion by 1 U/hr increment/decrement

If osmolality and BG are not falling as expected check IV lines
If equipment working but response to treatment inadequate, increase rate of hydration/insulin infusion by 1 unit/hr increments hourly until targets achieved.

Ward management		Resolution of HHS
6 - 12 hours	**12 - 24 hours**	**24 - 72 hours**
• Continue IV fluid via infusion pump at reduced rate, adjust according to patient's hydration status and urine output with K supplementation in each pint NaCl + concurrent 5% or 10% glucose maintenance fluid total 125 ml/hr if blood glucose falls below 14 mmol/L. • Aim and keep BG 10 - 15 mmol/L in first hours • Reassess hydration, aim positive balance 3-6 litres by 12 hours • Assess for complications - fluid overload / cerebral oedema • Continuous drop in serum osmolality 3 mOsm/kg - 8 mOsm/kg	• Continue IV fluid, hourly I/O charting, reassess hydration, aim replacement of rest of fluid losses within these 12 hours • Insulin infusion via infusion pump at reduced rate. • Keep BG 8 - 12 mmol/L in first 24 hours, adjust insulin and amount of dextrose to achieve this.	**Expectation:** • Biochemical parameters improving / normalised • If on insulin infusion may adjust to aim BG 8 - 12 mmol/L • Once HHS patient able to take orally convert to subcutaneous insulin regimen (basal bolus/ premix regimen). Stop intravenous insulin infusion 60 minutes after subcutaneous short acting insulin has been given. Assess fluid balance, IVD may still be needed if hydration inadequate • Rehabilitation & DVT prophylaxis until discharge

Calculate subcutaneous insulin dose in insulin-naïve patients; Calculating a Basal Bolus (QID) Regimen once HHS resolves :-

- Newly diagnosed patients or adult patients who have not previously received insulin can be started at a total daily dose (TDD) of 0.5 - 0.7 U/ kg/ day[7].

- However, patients with HHS are more insulin sensitive and may require lower insulin dose.

- In patients previously on insulin, previous regimen may be restarted and adjusted or estimation of TDD from hourly insulin dose which maintains BG 8 - 12 mmol/L after HHS resolves - Calculate the average insulin intravenous infusion rate to obtain the mean hourly rate then multiply by 24 to get the total daily insulin requirement.

- TDD is then divided into 50% TDD for basal and the remaining 50% TDD as prandial insulin divided equally by number of main meals per day.

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SECTION 8
MANAGEMENT OF HYPERGLYCAEMIA IN SPECIAL POPULATIONS

8.1 Continuous subcutaneous Insulin infusion pump (CSII)

Insulin pump is an electronic device that delivers subcutaneous (SC) insulin continuously. The principle of insulin administration is similar to basal bolus insulin regimen which involves maintaining a constant background insulin administration (basal insulin) and boluses of insulin (bolus insulin) administration before food is consumed. Correctional insulin doses can be given if blood glucose is out of target range. Successful management of inpatients with diabetes by use of a CSII has been previously demonstrated in selected patients[1,2].

Assessment of patient

Insulin pump is used primarily in T1DM and occasionally in type 2 diabetes mellitus (T2DM). It is not widely used in Malaysia except in specialised tertiary centres. When a patient on CSII is hospitalised, the endocrinologist responsible for the patient's insulin pump management should be contacted to make decisions about appropriate infusion adjustments during the hospital stay. If a specialised diabetes management team is available in the hospital, the team should be notified as soon as possible after the patient is admitted. If inpatient diabetes resources are not available and the attending doctors are not familiar with the management of insulin pump, discontinuation of insulin pump and transition to a SC basal bolus insulin regimen (pump holiday) may be the safest and most appropriate step.

To successfully transition from insulin pump therapy to a SC basal bolus insulin regimen, it is necessary to inquire directly from the patient or family the current insulin pump settings being used. Most patients would be able to display in their pump screen the average total daily insulin used for the past few days. Based on such information, safe estimations of SC basal, bolus, and supplemental insulin can be calculated[3].

The best person who can manage the pump during hospitalisation is the patient, however the attending doctor should decide whether the pump therapy should be withheld or continued based on the assessment of their physical and mental competency to manage the device and whether there is any contraindication to continue the insulin pump therapy[4,5].

The patients have to demonstrate physical and mental competency to manage the insulin pump. They are required to share with the HCP information regarding pump settings, and to report any problems. If the patient is deemed not competent in managing the insulin pump, it should be discontinued and place on a basal bolus insulin regimen during the hospital stay.

8.1.1 Contraindications

The use of insulin pump is contraindicated in situations where the patient's safety may be compromised by the physical illness or mental state of the patients.

1. Impaired level of consciousness
2. Critical illness requiring intensive care
3. Diabetes ketoacidosis
4. Psychiatric disturbances
5. Risk for suicide
6. Unwilling to participate in self-care

In any of the above situations, the insulin pump should be discontinued and refer to the sections on management of diabetes in specific situations.

8.1.2 Blood glucose monitoring

Patients on insulin pump should perform a minimum of four capillary BG test per day. Three tests before each meal and one test before bed. Additional BG may be performed if it is indicated clinically. (Refer to appendix 1)

8.1.3 Situations where the insulin pump need to be discontinued temporary

Insulin pump may need to be discontinued during surgery and radiological procedure.

Surgery

The use of insulin pump during surgery is not contraindicated. Since the perioperative period is mainly managed by the anaesthetist, its use should be discussed among the anaesthetist surgeon and physician. If the anaesthetist is not familiar with the management of insulin pump, it should be disconnected and refer to Section 4.2 for management of non-critical surgical patient.

The following procedures should be followed if insulin pump is continued:

1. The patient must consent to continue insulin pump therapy during the perioperative period.

2. Metal cannulas should be replaced with plastic cannulas before any surgical procedures that involve diathermy.

3. The patient's BG must be monitored hourly until they have regained consciousness and is capable of making decisions regarding management of the insulin pump.

4. Basal insulin infusion rate is continued and correctional insulin bolus according to patient's insulin sensitivity factor may be given if BG is higher than target range.

5. If the BG falls below 4 mmol/L, the insulin pump should be suspended temporarily and correct the hypoglycaemia with intravenous (IV) dextrose solution.

Radiology

Insulin pump has to be discontinued during radiological interventional procedures and during CT scan or MRI scan because the magnetic fields and radiation can make the insulin pump malfunction. The patient can safely disconnect the pump for up to one hour however hyperglycaemia may occur as soon as 30 minute after disconnection.

The patient's BG has to be monitored before discontinuation of insulin pump, hourly during the procedure and before pump is reconnected. Correctional SC bolus short acting insulin based on patient's insulin sensitivity factor may be given if BG is higher than target range.

Recommendations

- In the absence of contraindication, CSII can be continued during hospitalisation.
- If the attending doctors are unfamiliar with CSII, it can be discontinued and converted to SC basal bolus insulin.

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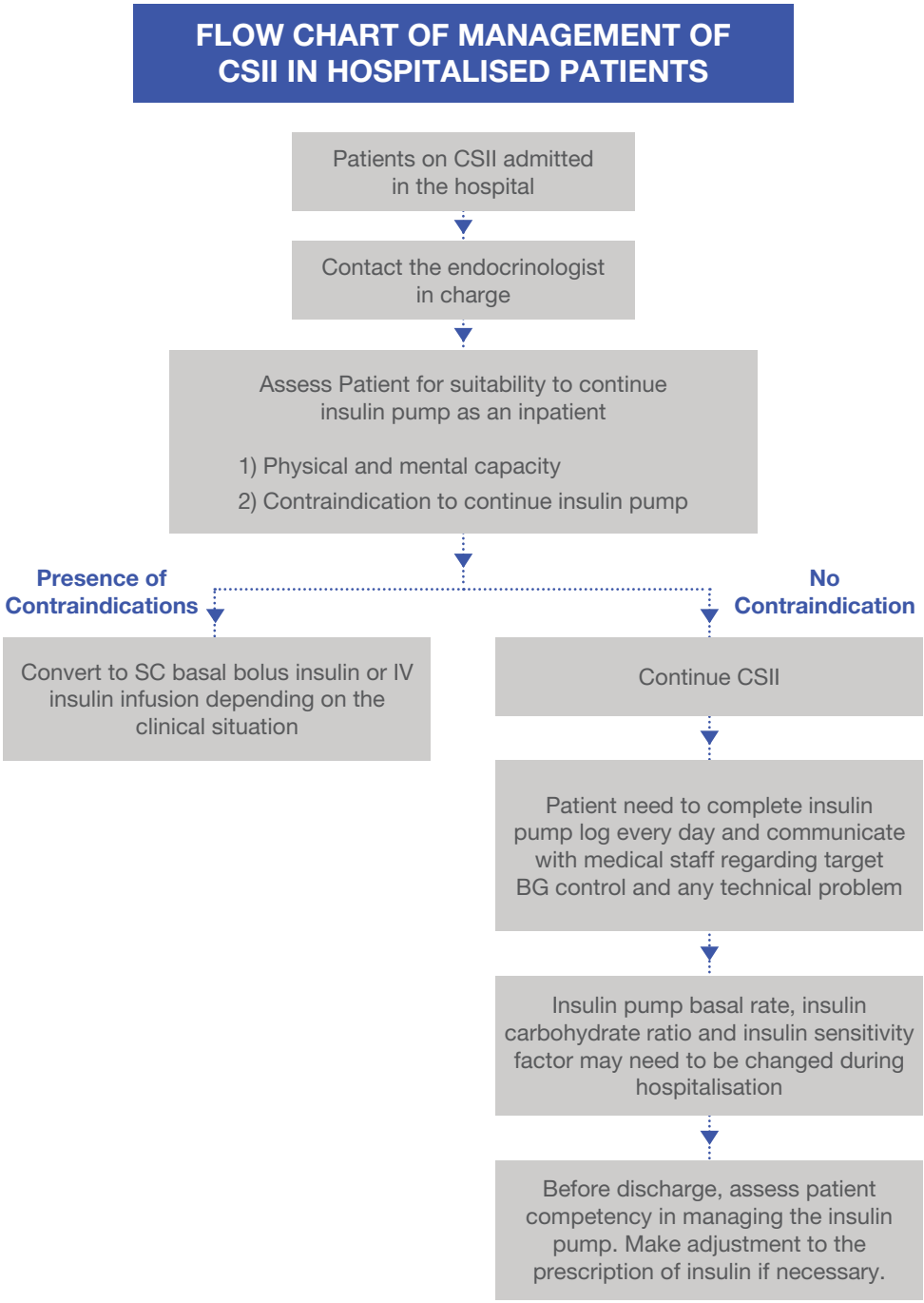
Figure 1: Flow chart of management of CSII in hospitalised patients



8.2 Pregnancy

Introduction

Diabetes mellitus in pregnancy is associated with adverse maternal and foetal outcome. Antenatal nutritional therapy and medical therapy consist of multiple daily insulin injections are recommended to optimise glycaemic control.

