Academic Department of Critical Care
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Portsmouth Hospitals NHS
NHS Trust

Insulin Infusion (Variable Rate) in Critical Care

Aim To provide guidance on administration of variable rate insulin infusion on adult patients on DCCQ

Scope This applies to all adult patients on DCCQ receiving variable rate intravenous insulin infusion. It does not apply to patients requiring fixed rate insulin infusion i.e. patients suffering from diabetic emergencies such as DKA and HHS.

Goals of variable rate intravenous insulin infusion

1. Treat and control hyperglycaemia in critical care patients not normally on insulin
2. To maintain euglycaemia in insulin dependent diabetics who are unable to maintain enteral carbohydrate intake and/or unable or unsuitable for their regular subcutaneous insulin.
3. To avoid harmful hypoglycaemia.

Consideration to start variable rate IV insulin

Non-diabetic patients/ diabetic patients not normally dependent on insulin

Confirm at least two consecutive BM readings >10mmol/L.

Commence non-diabetic IV insulin protocol at a rate determined by blood glucose-see insulin chart in Appendix B

Insulin dependent diabetics

Commence insulin dependent diabetic protocol at a rate determined by blood glucose-see insulin chart in Appendix B

Consideration should be given outside of critical illness or as critical illness resolves to restart long-acting insulin alongside variable rate IV insulin infusion

Prescription:
Insulin should be prescribed as a continuous infusion on CIS and also on the department's IV insulin bedside paper prescription. Patient details should be completed on the paper chart, the target blood glucose range specified, the chosen regimen circled and signed by the prescribing clinician along with their printed name and date of prescription. Nurses should adjust rate against BMs according to this paper chart.

Administration:
Administer via syringe pump using 50 units in 50ml syringe of insulin alongside a glucose containing infusion (including enteral tube feeding providing patient is absorbing). Use pre-filled pharmacy syringes.

Monitoring:
Check BMs hourly for 2 hours then 2-hourly for four hours if acceptable. Once stable and in target range go to 4-hourly monitoring. If BMs consistently out of range (>70% readings) consider protocol individualisation

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1. INTRODUCTION

Elevated blood glucose in critically ill patients is a common clinical finding and is associated with increased mortality and poorer outcomes. The aetiology of hyperglycaemia in critical illness is multi-factorial and occurs in both diabetic and non-diabetic patients. Endogenous cytokines and hormones such as cortisol and adrenaline reduce insulin production and increase insulin resistance, promoting glycogenolysis and gluconeogenesis whilst impairing peripheral utilization. Many of the critical care therapies such as exogenous steroids and catecholamines further exacerbate the situation. However the results of the NICE-SUGAR study in 2009 indicate that overly aggressive glucose control with intravenous insulin results in worse outcomes than moderate control due to increased tendency to develop hypoglycaemia. Thus critical care practitioners must walk a fine line between avoiding harmful hyper and hypoglycaemia.

2. PURPOSE

The purpose of this guideline is to inform the safe use of intravenous insulin for the control of blood sugars in critically ill patients. It guides the use of IV insulin infusions (sometimes referred to as sliding-scale insulin) in diabetic and non-diabetic patients for the purposes of maintaining moderate euglycaemia.

3. SCOPE

The guideline covers all adult patients on DCCQ who require variable rate intravenous insulin infusion (VRIII). The management of diabetic emergencies (DKA, HHS) with fixed rate insulin is beyond the scope of this guideline.

4. DEFINITIONS

BM: Boehringer Mannheim test: A blood glucose measurement performed on a glucose meter
IDDM: Insulin dependent diabetes mellitus
NIDDM: Non-insulin dependent diabetes mellitus
DKA: Diabetic Ketoacidosis
HHS: Hyperosmolar hyperglycaemic state
HONK: Hyperosmolar non-ketosis-old fashioned term for HHS
VRIII: Variable rate intravenous insulin infusion
GLP-1 analogues: Glucagon-like peptide-1 analogues. Anti-diabetic medicines which are subcutaneously injected but are NOT insulin. Examples include Exenatide (Byetta© & Bydureon©) and Liraglutide (Victoza©). Do not confuse with regular insulin.

5. DUTIES AND RESPONSIBILITIES

- The decision to implement this guideline is at the discretion of the on-call critical care consultant.
- Implementation of this guideline is the joint responsibility of appropriate critical care medical/ nursing staff.
- This guideline is subject to professional judgment and accountability.