8.2.1 Hospitalisation during antenatal period

Pregnant women who are hospitalised during antenatal period should continue their insulin treatment to keep their target BG within the recommended range as long as they are able to tolerate orally. Seven points BG (fasting, pre-meal, 1 or 2 hours after meal and prebed BG) should be monitored. (Refer to Table 1)

If there is a need to fast the patient, basal insulin should be continued and BG to be monitored 6 hourly with SC short acting correctional dose insulin (to be determined by the specific patient's insulin sensitivity factor) given after each BG check. IV dextrose containing solution is recommended if the patient is fasting, the volume will be determined by the patient's concomitant medical conditions and volume status.

Table 1: Blood Glucose targets in pregnancy (Antenatal)

Timing of Blood Glucose	Target value (mmol/L)
Fasting or pre-prandial	≤ 5.3
1 hour after meal	≤ 7.8
2 hours after meal	≤ 6.7

8.2.2 Management of diabetes during administration of dexamethasone for foetal lung maturation

Intramuscular(IM) dexamethasone is recommended to antenatal mother at risk of premature delivery to enhance foetal lung maturation. Hyperglycaemia will be expected especially in patients with underlying diabetes mellitus. In a retrospective study of 55 patients with diabetes who had received dexamethasone, over 90% of women had fasting glucose of greater than 5.3 mmol/L on day 2 and day 3. At least one post prandial glucose was greater than 6.7 mmol/L in 81-98% on day 1 to day 3 and over 60% on day 4 to 6[1].

The management of hyperglycaemia after dexamethasone has to be individualised as there is wide inter-individual variability in the degree and duration of hyperglycaemia. In a study of patients with GDM on diet control alone, insulin had to be started in 40 to 58% cases after

dexamethasone was given. An increase of 39% to 112% in the daily insulin dose was required in GDM on insulin whereas an increased requirement of 26% to 64% was documented in women with pre-existing T2DM on insulin therapy.[1,2]

Kaushal et al. published a nurse-driven protocol to manage diabetes and prevent hyperglycaemia after the use of IM dexamethasone in antenatal women.

The median amount of supplementary IV insulin required was 74 U (range 32-88 U). The median glucose values achieved were 5.8 - 8.9 mmol/L.[3]

Mathiesen et al suggested an increment of SC insulin between 20 - 40% after IM dexamethasone. On the first day, both the basal and bolus insulin were increased by 40%. On the second and third day, basal and bolus were increased by 40%. On the fourth day, the increment was 20% and by the fifth day 10 - 20%. Lastly on day 6 and 7, it was reduced to pre-existing regimen. The median glucose achieved on the second day was 8.2 (6.7 - 12.7) mmol/L and 9.6 (6.3 - 13.1) mmol/L on the third day. The total number of hypoglycaemia episodes was 0.5 per woman.[4]

In diabetic mothers receiving dexamethasone, BG need to be monitored closely (pre, 2HPP and prebed) for at least four to five days. GDM mothers on diet control previously may require insulin temporarily. In GDM or T2DM patients who are already taking insulin, an increase in the dosage of SC insulin by 20 - 40% may be necessary. If glycaemic control is suboptimum, IV insulin infusion may be used. Standard rate VRIII is most likely required since high dose glucocorticoid induces profound insulin resistance.

8.2.3 Management of diabetes during labour

These patients often require inpatient diabetes management prior to delivery because maternal hyperglycaemia during labour increases risk of neonatal hypoglycaemia.[5,6] Maintenance of euglycaemia for diabetic mother in labour has been shown to reduce risk of neonatal hypoglycaemia.[7]

Glucose target

The ideal intrapartum target BG to reduce risk of adverse neonatal outcome is not clear. Many factors including antepartum glycaemic control, gestational age, birth weight affect foetal outcome.

We recommend BG range between 4 to 7 mmol/L during labour for pregnant women with diabetes. This level is supported by The National Institute for Health and Care Excellence, UK (NICE) guideline and the endocrine society guideline.[8,9] These ranges have not been associated with clinically important neonatal hypoglycaemia in insulin requiring women.[7,10] Intrapartum glucose levels above 7.8 to 10 mmol are consistently associated with neonatal hypoglycaemia and increased risk of maternal ketoacidosis.[11,12]

Glucose monitoring

In Type 1 and Type 2 diabetes mellitus, BG should be monitored every two to four hours during latent phase of labor. BG should be monitored every hour during active phase especially if insulin is being infused intravenously.

In women with gestational diabetes who were managed antenatally with diet and lifestyle intervention only, BG should be measured every four to six hourly.

Intrapartum management

The management of diabetes during labour is influenced by the type of diabetes mellitus, insulin sensitivity, the progress and duration of labour.

Type 1 diabetic mothers who have insulin deficiency often require administration of glucose and insulin during labour to prevent diabetes ketoacidosis. Whereas women with gestational diabetes (GDM) and type 2 diabetes mellitus (T2DM) have variable insulin requirement depending upon the duration of diabetes mellitus, insulin resistance, antenatal glycaemic control and stage of labour. They may have sufficient glycogen stores during the latent phase of labour, however glucose requirement increases with prolong labour and during the active phase of labour[6] Refer to (Table 2).

Type 1 diabetes mellitus (T1DM)

The night before induction, the patient should take her usual bedtime dose of intermediate acting insulin. Patient using long acting insulin analogue should reduce the dose by half. Bolus insulin should be stopped on the morning of induction or at the onset of spontaneous labour.

IV insulin infusion with IV glucose regimen has been associated with low maternal and neonatal complications rates in women with T1DM. Several glucose insulin infusion protocols have been published. However, these protocols have not been directly compared in clinical trials. There is no single best way to recommend the insulin protocol to achieve glycaemic control during labour. Adjustment should consider the patient's degree of insulin resistance and insulin sensitivity factors used antenatally. Variable rate insulin infusion (VRIII) at reduced rate with IV Dextrose 5% infusion 125 ml/hr may be used and adjusted to achieve target glucose range.

Gestational diabetes mellitus (GDM) and type 2 diabetes mellitus (T2DM) on insulin

The night before induction, the patient should take her usual bedtime dose of intermediate acting insulin. Patient using long acting insulin analogue should reduce the dose by half. Bolus insulin should be stopped on the morning of induction or at the onset of spontaneous labour.

If oral intake is permitted during the latent phase, SC basal and bolus insulin regimen used during antenatal period can be continued. Bolus rapid insulin should be administered according to carbohydrate intake and correctional scale given in addition if blood glucose falls out of range.

During the active phase of labour, when oral intake is limited, VRIII at standard rate may be used to control blood glucose.

Gestational diabetes mellitus (GDM) on diet control

Women with GDM who are on diet control do not need IV insulin during delivery most of the time. A prospective observational study of women with GDM in labour showed that 86% of the participants were able to maintain CBG within target and did not require insulin during labour.[13] A rotational fluid protocol can be used to keep the maternal glucose within target range. (Appendix 2)

Urine ketone and serum potassium monitoring

Monitor urine ketone 4 hourly. Serum potassium need to be monitored if patient is on IV insulin infusion, keep serum potassium between 4 - 5.5 mmol/L.

Elective caesarean section

The night before induction, the patient should take her usual bedtime dose of intermediate acting insulin. Patient using long acting insulin analogue should reduce the dose by half. Bolus insulin should be stopped on the morning of the surgery. Surgery should be scheduled early in the morning.

BG should be tested on admission and hourly thereafter. If the BG is less than 4 mmol/L, IV dextrose drip should be commenced. Patient should be hydrated with a non-glucose containing solution if the BG between 4 to 7 mmol/L and commence VRIII if the BG is more than 7 mmol/L twice in a row.[14]

Table 2 Intrapartum management of Diabetes

Phases of labour	Management	Gestational DM on diet control	Gestational DM on insulin or T2DM on insulin	T1DM
Plan for induction of labour	Insulin prescription before admission	Not applicable	Continue bedtime dose of intermediate acting insulin Or 50% of long acting insulin	Continue bedtime dose of intermediate acting insulin Or 50% of long acting insulin
Latent phase of labour	BG monitoring	4-6 hourly	2-4 hourly	2-4 hourly or hourly if on IV insulin infusion
	Insulin regimen	No need insulin	Continue basal bolus insulin regimen if oral intake is permitted	Continue basal bolus insulin regimen if oral intake is permitted Or start VRIII at reduced rate with IV D5% 125 ml/hr
	Urine ketone	4 hourly	4 hourly	4 hourly
Active phase of labour	BG monitoring	Every hour	Every hour	Every hour
	Insulin regimen	Start rotational fluid regimen. Usually no need insulin unless BG persistently above 7 mmol/L	If BG > 7mmol/L start VRIII standard rate with IV D5% 125 ml/hr	VRIII reduced rate with IV D5% 125 ml/hr
	Urine ketone	4 hourly	4 hourly	4 hourly

Phases of labour	Management	Gestational DM on diet control	Gestational DM on insulin or T2DM on insulin	T1DM
Postpartum care	BG monitoring	Pre-meal and pre-bed	Pre-meal and pre-bed	Pre-meal and pre-bed
	Diabetes management	Diet control	Breast feeding: insulin therapy if glycaemic control inadequate with diet alone Or low dose metformin Non breast feeding: Oral diabetic agent can be used	Resume pre-pregnancy basal bolus regimen
Caesarean section	Insulin prescription before admission	Not applicable	Continue bedtime dose of intermediate acting insulin Or 50% of long acting insulin	Continue bedtime dose of intermediate acting insulin Or 50% of long acting insulin
	BG monitoring	Hourly	Hourly	Hourly
	IV drip	Dextrose drip if GM < 4 mmol/L Normal saline if GM 4 - 7 mmol/L	Dextrose drip if GM < 4 mmol/L Normal saline if GM 4-7 mmol/L	VRIII reduced rate with IV D5% 125 ml/hr
	Insulin regimen	Usually no need insulin	If BG >7 mmol/L start VRIII standard rate with IV D5% 125 ml/hr	VRIII reduced rate with IV D5% 125 ml/hr

8.2.4 Postpartum care

Maternal insulin requirement decreases by one third to one half after delivery of the placenta[9]. Postpartum glucose target range is less stringent compared to the target during pregnancy (refer to section 2 on inpatient glycaemic target).

Women with T1DM may resume the pre-pregnancy basal bolus regimen with the bolus insulin adjusted according to carbohydrate intake for each meal. Women with T2DM may not require medical therapy in the immediate postpartum period depending on their baseline degree of insulin sensitivity. BG should be monitored pre-meal and pre-bed. Medication should be resumed if hyperglycaemia is documented.

Most women with GDM are able to discontinue insulin immediately after delivery. In non-breast feeding mothers, oral diabetic agent can be continued[17]. Low dose metformin can be safely used in nursing mother[18]. If glycaemic control is still inadequate, insulin therapy at lower dose should be continued.

Recommendations

- Pregnant women who are hospitalised during antenatal period should continue insulin treatment as long as they are able to tolerate orally.

- Target BG are:-
  a. Fasting or pre-prandial ≤ 5.3mmol/L, 1 hour post-prandial ≤ 7.8mmol/L and 2 hour post-prandial ≤ 6.7mmol/L.

- In diabetic mothers receiving IV dexamethasone, BG need to be monitored for at least four to five days.
  a. GDM mothers receiving IV dexamethasone, BG need to be monitored for at least four to five days.
  b. In GDM or T2DM patients who are already taking insulin, an increment in the dosage of SC insulin by 20 - 40% may be necessary.
  c. If glycaemic control is suboptimum, VRIII may be used.

- Target BG during labour for pregnant women with diabetes is between 4 to 7 mmol/L

- For diabetic mother undergoing caesarean section or in active phase of labour, BG should be monitored hourly. T1DM mother should be on VRIII. Whereas for GDM and T2DM mother, VRIII should be started if their BG is more than 7 mmol/L.

- After delivery, metformin can be safely used in nursing mother with pre-existing T2DM. Insulin therapy should be commenced if glycaemic control is suboptimum.

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8.3 Glucocorticoid-Induced Hyperglycaemia

Introduction

The prevalence of glucocorticoid-induced hyperglycaemia is reported to be 20-50% among hospitalised patients.[1,2] The underlying mechanisms include the presence of impaired peripheral glucose uptake and increased hepatic gluconeogenesis mediated by supraphysiological levels of glucocorticoids in the circulation.[1]

All patients receiving pharmacological doses of glucocorticoids, i.e. 5mg and above of prednisolone per day or equivalent (Table 1) should have BG monitoring for 24 to 48 hours[1-3]. Insulin should be commenced if BG is persistently more than 7.8mmol/L at fasting or 10.0 mmol/L at 2-hour post-meal.[1] HbA1c should be obtained for patients without history of diabetes who develop glucocorticoid-induced hyperglycaemia.

The glycaemic effect of glucocorticoid is usually observed 4 - 8 hours after oral administration, sooner with IV formulation.[3] The duration of hyperglycaemia depends on the duration of action of the specific glucocorticoid formulation. The recommended first line regimen for most situations is scheduled s/c insulin. Insulin regimen should be individualised according to the glucocorticoid dosage, timing and severity of hyperglycaemia.[1,4]

Table 1: Steroid dose equivalents

Steroid	Potency/ Equivalent Dose	Duration of action (hours)
Hydrocortisone	20 mg	8
Cortisone	25 mg	8
Prednisolone	5 mg	16-36
Methylprednisolone	4 mg	18-40
Dexamethasone	0.75 mg	36-54

Adapted from Roberts A et al. Joint British Diabetes Societies for Inpatient Care 2014; 1-26.[3]

Initiation and Adjustment of Scheduled Subcutaneous Insulin in Glucocorticoid Induced Hyperglycaemia

Majority of patients with glucocorticoid-induced hyperglycaemia can be controlled with scheduled SC insulin (Table 2). There is a lack of randomised control trials comparing efficacy and safety of different SC insulin protocols in management of inpatient glucocorticoid-induced hyperglycaemia except a small study by Grommesh B et al.[4]

IV insulin infusion is rarely required except in critically ill patients.[3] The most conventionally used regimen is basal bolus insulin. Higher prandial dose is often required for lunch and occasionally dinner when glucocorticoid is given as a daily dose in the morning. The total insulin dose requirement may need to be to up-titrated to 70% above the baseline TDD.

If BG is not well controlled on basal bolus insulin regimen, additional NPH may be added into the basal bolus regimen.[4] This regimen is able to accommodate various glucocorticoid dosing, formulations and frequency by utlising additional NPH dosing which simulate the BG excursion induced by each dose of glucocorticoid (Table 3).[3,4]

Table 2: Insulin regimen for glucocorticoid-induced hyperglycaemia

Insulin Regimen	Description
A. Basal bolus insulin	• SC correctional bolus insulin to coincide with scheduled bolus insulin, 3x/ day • If TDD is known, start with 120% of previous TDD[5] • If TDD is unknown, start with 0.3 - 0.5 U/ kg/ d. The lower dose range is recommended for patient without history of diabetes, type 1 diabetes, elderly or presence of chronic kidney disease at risk of hypoglycaemia. • Higher dose range is recommended for pre-existing type 2 diabetes without risk factor for hypoglycaemia[1]. • Divide TDD into 30% basal, 70% bolus[3,5].
B. Basal bolus insulin + NPH OM/ BD[3-5]	• Start basal bolus insulin with the previous or estimated TDD but divide TDD into 50% basal, 50% bolus. • Add additional NPH with initial dosing according to glucocorticoid dose and diabetes status (cf. Table 3). • NPH OM if glucocorticoid is administered in the morning. • NPH BD if glucocorticoid is administered as multiple dosing throughout the day.
C. VRIII[1,3,5]	Recommended in: • Critically ill patient[3] • BG remains uncontrolled on scheduled SC insulin[1]

TDD, total daily dose; NPH, neutral protamine Hagedorn; VRIII, variable rate intravenous insulin infusion.

Table 3: NPH dosing protocol

Glucocorticoid Regimen	Glucocorticoid Dosage	NPH Initial Added Dose
Prednisolone OM	Low dose (< 40 mg/day)	Non-DM: NPH 5 u OM T2DM: NPH 10 u OM
	High dose (> 40 mg/day)	Non-DM: NPH 10 u OM T2DM: NPH 20 u OM
Hydrocortisone, Dexamethasone or Methylprednisolone TDS/QID	Low dose: Hydrocortisone < 160 mg/day Dexamethasone < 6 mg/day Methylprednisolone < 32 mg/day	Non-DM: NPH 5 u BD T2DM: NPH 10 u BD
	High dose: Hydrocortisone < 160 mg/day Dexamethasone < 6 mg/day Methylprednisolone < 32 mg/day	Non-DM: NPH 10 u BD T2DM: NPH 20 u BD

Non-DM, Non-diabetic or pre-existing diabetic patients with HbA1c < 6.5% not on any glucose lowering medications; T2DM, pre-existing type 2 diabetic patients on medications or HbA1c > 6.5% if not on medications or newly diagnosed type 2 diabetic patients with HbA1c > 8%

N.B.

i. If patient is nil by mouth, reduce NPH added dose by 50%
ii. Uptitrate NPH dose by 25 - 50% if BG is > 10 - 16.7 mmol/L
iii. Discontinue NPH when glucocorticoid dose is < 10 mg of prednisolone or equivalent

Modified from Grommesh B et al. Endocr Prac 2016; 22(2): 180 - 9[4].

When glucocorticoid dose is being tapered, insulin dose should be reduced accordingly to prevent hypoglycaemia. The percentage of insulin dosage reduction should be at the same percentage reduction in glucocorticoid dosage[3]. When glucocorticoid dose is reduced to physiological range, i.e. 5mg prednisolone or below per day or equivalent, stop insulin for patients without history of diabetes or resume previous glucose lowering regimen for patients with pre-existing diabetes.

Discharge plan for patients with glucocorticoid-induced hyperglycaemia[3]

If patients are to be discharged with a protracted course of pharmacological dose of glucocorticoid, they should be educated on lifestyle and dietary modifications; regular BG monitoring; symptoms and signs of hyperglycaemia and hypoglycaemia; adjustment of glucose lowering medications upon glucocorticoid dose tapering or increment. An early review with the primary care provider coinciding with the anticipated glucocorticoid dose adjustment should be arranged. A screening test in the form of fasting BG or oral glucose tolerance test to look for persistent glucose intolerance should be arranged 6 weeks after cessation of glucocorticoid. If HbA1c is chosen as a screening test, it should only be performed 3 months after glucocorticoid cessation.

Recommendations

- All patients receiving pharmacological doses of glucocorticoids, i.e. 5 mg and above of prednisolone per day or equivalent should have BG monitoring for 24 to 48 hours and commenced on insulin if BG is persistently more than 7.8 mmol/L at fasting or 10.00 mmol/L at 2-hour post-meal.

- The recommended first line regimen for most situations is scheduled SC insulin with its regimen individualised according to the glucocorticoid dosage, timing and severity of hyperglycaemia.

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8.4 Chronic Kidney Disease (CKD)

8.4.1 Introduction

No guidelines have been published for hospitalised patient with diabetes and CKD. The principle of management of diabetes in this group of patient should follow the general population. In general, it is advised that most non-insulin therapies be discontinued at hospital admission.

In diabetic patients receiving exogenous insulin, renal metabolism plays a more significant role since there is no first pass metabolism in the liver. Once the glomerular filtration rate (GFR) drops below 20 ml/min, the kidneys clear markedly less insulin. This effect is compounded by a decrease in the hepatic metabolism of insulin which occurs in uraemia[1]. Despite the increase in insulin resistance caused by renal failure, the net effect is reduced requirement for exogenous insulin[2].

When GFR drops to between 10 and 50 ml/min, the total insulin dose should be reduced by 25%. Once the filtration rate is below 10 ml/min, the insulin dose should be decreased by 50% from the previous amount[3].

If the patient is insulin naïve, the starting total insulin dose should be 0.2 - 0.3 U/kg/day. Basal insulin should consist of half of the total daily dose and the other half divided into 3 doses of bolus insulin before each meal. Aggressive glycaemic control should be avoided to reduce the risk of hypoglycaemia.

8.4.2 Management of diabetes in End Stage Renal Disease (ESRD)

Upon initiation of dialysis, peripheral insulin resistance may improve, further reduce insulin requirement[4].

Haemodialysis increases the risk of hypoglycaemia due to glucose elimination from blood circulation during the sessions and improvement of sensitivity to insulin. A study in diabetic patients with ESRD on haemodialysis using a 24 hour euglycaemic clamp demonstrated a significant reduction of basal hourly insulin requirement by 25% on the day after dialysis compared with the day before, however bolus insulin requirement was unchanged[5].

Among patients on peritoneal dialysis, glucose content in peritoneal dialysate may confer as much as 10-30% of a patient's total caloric intake[6]. The glucose load increased the need for insulin therapy.

Treatment in this group of patients will need to be individualised. For patient on haemodialysis, basal insulin dose may need to be reduced on the day after dialysis whereas for patient on peritoneal dialysis, insulin requirement increase depending on the glucose content of dialysate used.