6. PROCESS

Action	Rationale
Inclusion Criteria • All adult patients admitted to intensive care requiring variable rate intravenous insulin infusion	The protocol used in this guideline is based on the NICE-SUGAR study which included type 1, type 2 and non-diabetic patients with hyperglycaemia admitted to intensive care.
Exclusion Criteria *DKA/HHS *Paediatric patients	*The management of DKA and HHS/HONK requires fixed rate intravenous insulin infusion with potentially large volumes of fluid delivered and close attention to the rate of decline in serum glucose. This is normally dictated and modified on case-by-case basis by the duty consultant and is outside the scope of this guideline. *The NICE-SUGAR protocol was not validated in children whose insulin sensitivity and fluid requirements are significantly different to that of an adult. The use of variable rate IV insulin in paediatric patients on DCCQ is to be guided by the expertise of the duty consultant.
In DCCQ Guidance *Patients should be stratified onto the correct protocol depending on whether they are insulin dependent diabetics or non-insulin dependent: -Insulin dependent: Type 1 diabetics or type 2 diabetics established on subcutaneous insulin therapy at home -Non-insulin dependent: Type 2 diabetics on tablets (or injectable GLP-1 analogues) or those with hyperglycaemia but not diabetic.	.Patients with type 2 diabetes and non-diabetic patients experiencing hyperglycaemia will still retain some residual insulin producing pancreatic function. Type 1 diabetics have no endogenous insulin secretion and so require a basal level of insulin even within range to inhibit ketogenesis. Therefore it is necessary to have a protocol for each patient group.
*Prescribing clinician to complete paper insulin prescription at the bed-space with patient details filled in. Select, by circling, which regimen the nurse is to follow. Sign, print name and date underneath the prescription.	Due to the limitations of CIS in guiding the nurse as to insulin dosage and the high risk nature of the infusion it is mandatory that all VRII prescriptions have a paper chart as well as a CIS prescription
*Prescribe on CIS intravenous insulin infusion. For VRII this is the option titled: -"Insulin soluble (human) pre-filled syringe" Ensure that the pre-set is properly selected so all details of the preparation including volume and concentration are carried across.	The infusion should be prescribed on CIS so that the rate of insulin can be tracked on the system against blood results and the volume can be included in the patient's total fluid intake.
*Continue patient's regular long-acting insulins particularly in type 1 diabetics once the patient is in the convalescent phase of their illness or time on IV insulin	Hyperglycaemia and DKA have been reported in type 1 diabetics who have variable rate IV insulin discontinued without long-acting agent already on board. IV insulin has a very short half life and effects

infusion is likely to be short.	will dissipate in a matter of minutes once the infusion is stopped. Physiologically a healthy pancreas produces a continuous background level of insulin to suppress ketogenesis. Type 1 diabetics will not produce sufficient background insulin on cessation of the infusion and are at risk of DKA. Keeping the long-acting insulin on board from beginning the VRIII ensures smooth and safe continuity of care when the infusion is taken down.
*Ensure a source of glucose is prescribed and is run at all times alongside the insulin infusion. Acceptable sources of glucose include: • Glucose 4%/NaCl 0.18% ± potassium • Glucose 10%, 20%, 30% ± potassium • Nasogastric/nasojejunal feed (at full feed • Total parenteral nutrition (TPN)	Incidents have occurred where patients have had IV insulin without a source of glucose and have developed severe hypoglycaemia. Always run a source of glucose to oppose the insulin and prevent this. The National Diabetes Association Guidelines state that critical care units are permitted to use a wider range of glucose sources than are permitted for lower dependency wards including enteral feeds which are not acceptable in ward patients.
*The bed-space nurse should run the insulin infusion at a rate determined by the blood sugars.	The protocols used were validated in the NICE-SUGAR trial in critically ill patients as a means of attaining adequate control of BMs.
*Blood sugars should be monitored either via BM monitoring or derived from arterial blood gas analysis. Monitoring should be hourly initially for two hours, reducing to two-hourly for four hours and then four-hourly if BMs remain in target range. Increase frequency of monitoring if BMs move persistently out of range (>2 readings of >10mmol/L despite adjustment of the rate) Target a range of 4.6-10mmol/L unless specified otherwise by the duty consultant.	The frequency of monitoring is as per the NICE-SUGAR protocol. Overly intensive blood glucose control was associated in the study with a higher mortality than tight glycaemic control. Excessive finger-prick testing is unpleasant for patients and excessive arterial blood sampling can contribute to anaemia. A range of 4.6-10mmol/L is sufficient in most patients to reduce the harmful effects of hyperglycaemia in critical illness without chasing a range that is too tight and producing hypoglycaemia.
*The clinician should review the prescription every 6 hours and adjust the prescription, individualizing the algorithm where necessary to attain > 70% blood glucose readings within target range.	Patients have variable insulin sensitivities and for some the standard algorithm may have too little or too much of an effect. For example obese patients, those in septic shock or those receiving corticosteroids may have up to 4x the requirement of those that are not whilst renal patients often have much lower insulin requirement Prescribers should therefore tailor the guideline rates to the patient's specific insulin sensitivity. For assistance in how to individualise sliding scale speak to the duty consultant, senior doctor or pharmacist for advice.
Ensure in the absence of hyperkalaemia that adequate potassium is included with infusion fluids in all patients on IV insulin. Closely monitor potassium and correct abnormalities as they occur	Insulin induces the movement of potassium ions into cells via action at the insulin receptor. Inadequate supplementation of potassium in the face of continuing insulin can precipitate hypokalaemia.