Recommendations

- For hospitalised patient with CKD and diabetes, total insulin dose should be 0.2- 0.3 U/ kg/ day.
- Insulin requirement is reduced in insulin treated patients undergoing haemodialysis.
- Insulin requirement is increased in insulin treated patients undergoing peritoneal dialysis.

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8.5 Enteral and Parenteral Nutrition

Introduction

The use of enteral (EN) or parenteral nutrition (PN) is an independent risk factor for new onset or aggravation of inpatient hyperglycaemia for patients with or without history of diabetes[1]. The prevalence of inpatient hyperglycaemia is up to 30% for patients receiving EN and more than 50% for patients receiving PN[2]. Development of hyperglycaemia during nutritional support is associated with increased risk of infection and mortality in hospitalised patients[2].

It is recommended to initiate BG monitoring 6 hourly for all patients commenced on EN or PN in the hospital[3]. After achievement of the desired caloric intake, BG monitoring can be discontinued in patients with no history of diabetes if all the BG readings are less than 7.8 mmol/L at 24 to 48 hours[1]. If the BG are persistently more than 7.8 mmol/L for more than 24 hours, scheduled insulin should be commenced[1]. The insulin regimen should be individualised according to the feeding schedule.

Enteral Nutrition: Bolus Feeding

A typical enteral feeding regimen for patients in non-critical wards is administration of three hourly bolus feeding during the day. All SC insulin should be administered at the start of a bolus feed away from the rest period to avoid hypoglycaemia.

The recommended insulin regimen with established feeding is basal bolus insulin. Short-acting insulin (SAI) is preferred over rapid-acting insulin as bolus insulin due to its longer duration of action thus requiring less number of injections per day[1,5]. One may start with basal only with correctional insulin regimen and delay the initiation of scheduled bolus insulin until achievement of at least 50% of the desired caloric intake. If bolus feeding is given overnight, the basal insulin can be replaced by a bolus insulin, i.e. bolus insulin only regimen.

Crushing of oral anti-diabetic agent is generally not recommended[3] (Table 1).

Table 1: Insulin regimen for bolus enteral feeding

Insulin Regimen	Description
A. Basal only with correctional insulin[2,4]	• SC NPH: 12Hly at the start of a feed or • SC basal analogue: Once daily at the start of last feed of the day • SC correctional bolus insulin 6Hly
B. Basal bolus insulin[3,5,6]	• SC NPH: 12Hly at the start of a feed or • SC basal analogue: Once daily at the start of last feed of the day • Scheduled SC SAI 20 min before a bolus feed with correctional insulin 3^{x} / day[3]
C. Bolus insulin only[3]	• Scheduled SC SAI 20 min before a bolus feed with correctional insulin 4^{x} / day

NPH, neutral protaminated Hagedorn; SAI, short-acting insulin

Enteral Nutrition: Continuous Feeding

Continuous enteral feeding is conventionally delivered via an infusion pump in a cyclical manner with each cycle consisting of continuous feeding over 4 hours followed by 2 hour rest to a total of 4 cycles per day. For patients not tolerating the cyclical regimen, the feeding period can be extended to 20 hours with 4 hour rest overnight.

If the total daily insulin requirement, i.e. TDD of insulin is known, a basal only with correctional insulin can be used. For patients at risk of hypoglycaemia during the rest period of cyclical feeding on basal insulin only regimen, basal bolus insulin is recommended. Scheduled bolus insulin should be administered prior to the start of each cycle away from the rest period. For patients with unknown TDD, VRIII should be utilised to estimate the TDD[1]. When the BG is stabilised after achievement of the desired caloric intake, it may then be converted to scheduled SC basal bolus or basal insulin only regimen in non-critically ill patients (Table 2).

Table 2: Insulin regimen for continuous enteral feeding

Insulin Regimen	Description
A. Basal only with correctional insulin[3,5,6]	• SC NPH 12Hly at the start of a cycle (for cyclical feeding) or at onset and midpoint of the feed (for extended feeding over 12-24 hours). • SC basal analogue at the start of last cycle of the day (for cyclical feeding) or at the start of feed (for extended feeding over 12-24 hours). • SC correctional bolus insulin 6Hly (if cyclical: prior the start of each cycle).
B. Basal bolus insulin[1,3]	• SC basal insulin administered as above. • Scheduled SC SAI with correctional insulin at the start of a cycle, 3x/day.
C. VRIII	Recommended when: • TDD of insulin is not known[6]. • Before achievement of desired caloric intake. • Patient is clinically unstable[2]. • Patient with gastroparesis on 20H feeding/day. • BG not controlled on basal only or basal bolus regimen.

NPH, neutral protaminated Hagedorn; VRIII, variable rate intravenous insulin infusion; TDD, total daily dose

Parenteral Nutrition

Hyperglycaemia is more common during PN compared to EN due to a high glucose load to the systemic circulation bypassing the enteral system[(4,6)]. It is recommended to initiate VRIII first to estimate the TDD for patients with persistent hyperglycaemia[(1,2,5,6)]. For non-critically ill patients on full rate of PN, scheduled SC insulin can be considered after BG is stabilised on VRIII. It is generally not recommended to add insulin into the PN bag (Table 3).

Table 3: Insulin Regimen for Parenteral Nutrition

Insulin Regimen	Description
A. VRIII[1,2,5.6]	• TDD of insulin can be calculated when PN is infused at full rate with stable BG. • May be converted to basal or bolus insulin only regimen when BG is stable after achievement of desired calorie intake.
B. Basal only with correctional insulin	• TDD of insulin can be derived from the total amount of insulin infused per day from VRIII. • SC NPH 12Hly or basal analogue once daily. • SC correctional bolus insulin 6Hly.
C. Bolus insulin only	• TDD of insulin can be derived from the total amount of insulin used per day from VRIII. • Continuous feeding over 24H: Scheduled SAI 6Hly. • *Cyclical feeding over 16H: Scheduled SAI 4Hly over the feeding period. • SC correctional SAI to coincide with scheduled SAI.

VRIII, variable rate intravenous insulin infusion; TDD, total daily dose; NPH, neutral protaminated Hagedorn; SAI, short-acting insulin.

* Cyclical regimen with feeding withheld for 8 hours during day time, typically from 10am to 6pm to rest the liver or to encourage ambulation in non-critically ill patients.

Table 4: Insulin adjustment when EN/ PN is interrupted

Previous Insulin Regimen	Recommended Insulin Adjustment
A. Basal bolus insulin	• Withhold the bolus insulin. • Continue the basal insulin. • If NPH insulin was used as basal insulin, ensure 24 hours coverage by 12 hourly administration.
B. Basal insulin only	• Continue basal insulin at 40-50% of previous TDD[6].
C. Bolus insulin only	• Replace bolus insulin with a basal insulin at 50% of previous TDD.
D. VRIII	• Consider scale de-escalation.

N.B.

i. Start IV dextrose to avoid hypoglycaemia[3,5,6]
ii. Monitor BG hourly until the end of duration of action from the last dose of SC insulin administered prior to the feeding interruption[3]
iii. VRIII is recommended for patients with type 1 diabetes if the feeding interruption exceeded 2 hours[3]

Recommendations

- Initiate BG monitoring 6 hourly for all patients commenced on EN or PN. Monitoring can be discontinued in patients with no history of diabetes if all the BG readings are less than 7.8 mmol/L at 24 to 48 hours after achievement of the desired caloric intake.
- Insulin regimen and dosing should be tailored and adjusted on a daily basis to the feeding type and schedule, achievement of desirable caloric intake and stability of the patients.

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SECTION 9
MANAGEMENT OF HYPOGLYCAEMIA

Introduction

Hypoglycaemia is the commonest and most feared side effect of insulin and insulin secretagogues i.e., sulphonylureas in the treatment of diabetes and has been associated with increased rates of mortality, readmission within 30 days and longer hospital stay[1-2].

Hypoglycaemia results from an imbalance between glucose supply and utilisation, and insulin levels[3]. Insulin treated T2DM patients are more likely to experience severe hypoglycaemia requiring hospital admission than patients with T1DM[4]. Other possible causes of hypoglycaemia in adults are as outlined in Table 1. Hypoglycaemia in patients with diabetes mellitus is defined as blood glucose < 4 mmol/L regardless of whether symptoms of hypoglycaemia are present.

Table 1: Causes of hypoglycaemia in adults[6]

Ill or medicated individual	Seemingly well individual
Drugs • Insulin • Insulin secretagogue (sulphonyurea, glinides) • Alcohol • Others - gatifloxacin, pentamidine, quinine	**Endogenous hyperinsulinism** • Insulinoma • "Dumping syndrome" post gastric bypass • Insulin autoimmune hypoglycaemia • Insulin secretagogue • Accidental, surreptitious or malicious hypoglycaemia
Critical illnesses • Hepatic, renal or cardiac failure • Sepsis (including malaria) • Starvation	
Hormone deficiency • Cortisol deficiency • Glucagon and epinephrine deficiency (in insulin - deficient diabetes mellitus) Non-islet cell tumour especially if huge tumour burden	

No local data is available regarding inpatient hypoglycaemia and its prevalence. Prevalence of severe hypoglycaemia in inpatients treated with insulin elsewhere reported to range from 5% to 32%[5]. Hypoglycaemia is preventable. Patient safety can be improved by:-

1. Increasing awareness and knowledge on hypoglycaemia among HCP and patients.
2. Identification of risk factors and potential iatrogenic trigger whether pertaining to the patient, his/her management and treatment, and even the hospital environment.
3. Subsequent preventative measures to minimise these risks and avoid potential triggers.

Signs and symptoms of hypoglycaemia are as outlined in Table 2. However it is important to note that some patients symptoms even when BG is below 4 mmol/L. This is called "hypoglycaemia unawareness". Patients with hypoglycaemia unawareness are at especially high risk for subsequent hypoglycaemia. Therefore, their medications should be reviewed and glycaemic targets temporarily relaxed with strict avoidance of hypoglycaemia for 2 days to 3 months. This would improve counter-regulatory hormone responses and help them regain early warning symptoms of hypoglycaemia. On the other hand, some patients may experience symptoms despite BG being more than 4 mmol/L. This is called "relative hypoglycaemia" and can be treated with giving 15 g long-acting carbohydrate.

Table 2: Signs and symptoms of hypoglycaemia

Autonomic*	Neuroglycopaenic
Palpitations	Confusion
Tremor	Drowsiness
Anxiety/ nervousness	Abnormal or altered behaviour
Diaphoresis	Focal or generalised neurologic complaints such as speech difficulty or incoordination
Hunger	
Numbness	Seizure
Headache	Coma
Nausea	Death

* Caution: May not be present in patients with hypoglycaemia unawareness

Patient Factors:

- Elderly
- Co-morbidities - renal impairment, renal dialysis, severe liver dysfunction
- Endocrine dysfunction – exogenous Cushing's with sudden cessation or reduction of steroids, primary adrenal insufficiency, growth hormone deficiency, hypothyroidism, hypopituitarism
- History - previous hypoglycaemia especially severe hypoglycaemia or undetected nocturnal hypoglycaemia, long-standing diabetes
- Reduced carbohydrate intake – vomiting, reduced appetite, malabsorption syndromes
- Hypoglycaemia unawareness (loss of, diminished or altered warning symptoms of hypoglycaemia)
- Poor injection technique
- Physically or cognitively incapacitated - unable to report symptoms or self-correct e.g., intubated, bedbound, dementia
- Change in clinical status - resolution of stress, convalescence, mobilisation, major limb amputation
- Early pregnancy, breastfeeding
- Inadequate monitoring
- Rapidly dropping blood glucose e.g., > 5 mmol/L per hour while on insulin infusion

Potential Iatrogenic Triggers:

- Prescription error
  - Poorly written prescriptions
  - Misinterpretation e.g., 2U read as 20 units
  - Confusing insulin name with dose e.g., Mixtard 30/70 read as Mixtard 30 units
- Transcription error
- Tight glycaemic control
- Insulin infusion (with or without dextrose infusion)
- Sudden cessation or reduction of corticosteroid dose
- Nutrition-insulin mismatch - unexpected interruption or reduction of nutrition (oral, enteral or parental feedings) or IV dextrose infusion
- New or prolonged "nil-by-mouth" status
- Inappropriate timing of short-acting insulin or diabetic medication for meal/ enteral feed
- Inappropriate use of short-acting insulin "stat" or "PRN"
- Missed or delayed meals due to transfer out of ward for imaging or procedures

All patients with diabetes mellitus should be reviewed daily for their risk of hypoglycaemia and especially when there is a change in their condition or if a procedure is planned especially if "nil-by-mouth" is required. There should be a plan placed in advance and written clearly in the notes to monitor BG more closely, withhold insulin or OAD and whether dextrose infusion need to be started when NBM is commenced.

REVIEW to reduce or stop insulin and/ or OAD WHEN
• Patient has recent history of severe hypoglycaemia • Patient has hypoglycaemia unawareness • Patient has recent history of weight loss • Immediately after an episode of hypoglycaemia (BG < 4.0 mmol/L) • There is rapid drop in BG or BG < 5.6 mmol/L • Planned for NBM - consider giving dextrose-containing IV fluids • Reduced appetite or if vomiting and/ or diarrhoea • Feeding (whether enteral or parental) is reduced, omitted or stopped • Dextrose-containing IV fluids is reduced (in rate or volume) or stopped • After major limb amputation • Deteriorating renal or liver function • There is renal or liver impairment • Steroids dose is reduced or stopped • Increased in physical activity or improved mobilisation and ambulation • Change in clinical status particularly if improving with amelioration of stress such as treated infection with settling fever or infected wound that has been surgically debrided and is now clean and healing • Pregnant women with pre-existing DM after delivery

Treatment of Hypoglycaemia

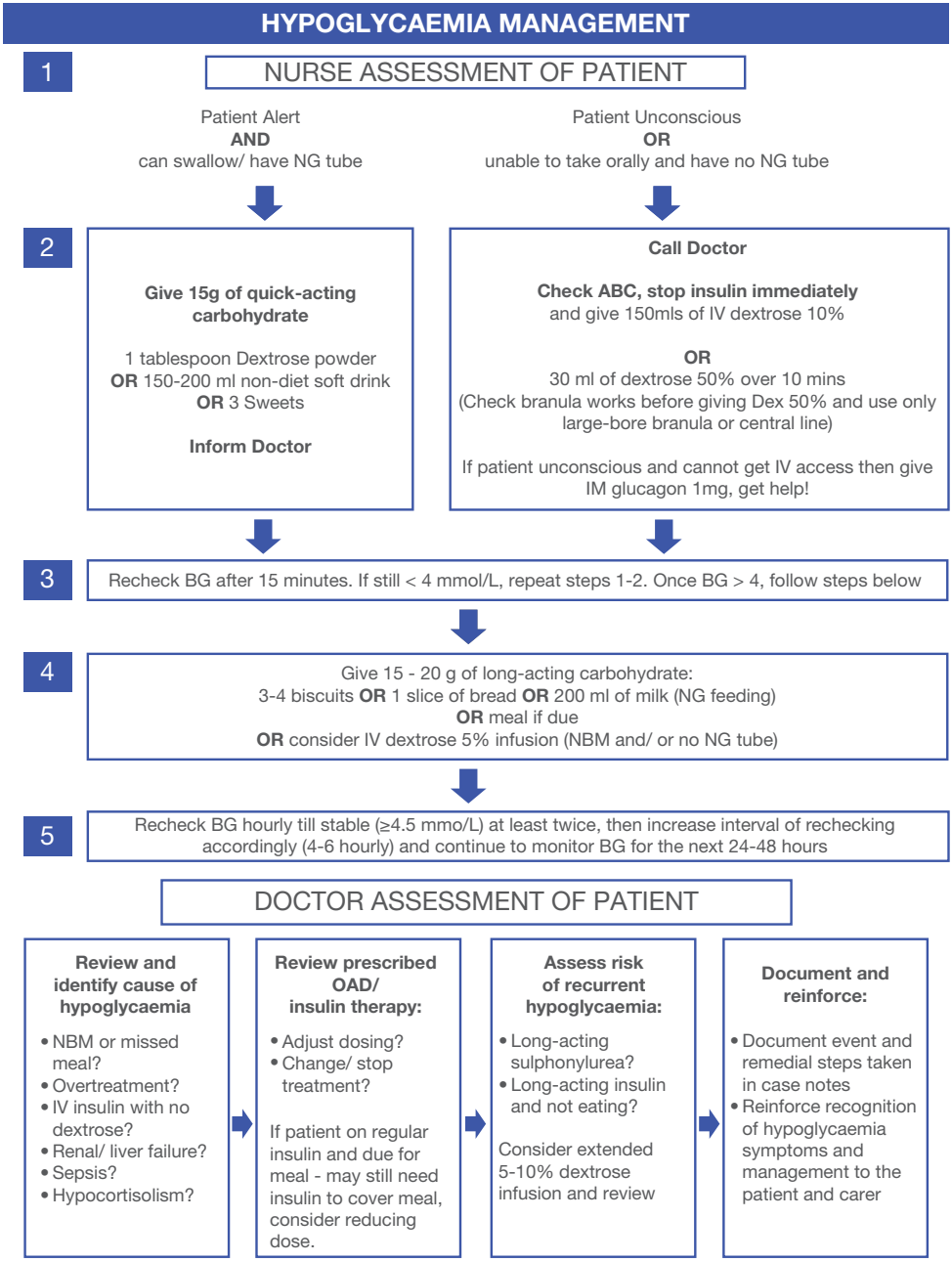
Hypoglycaemia is a medical emergency and should be treated urgently by ingestion of quick-acting carbohydrates, or by parenteral glucose or glucagon if oral ingestion is not feasible. When BG is above 4.0 mmol/L following correction of hypoglycaemia, ingestion of long-acting carbohydrate is recommended to prevent recurrent hypoglycaemia. Infusion of dextrose-containing intravenous fluids can be considered for those who are unable to take orally and BG should be monitored for the next 24 to 48 hours. **An easy way to remember how to treat hypoglycaemia is the RULE OF 15.**

RULE OF 15

STEP 1:	**15** g of quick-acting carbohydrate given immediately
STEP 2:	Recheck BG in **15** minutes and repeat steps 1 and 2 till BG > 4 mmol/L
STEP 3:	**15** g of long-acting carbohydrate once BG > 4 mmol/L

Below is an algorithm for treatment of hypoglycaemia that can be used as part of nursing protocols.

Figure 1: Hypoglycaemia management



Document and reinforce

The attending doctor should document every event and remedial steps taken clearly in the patient's notes. Subsequently hypoglycaemia education should be reinforced on both the patient and the carer. Insulin and sulphonylurea are antidiabetic medications associated with high risk of hypoglycaemia and should therefore be reviewed first to consider withholding or reducing dose when hypoglycaemia happens. Consider changing to other antidiabetic medications such as metformin, DPP4-inhibitors, SGLT2-inhibitors and GLP1 receptor agonists that are associated with relatively lower risk of hypoglycaemia. However for insulin deficient patients (T1DM, long-standing T2DM or recovering DKA), insulin should be resumed at a lower dose once hypoglycaemia is treated.

Please refer to Appendix 9 - Hypoglycaemia Action Sheet that can be used to guide doctors in treating hypoglycaemia when it happens in the hospital and to give an action plan to prevent recurrence.

****Important Notes:**

1. Dextrose 50% is caustic. In patients who have a long line in situ, a higher volume of 40-50 ml of Dextrose 50% can be given through the long line for correction of severe hypoglycaemia.

2. Glucagon may be less effective in the following situations:
   - Treatment with sulphonylureas
   - Chronically malnourished
   - Under the influence of alcohol
   - Period of prolonged fasting
   - Depleted glycogen stores
   - Severe liver impairment

3. If glucagon is given, TWICE the suggested amount of long-acting carbohydrate should be given to replenish glycogen stores.

4. If the cause of hypoglycaemia is due to sulphonylurea or long-acting insulin therapy, risk of hypoglycaemia may persist up to 24-36 hours from the last dose particularly if patient has concurrent renal impairment. Close BG monitoring should therefore be continued till the offending drug is metabolically excreted.

5. Insulin injection if due may be continued after adequate treatment of hypoglycaemia but review of the dose and regimen may be required.

6. Preventative measures should be taken to prevent recurrent hypoglycaemia.

7. Insulin should not be stopped completely for those with insulin deficiency particularly in patients with Type 1 diabetes mellitus, those recovering from DKA or on long-standing Type 2 diabetes mellitus on insulin. Consider dose reduction instead.

8. For patients with renal impairment suffering hypoglycaemia due to sulphonylurea, subcutaneous octreotide (50 µg stat and to repeat in 6-12 hours can be considered if hypoglycaemia is prolonged or refractory to dextrose infusion[9-10].

9. **In persons without diabetes mellitus,** cause for the hypoglycaemia need to be determined by reviewing the history, physical findings and all available laboratory data. Further investigations such as serum cortisol (to look for hypocortisolism), plasma glucose, insulin, C-peptide (to look for endogenous hyperinsulinism) and blood for sulphonylurea (to look for ingestion of sulphonylurea) during an episode of spontaneous hypoglycaemia may be required. Possible causes to consider are as outlined in Table 1.