Discontinuing insulin infusion	
In non-insulin dependent patients the IV insulin can be discontinued from the CIS prescription when the patient has been on 0ml/hr of insulin for ….	Blood sugars remaining in normal range without IV insulin for a protracted period in such patients suggests the driver for their hyperglycaemia has resolved and the prescription is no longer required.
For type 1 diabetics the IV insulin infusion should be discontinued around a mealtime. Give the usual dose of their short-acting insulin prior to a meal (30 mins prior for short-acting, immediately prior for rapid acting e.g. Novorapid). 15 mins after they have finished their meal switch off IV insulin	A meal time is the safest time to discontinue IV insulin in type 1 diabetics as this allows a short-acting insulin to be given, in conjunction with food to mimic normal physiological profile of endogenous insulin.
Check BMs 1 hour after stopping insulin infusion in type 1 diabetics	This ensures there is not rebound hyperglycaemia upon cessation of IV insulin. Speak to the duty consultant for advice if this occurs.
Patients who have required sliding scale insulin due to TPN-induced hyperglycaemia can be transitioned to subcutaneous insulin by prescribing the total daily dose of IV insulin (once stable) as Insulatard/Humulin I. Give 50% of this calculated dose and stop the infusion 30 mins later. Give the other 50% 12 hours later	This is the most efficient regimen for controlling BMs in patients on continuous parenteral nutrition. Regimens containing short-acting insulins are ineffective since the IV administration of glucose is continuous whilst long acting insulins pose greater risk of hypoglycaemia and are difficult to titrate.
Patients normally on continuous subcutaneous insulin pumps at home should have input from the diabetes team prior to IV insulin being discontinued.	Such patients are a specialist population with the pump technology not being in the remit of expertise of DCCQ staff.
Starting subcutaneous insulin in previously naïve patients who are now insulin dependent	
The following guidance should ideally be applied in conjunction with guidance from the diabetes team	
Weight based calculation: Frail, elderly patients, those in severe hepatic failure, renal failure (CKD stage 4 or 5) newly diagnosed type 1 diabetes: **Total daily insulin dose (units/day)= 0.3 x weight (kg)** All other patients: **Total daily insulin dose (units/day) = 0.5 x weight (kg)**	There is an adjustment for patients who may have impaired handling of insulin such as hepatic failure where the sensitivity is greater increasing the risk of hypoglycaemia.
Using insulin requirements during VRIII: Assuming rate has been stable for last 6 hours: **Total insulin over 6hrs x 20 = total daily dose** **6**	The method calculates the average insulin requirement over 20 rather than 24 hours to prevent hypoglycaemia.
When dividing the total daily dose: -For basal bolus give 50% as the basal dose (evening) and 50% divided as short-acting insulins (breakfast, lunch dinner). -For twice daily pre-mixed insulin regimen (e.g. Humulin M3) give 60% with breakfast and 40% with the evening meal.	This is based on guidance from the Joint British Diabetes Society.

Transfer of patients to the ward from DCCQ on IV insulin infusion	
The discharging clinician should complete a pink IV insulin prescription suitable for non-DCCQ ward use. There are currently three prescriptions to choose from based on patient weight and/or total daily insulin dose. Select the regimen that most closely correlates with the IV insulin regimen the patient is currently taking. In patients on an individualised regimen transcribe this onto the new prescription	The DCCQ chart is not suitable for ward use as it is designed to be used in conjunction with CIS. It is vital the correct ward prescription be completed before the patient leaves the unit to enable nurses on the ward to continue to monitor and adjust IV insulin rate.
The glucose source the patient is having to oppose their insulin should be switched to match trust guidelines. Outside of DCCQ the approved fluids are: • 10% Glucose ± 20mmol KCl • 5% glucose/0.45% NaCl ± 20mmol KCl • 5% glucose ± 20mmol KCl Recommended rates of infusion can be found on the pink insulin prescription charts. These fluids should be prescribed on a ward fluid chart.	NG feed and maintenance fluids are not approved by trust guidelines or national guidelines to oppose IV insulin. This is because variation in calorific intake and fluid requirement can precipitate hypoglycaemia without adequate intensive monitoring which is not reliably guaranteed outside of DCCQ. TPN poses a therapeutic problem however. Wherever practicable the patient should be transitioned to subcutaneous insulatard/humulin I as per above guidance prior to transfer. Where this is not possible consider discussion with diabetes team prior to discharge.
Ensure the receiving ward are made aware in handover the patient is on an insulin IV infusion and have nursing capability to comply with monitoring	Nationally cases of fatalities have occurred where patients on IV insulin were not appropriately monitored due to a lack of awareness on wards of the infusion when patients were transferred.
Insulin syringes	
Pharmacy pre-filled syringes must be used for administering IV insulin infusions. Nurses should not prepare syringes themselves for this indication.	There is a trust-wide mandate to use pre-made insulin syringes for insulin infusions to avoid risks of incorrect administration and overdose. Insulin syringes are available on every ward in the trust and in the emergency cupboard. The circumstances where it is not possible to borrow from any other location, in preference to preparing on the ward, are no longer likely to be encountered in practice.