Prevention strategies[1, 7-8]

1. Root cause analysis of all hypoglycaemia episodes.

2 All hypoglycaemia episodes be aggregated, documented clearly, tracked in the medical records and reviewed for systemic issues.

3. Treatment regimen be reviewed when BG is < 5.6 mmol/L or when a rapid drop of BG occurs.

4. Adoption and implementation of a hypoglycaemia protocol in each hospital.

5. Risk stratification for all patients with diabetes mellitus admitted to the hospital using the Hypoglycaemia Risk Stratification Tool (Appendix 10)[11] with subsequent intensive interventions to minimise hypoglycaemia risk targeted at the intermediate to high risk group which should be continued even at discharge and subsequent outpatient follow-up. This tool can be incorporated as part of nursing care or developed as a software for hospitals with EMR.

Recommendations

- Hypoglycaemia in patients with diabetes mellitus is defined as BG < 4.0 mmol/L and should be treated immediately even if no symptoms with 15g of quick-acting carbohydrate followed by rechecking of BG in 15 minutes, repeat administration of simple sugar if necessary till BG > 4.0 mmol/L then give 15 g long-acting carbohydrate to prevent rebound hypoglycaemia (Rule of 15). The cause of hypoglycaemia should be identified, treated and an action plan given to prevent recurrence.

- All patients with DM admitted to the hospital should be risk stratified and those at intermediate to high risk of hypoglycaemia should have their insulin or antidiabetic medications reviewed to reduce dosage, stopped or changed to prevent hypoglycaemia.

- Adoption and implementation of a hypoglycaemia protocol in each hospital.

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1. Walden E, Stanisstreet D, Jones C, et al. The hospital management of hypoglycaemia in adults with diabetes mellitus. Joint British Diabetes Societies for Inpatient Care. Revised September 2013.

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5. Farrokhi F, Umpierrez G, Smiley D. Hypoglycemia in the hospital setting, Diabetic Hypoglycemia (www.hypodiab.com), 5: 3-8.

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9. Glatstein M, Scolnik D, Bentur Y. Octreotide for the treatment of sulfonylurea poisoning. Clinical Toxicology. 2012 Nov 1;50(9):795-804.

10. Gonzalez R, Zweig S, Rao J, et al. Octreotide therapy for recurrent refractory hypoglycemia due to sulfonylurea in diabetes-related kidney failure. Endocrine Practice. 2007 Jul 1;13(4):417-23.

11. Karter AJ, Warton EM, Lipska KJ, et al. Development and validation of a tool to identify patients with type 2 diabetes at high risk of hypoglycemia-related emergency department or hospital use. JAMA Internal Med. 2017 Oct 1; 177(10):1461-70.

SECTION 10
INPATIENT MEDICAL NUTRITION THERAPY

Introduction

Medical nutrition therapy (MNT) is an essential component of inpatient glycaemic care for patients with diabetes and hyperglycaemia. The goals of MNT are essentially to optimise glycaemic control, ensure sufficient caloric intake in the setting of increased metabolic demands of acute illness, optimise glycaemic control and subsequently provide a suitable home nutrition plan following hospital discharge.[1] There are many challenges and barriers to optimal inpatient MNT[2] (refer Table 1).

TABLE 1

- Changes in appetite and ability to eat secondary to medications and acute illness.
- Decreased activity levels
- Inconsistent carbohydrate intake
- Lack of understanding of current diabetes nutrition principles by staff, patients and their families
- Meal timing and modifications based on need for testing, procedures, and surgery
- Meal timing and modifications vary from those at home and are based on need for testing, procedures, and surgery
- Suboptimal coordination of nutrition delivery with point of care glucose testing and insulin administration
- Variation in insulin requirements with enteral and parenteral feedings
- Visitors bring in outside food that is not included in the meal plan

Specialized nutrition support has been shown to be cost effective, reduces infectious complications and length of hospital stay[3].

The general approach to MNT in hospitalised patients with diabetes and hyperglycaemia consists of a nutritional assessment by a dietitian followed by individualised nutrition recommendations and meal planning that provide consistent carbohydrate content.

Diabetes educators should assist in the coordination of hospital food delivery, insulin administration, and POC BG testing schedules to optimise glycaemic control. Coordinating care with the hospital dietitian is essential due to the many nutrition challenges in the inpatient. Educating and involving patients and family members in meal planning throughout hospitalisation will facilitate self-care behaviour during and beyond hospitalisation[2].

Nutritional Recommendations and Meal Planning

a. Total calorie requirement

Most hospitalised patients will require a diet providing 25 – 35 calories/kg body weightper day, which is an average of 1500 – 2000 calories per day and containing approximately 200g carbohydrate, divided between 3 separate meals with or without scheduled snacks depending on patient's need and glycaemic profiles[4].

b. Carbohydrate requirement

Dietary carbohydrate is the main nutrient affecting glycaemic level. Hence, the daily carbohydrate content of specific meals should be kept constant to facilitate coordination of meal / prandial insulin doses[4]. Care must be taken not to overfeed patients as this can exacerbate hyperglycaemia.

c. Protein requirement

Protein intake goals for inpatient should be individualised based on patient's nutritional status and metabolic needs. The protein recommendations would be between 1.0 – 1.5 g / kg body weight per day[5]. Those with diabetic kidney disease, the aim is to maintain dietary protein at the recommended daily allowance of 0.8 g/kg body weight per day[5].

d. Post-operative inpatient nutrition

Following surgery, food intake is recommended early as tolerated with clear fluids then progressing promptly to full liquids then solid foods. In patients where nutritional requirements cannot be met orally, enteral nutrition (EN) or parenteral nutrition (PN) support can be initiated, both of which may aggravate hyperglycaemia and worsening metabolic control. However, oral nutrition and EN are preferable to PN in clinical practice[4]. Hyperglycaemia related to PN can be reduced by limiting the amount of dextrose infusion to 100 - 150 mg /day, sufficient to fulfil metabolic demands of brain and basic cellular function[8].

e. Diabetes Specific Formulas (DSFs)

Diabetes specific formulas (DSFs) are superior to standard formulas in controlling postprandial glucose elevation, glycaemic variability and insulin response due to reduced carbohydrate, high fat and fibre content[6]. Providing DSFs for EN has been shown to be associated with reduced need for insulin, reduced length of ICU stays, reduced ICU costs and reduced mortality[7] (refer Table 2).

Table 2: Diabetes Specific Formulas (DSFs)

No*	Enteral Formula	Standard Dilution	Weight/ can (g)	Caloric density (kcal/ml)	Scoop (g)
1	Nutren Diabetik powder (Nestle)	7 scoops in 210 ml water	400	1.0	7.9
2	Glucerna Triple Care Powder (Abbott)	5 scoops in 200 ml water	400	1.0	10.4
3	Diabetasol powder (Kalbe International)	4 scoops in 200 ml water	180	1.0	15.0
4	Wellness 60+ Diabetic Vanilla (Appeton)	5 scoops in 200 ml water	450	1.2	10.6
5	Pentra Sure DM (AJ Pharma)	4 scoops in 200 ml water	400	1.0	12.5
6	Supplement D powder (British Biologicals)	6 scoops in 210 ml water	400	1.0	10.0
7	Nutren Diabetik RTD (Nestle)	-	237 ml	1.0	-
8	Glucerna RTD	-	250 ml	1.0	-

Calories and nutrient composition per scoop						
No*	Calories (kcal)	Carbs (g)	Protein (g)	Fat (g)	Calcium (mg)	Potassium (mg)
1	36.1	3.5	1.6	1.6	29.1	34.3
2	45.2	5.4	2.0	1.65	33.6	74.0
3	65.0	9.8	2.5	1.8	42.5	55.0
4	49.8	6.5	1.7	1.9	34.0	56.8
5	55.0	7.8	2.8	1.4	49.9	59.5
6	45.1	5.04	2.0	1.7	20.0	52.3

Table 3: Calories and nutrient content per scoop DSFs

Calories and nutrient composition per can for Ready-to-drink (RTD)						
7	240	23.2	10.7	10.4	187	228
8	250	20.0	10.0	14.0	180	390

Note: No. refers to the corresponding DSFs with similar number in Table 2.

Recommendations

- Inpatients with diabetes or stress hyperglycaemia should undergo a nutrition assessment by a dietician and provided with individualised meal plans with consistent distribution of carbohydrate content.

- For enteral nutrition, diabetes specific formulas (DSFs) should be used to reduce postprandial hyperglycaemia and glycaemic variability.

References:

1. Gusmanov AR, Umpierrez GE. Medical nutrition therapy in hospitalised patients with diabetes. Curr Diab Rep. 2012 February; 12(1): 93 - 100.

2. Role of Diabetes Educator in Inpatient Diabetes Management. AADE Position Statement 2016

3. Zaloga GP. Improving outcomes with specialized nutrition support. JPEN. 2005; 29:S49 - S52.

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SECTION 11
PATIENT EDUCATION

During hospitalisation, in non-ICU setting, there is an opportunity to provide diabetes related patient and family education. The goal is to prepare the patient and/or caregiver to perform self-management skills by the time of hospital discharge. In the hospital setting, trained and certified diabetes educators are an essential part of the diabetes care team and have a key role towards both inpatient and outpatient diabetes education for patients and caregivers as well as for other hospital staff.

Diabetes self-management education and support is an important component of patient care and recovery, and shown to reduce cost in the hospital setting. Patient education planning by the inpatient diabetes care team should start following patient assessment and identification of specific learning needs of the patient. Early intervention provides time to identify and address barriers, offer opportunities for practice and facilitates problem-solving and coping skills.

Inpatient patient education focuses on developing and enhancing basic skills and knowledge, and represents a bridge to ongoing outpatient education.

Diabetes educators (DE) have an important role to ensure the following practices

- Assessment of learning needs including health literacy, and setting and prioritising goals
- Evaluating patient and / or caregiver prior diabetes knowledge and giving updated information
- Optimise patient and/ or caregiver learning by giving short and focused teaching sessions
- Focus on self-management survival skills - meal planning, safe medication administration, monitoring BG including targets, timing and technique of testing, prevention and treatment of hypoglycaemia and hyperglycaemia
- Document and communicate status of self-management education and identified needs to other health care professionals
- Evaluate the ability of the patient to obtain diabetes supplies and medication
- Coordinate continued diabetes self-management education at primary care health facilities

Commonly insulin therapy is initiated for the first time during hospitalisation. Use of insulin in acute care may often be transient and should be explained to patients to avoid unnecessary anxiety concerning use of insulin therapy after discharge. In patients transitioning to insulin therapy for home use (especially those who are new to using insulin) self-administration of insulin should be initiated as soon as possible under supervision in order to assess the patient's ability. In patients with pre-existing diabetes, hospitalisation is an opportunity to evaluate and improve home diabetes medication regimens and promote self-care.

Recommendations

- Inpatients with diabetes should be referred to a diabetes educator for diabetes self-management education and support.

References:

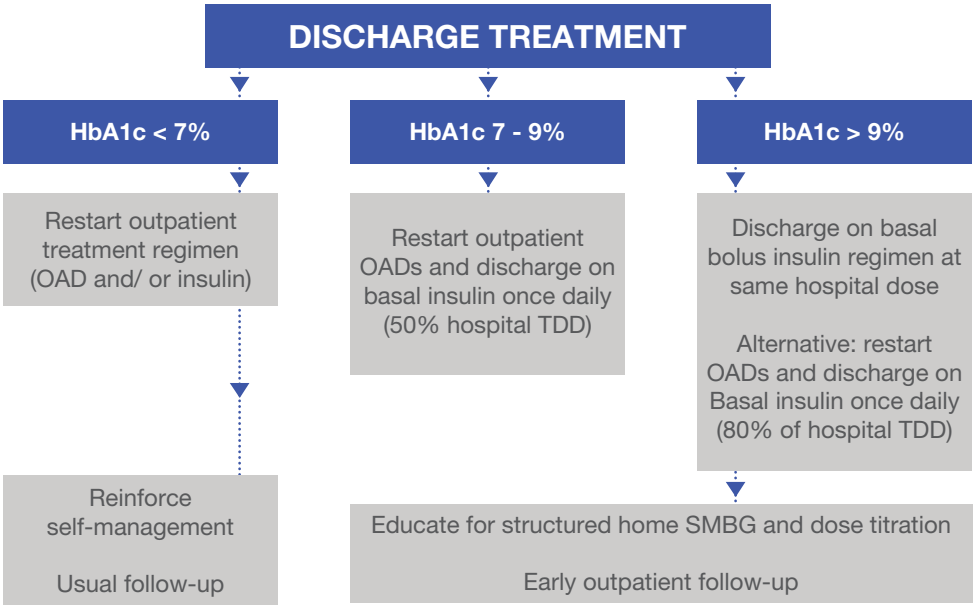
1. Role of Diabetes Educator in Inpatient Diabetes Management. AADE Position Statement 2016.

SECTION 12
DISCHARGE PLANNING/ TRANSITION FROM HOSPITAL TO HOME

Admission to hospital represents an important opportunity to improve glycaemic control among poorly controlled diabetes patients. Many issues of importance in outpatient diabetes care may be addressed during hospital admission and discharge planning such as adjustment outpatient medications at the point of discharge and providing appropriate outpatient clinical follow-up. Inpatients may be discharged to varied settings, including homes, assisted living or skilled nursing facilities. Diabetes-focused discharge planning should begin upon admission and continue throughout hospitalisation to prepare for a smooth transition from hospital to outpatient care. Preventing readmissions is an important strategy.

Medication adjustment at discharge

Prior to discharge, the decision for suitable anti-diabetic therapy (OAD and/ or insulin) would require consideration of the HbA1c on admission or within 3 months of admission as in the proposed discharge algorithm for medication adjustment (see Figure below)



Footnote
Adapted from Umpierrez et al Diabetes Care 2014 Nov 37 (11) 2934 - 2939
- Used in patients with 'straightforward' established Type 2 DM
- Use of pre-admission OADs only if not contra-indicated
- Patients with advanced comorbidities (CKD, liver disease, IHD, aged and frail, malignancies) are not suitable for this algorithm as they need individualised discharge medications depending on respective target HbA1c

Clear communication with outpatient health care providers (e.g.; primary care doctors, specialists) either via direct verbal/ written communication or via hospital discharge summaries facilitates safe transition to outpatient care. Information to include would be the cause of hyperglycaemia, related complications and comorbidities, recommended treatments and medication changes, pending tests and studies and follow-up needs.

Optimal Discharge Regimen / Checklist should include the following details

- A1c on admission
- Home medications
- Current medical problems
- Nutritional Status
- Renal Function
- New contraindications to oral medications
- Hypoglycaemia risk factors
- Goals of care and life expectancy
- Patient motivation and self-management abilities
- Family member support
- Outpatient follow-up appointments

The following areas of to be ascertained pre-discharge

- Identification of HCP who will provide follow-up diabetes care
- Level of understanding related to diabetes diagnosis. SMBG, home BG goals
- Definition, recognition, treatment and prevention of hyperglycaemia and hypoglycaemia
- Information on healthy food choices, referral to outpatient dietician, individualised meal plans (for patients discharged with tube feeding - ensure training is provided to caregivers and individualised regimen are prescribed)
- Ensure patients receive detailed discharge counselling especially on altered doses to ensure no errors are introduced on discharge
- For those discharge with insulin therapy to ensure they are educated on correct injection technique
- Physical activity, fall prevention (for elderly or with complications) and rehabilitation (e.g., post-MI, post surgical intervention)
- Sick day management
- For admission with foot ulcer - continuous wound management planning post-discharge is important
- All patients and their caregivers must be provided with contact details to access emergency support for diabetes care if required.

Recommendations

- All patients transitioning from acute care require a structured individualised discharge plan.

SECTION 13
MEDICAL PROFESSIONAL EDUCATION

All HCPs who care for patients with diabetes should receive ongoing diabetes management updates. This includes nurses, physician assistants, physicians, dietitians and pharmacists. It is important to address the following areas

- Assessment of staff diabetes knowledge and skill
- Enhancement of staff competencies
- Provision of education in a variety of settings, including staff orientation, clinical areas, and grand rounds
- Development of shared curriculum within members of the team
- Utilisation of a variety of learning tools, such as case studies, self-learning modules, journal clubs, survival skills toolkits to accommodate all settings and learners' needs and preferences.

Topics for updates should include

- Types of diabetes
- Early recognition and screening for hyperglycaemia
- Rationale for inpatient glycaemic control
- Glycaemic targets
- Nutrition therapy
- Insulin therapy
- Bedside blood glucose monitoring data
- OAD in the hospital
- Acute complications, diabetic ketoacidosis, hyperosmolar, hyperglycaemic non-ketotic syndrome
- Perioperative care, hypoglycaemia prevention and treatment
- Insulin pumps
- Documentation, including type of diabetes and complications

Recommendations

- All health care professionals who care for patients with diabetes should receive ongoing diabetes management updates.

APPENDICES

APPENDIX 1

Preparation for Variable Rate Insulin Infusion (VRIII)

Steps to set up VRIII:

- Insulin is drawn up using insulin syringe
- 50 units of human rapid acting insulin is drawn up an added to 49.5 ml of sodium chloride in a 50 ml syringe and mixed thoroughly (1 unit insulin = 1 ml)
- Label the syringe with content and time it is prepared
- Priming is done
- Syringe is set up in the infusion pump set.
- Insulin rate is commenced as per VRIII scale
- CBG is checked hourly
- Serum potassium to be checked 6-8 hourly to prevent hypokalaemia
- Intravenous fluid infusion as prescribed

APPENDIX 2

Variable Rate Insulin Infusion (VRIII) Dosing Protocol

	VRIII (units/ hr)			
Blood glucose (mmol/ l)	**Reduced rate**	**Standard rate**	**Increased rate**	**Customised scale**
<4 **	0	0	0	
4.0-6.9	0.5	1.0	2.0	
7.0-9.9	1.0	2.0	3.0	
10.0-12.9	1.5	3.0	4.0	
13.0-15.9	2.0	4.0	6.0	
16.0-18.9	3.0	5.0	7.0	
>19	4.0	6.0	8.0	

Steps to set up VRIII:

- The standard rate is recommended for most patients
- The reduced rate is recommended for patients who are more sensitive to insulin for example patients with type 1 diabetes
- The increased rate is recommended for patients who are insulin resistant,for example obese patients or those with daily requirement of insulin > 100 units per day
- ** in event of BG < 4.0 mmol/L, stop the insulin infusion, treat the hypoglycaemia and recheck the BG after 15 minutes. Once BG > 4.0 mmol/L, restart VRIII

APPENDIX 3

Peri-operative adjustment of insulin dose

Adapted from Joint British Diabetes Societies (JBDS) Management of adults with diabetes undergoing surgery and elective procedures: Improving standards Revised September 2015.[8]

Guideline for peri-operative adjustment of insulin dose

<table>
<tr><th rowspan="2">Insulins</th><th rowspan="2">Day prior to surgery</th><th colspan="3">Day of surgery/ whilst on VRIII</th></tr>
<tr><th>AM surgery</th><th>PM surgery</th><th>If VRIII is being used</th></tr>
<tr><td>Once Daily Basal (evening)
Lantus, Toujeo, Levemir, Tresiba, Insulatard, Humulin, Insuman basal</td><td>Reduce dose by 20%</td><td>No dose adjustment needed</td><td>No dose adjustment needed</td><td>Continue at 80% of the usual dose</td></tr>
<tr><td>Once Daily Basal (morning)
Lantus, Toujeo, Levemir, Tresiba, Insulatard, Humulin, Insuman basal</td><td colspan="2">Reduce dose by 20%</td><td></td><td>Continue at 80% of the usual dose</td></tr>
<tr><td>Twice Daily
Insuman Combo 25, 50, Mixtard 30, Humulin M3, Humolog Mix 25, 50, Novomix 30 Levemir BD, Lantus BD, Toujeo BD</td><td>No dose change</td><td colspan="2">Halve the usual morning dose
For evening dose:
• If able to resume meal normally
- leave the evening meal dose unchanged.
• If unable to resume meal normally; monitor BG.</td><td>Omit till able to resume meal normally</td></tr>
</table>

<table>
<tr><td rowspan="2">3, 4, 5 injections Daily
(Premixed Insulin 3 times a day, Basal bolus regimen; 3 short/rapid acting insulin with BD or Daily basal insulin)</td><td rowspan="2"></td><td>Premixed: halve morning dose and omit lunch time dose
Basal bolus: Halve morning dose and omit lunchtime dose.
Keep basal at 80% dose for those taking basal insulin in the morning.</td><td>Take usual morning insulin dose and omit lunch time dose.

Keep basal at 80% dose for those taking basal insulin in the morning.</td><td rowspan="2">Premixed and Short acting: Omit till able to resume meal normally
Basal insulin: Continue at 80% of the usual dose</td></tr>
<tr><td colspan="2">For evening dose:
• If able to resume meal normally
- leave the evening meal dose unchanged.

• If unable to resume meal normally; monitor BG.</td></tr>
</table>

APPENDIX 4

Peri-operative adjustment of oral antidiabetics (OAD)

Adapted from JBDS Management of adults with diabetes undergoing surgery and elective procedures: Improving Standards Revised September 2015[8]
Guideline for peri-operative adjustment of OAD

Medication	Day prior to admission	Day of surgery/ whilst on VRIII		
		AM surgery	PM surgery	If VRIII is being used
Acarbose	Take as normal	Omit morning dose	Take morning dose if eating. Omit lunch time dose	Omit once VRIII commenced, do not commence until eating and drinking normally
Meglitinides (Repaglinide, Nateglinide)		Omit morning dose	Take morning dose if eating. Omit lunch time dose	
Metformin (if GFR > 60 ml/min/1.73m^3 and procedure not requiring use of contrast media		If taken once or twice a day - take as normal If taken thrice a day - omit lunch time dose	If taken once or twice a day - take as normal If taken thrice a day - omit lunch time dose	
Sulphonylurea (Glibenclamide, Gliclazide, Glimeperide, Glipizide)		If taken once daily in the morning - omit the dose that day. If taken twice daily - omit the morning dose that day	If taken once daily in the morning - omit the dose that day. If taken twice daily - omit the morning dose that day	
Pioglitazone		Take as normal	Take as normal	
DPPIV Inhibitor (Sitagliptin, Vildagliptin, Linagliptin, Saxagliptin, Alogliptin)		Take as normal	Take as normal	

GLP-1 Analogue (Exenatide, Liraglutide, Lixisenatide, Dulaglutide)		Take as normal	Take as normal	Take as normal
SGLT 2 Inhibitor (Dapagliflozin, Canagliflozin, Empagliflozin)	Omit on the day before surgery*[9]	Omit on the day of surgery	Omit on the day of surgery	Omit on the day of surgery

* Due to risk of diabetic ketoacidosis (DKA) with sodium glucose-cotransporter 2 (SGLT-2) inhibitor the American College of Endocrinology (ACE) recommend stopping the drug in patients undergoing emergency surgery and holding the medication 24 hours before an elective surgery or invasive procedure.

APPENDIX 5

Hyperglycaemic emergencies inpatient monitoring chart

DKA / HHS MONITORING SHEET

DIAGNOSIS:

DIAGNOSIS:	MRN:	Date of Dx:	Time:	BW:
RBS:	pH/ HCO_3	Blood Ketone:	Anion Gap:	Se osm:
Old medication:				

Date/Time										
RBS:										
BG hourly										
Serum Osmolality (HHS)										
Serum Ketone (DKA)										
Next check										
K*										
Next check										
pH										
HC0[3]										
Next check										
Insulin (units/hr)										
IVD Resus (ml)										
IVD Maintenance										
Saline (ml)										
Dextrose (ml)										
K* in IVD Maintenance										
Hrly fluid input (ml)										
Hrly urine output (ml)										

APPENDIX 6

Continuous subcutaneous insulin infusion (CSII) pump log

Time	Blood glucose (mmol/L)	Carbohydrate (grams)	Meal bolus (unit)	Correctional bolus (unit)	Basal rate (unit/hour)
8am					
9am					
10am					
11am					

APPENDIX 7

Rotating fluid protocol (edited)

Maternal plasma glucose	Intravenous Insulin (unit/ hour)	Intravenous solution
< 4 mmol/L	Hold	Dextrose saline at 125ml/ hour
4-7 mmol/L	Hold	Normal saline at 125ml/ hour
> 7 mmol/L	Insulin infusion	Dextrose saline at 125ml/ hour

Edited from: Rosenberg VA, Eglinton GS, Rauch ER, Skupski DW. Intrapartum maternal glycemic control in women with insulin requiring diabetes: a randomized clinical trial of rotating fluids versus insulin drip. Am J ObstetGynecol 2006; 195: 1095.

APPENDIX 8

Blood Glucose Monitoring and insulin Prescription Chart

Name: MRN: IC:

BLOOD GLUCOSE MONITORING AND INSULIN PRESCRIPTION CHART

BG Monitoring																
Date																
Diet	☐ Normal ☐ NBM ☐ Fluids ☐ NG feed ☐ TPN								☐ Normal ☐ NBM ☐ Fluids ☐ NG feed ☐ TPN							
Meds	☐ OAD ☐ Steroids								☐ OAD ☐ Steroids							
BG Freq	☐ BD ☐ QID ☐ 7-point								☐ BD ☐ QID ☐ 7-point							
	0000 -1300				*1300 -2359*				0000 -1300				*1300 -2359*			
TIME																
20+ (Call Doctor)																
14.1 - 20.0																
10.1 - 14.0																
8.1 - 10.0																
4.0 - 8.0																
< 4 (Fill HYPO Chart)																
Ketone																
Insulin Administration																
Time given																
Signature																

Regular Insulin Orders

Date	Insulin	6am	Bfast	Lunch	Dinner	6pm	Bed	Top up	Name + Signature
								Y / N	
								Y / N	
								Y / N	
								Y / N	

Stat Insulin Orders

Date	Insulin	Units	Time	Name + Signature

TOPUP SCALE

Pre-mean insulin	
Top up Amount	
	6
	4
	2
	0
Changed by: Date:	

To change topup scale, cross off default values, write new values in the empty boxes and sign in changed box.

APPENDIX 9

Hypoglycaemia Action Sheet

HYPOGLYCAEMIA ACTION SHEET **CBG/RBS: _____ Time/Date:_____**

Patient's Name:		**Hypoglycaemia first noted by:** Name of SN/Doctor
IC:	**Ward/Bed:**	**Attended by Doctor:** Name of Doctor
Diagnosis:		**Time seen by Doctor:**
Current medications:		**Ward Consultant in-charge:**

GIVE 15g QUICK-ACTING CARBOHYDRATE

- ☐ *If patient is alert, can swallow or on NG feeding* – Give 1tbsp sugar dissolved in water or 150-200 mls non-diet soft drink
- ☐ *If patient is unconscious, unable to take orally, or no NG tube* - Give 30mls Dextrose 50% over 10 mins through a large bore cannula or 150mls Dextose 10%

RECHECK CBG IN 15 MINS: _____

REPEAT TREATMENT WITH 15G QUICK-ACTING CARBOHYDRATE AND RECHECK CBG EVERY 15 MINS TILL CBG > 4.0 MMOL/l

*If BG persistently < 4 mmol/L after 2 cycles to consider starting Dextrose infusion:

Dextrose _____% at _____ml/hour, started at _____

ONCE CBG > 4.0 MMOL/l

- ☒ **GIVE 20g SLOW-ACTING CARBOHYDRATE**
  - ☐ **Oral**_____
  - ☐ **NG feeding**_____
- ☒ **MONITOR: CBG HOURLY, to inform doctor if recurrent hypoglycaemia (BG < 4.0 mmol/L)**
- ☒ **IDENTIFY CAUSE OF HYPOGLYCAEMIA (please tick √)**
  - ☐ **NBM or missed meal**
  - ☐ **Suspected hypocortisolism** (take random cortisol stat and start hydrocortisone)
  - ☐ **Overtreatment**
  - ☐ **Insulin infusion without dextrose drip**
  - ☐ **Others, please specify** _____
- ☒ **REVIEW MEDICATIONS**
  - ☐ **Stop**_____
  - ☐ **Reduce or change to**_____
  - ☐ **Adjust VRIII**_____
- ☒ **REVIEW DEXTROSE INFUSION IF STARTED**
  - ☐ **Dextrose infusion**_____
- ☒ **REINFORCE HYPOGLYCAEMIA EDUCATION**

Review and plan by,
Signature of attending doctor

_____
Name and Stamp:
Time and Date:

*CBG=capillary blood glucose, OAD=oral antidiabetic agent

APPENDIX 10

Hypoglycaemia Risk Stratification Tool (For T2DM)

Tool inputs
- How many times has the patient ever had hypoglycaemia-related utilisation in an ED (primary diagnosis of hypoglycaemia) or hospital (principal diagnosis of hypoglycaemia) (0, 1-2, ≥3 times)?
- How many times has the patient gone to an ED for any reason in the past 12 month (<2, ≥2 times)?
- Does the patient use insulin (yes/no)?
- Does the patient use sulphonylureas (yes/no)?
- Does the patient have severe or end-stage renal disease (CKD stage 4 or 5) (yes/no)?
- Is the patient <77 year old (yes/no)?

☐	3 Prior hypoglycaemia-related ED or hospital utilisation	High risk (>5%)
☐	3 Prior hypoglycaemia-related ED or hospital utilisation AND Insulin user	

☐	No Prior hypoglycaemia-related ED or hospital utilisation AND No insulin AND No sulphonylurea use	Low risk (>1%)
☐	No Prior hypoglycaemia-related ED or hospital utilisation AND No insulin AND No sulphonylurea AND Age <77 years AND Does not have severe or end-stage renal disease	
☐	No Prior hypoglycaemia-related ED or hospital utilisation AND No insulin AND Age <77 years AND <2 ED visits in prior year	

☐	All other risk factor combinations	Intermediate risk (1%-5%)

GLOSSARY OF TERMS

AMI	Acute Myocardial Infarction
BG	Blood Glucose
CAP	Community-Acquired Pneumonia
CBG	Capillary Blood Glucose
CGM	Continuous Glucose Monitoring
CKD	Chronic Kidney Disease
COPD	Chronic Obstructive Pulmonary Disease
CSII	Continuous Subcutaneous Insulin Infusion
DKA	Diabetic Ketoacidosis
DM	Diabetes Mellitus
DPPIV	Dipeptidyl Peptidase IV
eGFR	Estimated Glomerular Filtration Rate
EN	Enteral Nutrition
ESRD	End Stage Renal Disease
FIGO	International Federation of Gynecology and Obstetrics
GCS	Glasgow Coma Scale
GDM	Gestational Diabetes
GV	Glycaemic Variability
HbA1c	Haemoglobin A1c
HCP	Health Care Professional
HDU	High Dependency Unit
HHS	Hyperosmolar Hyperglycaemic State
ICU	Intensive Care Unit
IV	Intravenous
LMWH	Low Molecular Weight Heparin
MAGE	Mean Amplitude of Glycaemic Excursions
MI	Myocardial Infarction
MNT	Medical Nutrition Therapy
NBM	Nil by Mouth
NHMS	National Health and Morbidity Survey
NICE	National Institute for Health and Care Excellence

NPH	Intermediate Acting Insulin
NPO	Nil per Oral
PCOS	Polycystic Ovary Syndrome
PN	Parenteral Nutrition
POC	Point-of-Care
POCT	Point-of-Care Testing
OAD	Oral Anti-Diabetic
QID	Quarter in Die, four times day
SAI	Short-Acting Insulin
SC	Subcutaneous
SGLT2	Sodium Glucose Transporter-2
SSIR	Scheduled Subcutaneous Insulin Regimen
T2DM	Type 2 Diabetes Mellitus
TDD	Total Daily Dose
TDS	Ter Die Sumendum, three times a day
TPN	Total Parenteral Nutrition
VRIII	Variable Rate Intravenous Insulin Infusion

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