7. TRAINING REQUIREMENTS

Training on the use of variable rate insulin in critical care will be cascaded out to trainees and new staff in the usual manner of MDT meetings, doctors and nurses induction and senior nurse and medical staff teaching.

8. MONITORING COMPLIANCE WITH, AND THE EFFECTIVENESS OF, PROCEDURAL DOCUMENTS

Compliance to this guideline will be assessed by a cycle of regular audit as part of the core DCCQ audit program.

9. REFERENCES AND ASSOCIATED DOCUMENTATION

- George Institute. NICE SUGAR protocol (2009). Available via: http://studies.thegeorgeinstitute.org/nice/ Date last accessed 03/05/17
- Joint British Diabetes Societies for Inpatient care [JBDS-IP]. The use of variable rate intravenous insulin infusion (VRIII) in medical inpatients. (2014). Available via: www.diabetologists-abcd.org.uk/JBDS/JBDS_IP_VRIII.pdf Date last accessed 03/05/17
- NICE-SUGAR trial investigators. Intensive versus conventional glucose control in critically ill patients. *New England Journal of Medicine.* (2009). 360, 1283-1297
- PHT F&M group. Glucose, insulin and potassium Infusion Guideline (2013). Available via trust intranet

Appendix A: Examples of Insulins & insulin conversions

Long-acting insulins:

- Insulin Degludec (Tresiba©)-Ultra-long acting; half life approx. 25 hours- Available in standard strength (100 unit/ml) and concentrated (200 unit/ml) Flexpens and standard strength (100 unit/ml) cartridges

- Insulin Detemir (Levemir©)-Available as Flexpens, Innolets and cartridges all at standard strength (100 units/ml)

- Insulin Glargine (Lantus©, Abasaglar©, Toujeo©). Available as cartridges for Abasaglar and Lantus, Solostar for Lantus and Kwikpen for Abasaglar. Toujeo is a concentrated insulin (300 units/ml) cartridge.

Intermediate-acting insulins:

- Isophane Insulin (Humulin I ©, Insulatard©, Hypurin Bovine Isophane etc): Also known as isophane protamine insulin, NPH insulin. Available in numerous formulations and devices.

Mixed Insulins:

- Novomix 30© (Insulin Aspart and Insulin Aspart Isophane): 30% short-acting, 70% intermediate acting.
- Humalog Mix 25© and Humalog Mix 50© (Insulin Lispro and Insulin lispro protamine): Number refers to % short-acting component.
- Humulin M3© (Soluble human insulin and isophane insulin): 30% short-acting, 70% long-acting.

Short and Rapid acting insulins:

- Soluble human insulin (Actrapid©, Humulin S©, Insuman rapid©): The natural human insulin is available in a variety of brands and formulations and devices. It acts within 30 mins to an hour. Where giving as part of basal-bolus therapy it should be given 30 minutes prior to a meal.
- Humulin R: A formulation of human soluble insulin available as a hyper-concentrated strength (500 units/mL)
- Insulin Aspart (Novorapid©) →
- Insulin Lispro (Humalog©) →
- Insulin Glulisine (Apidra©) →

These three insulins are rapid acting, kicking in within a few minutes. They should therefore be given immediately before a meal.

Converting between insulin formulations:

In theory long acting insulins can be inter-converted at the same dose, brands of isophane insulin can be interconverted at the same dose and short/rapid acting insulins can be interconverted at the same dose. When moving between short and rapid acting insulins remember to alter the timing of administration. Mixed insulins can be converted to intermediate insulins by calculating the fraction of the dose than is intermediate acting using the above ratios. Concentrated insulin should NEVER be given on DCCQ as trust insulin syringes are calibrated to 100 unit/ml strength-give the same dose of concentrated insulin (in units) in a non-concentrated strength.

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Critical Care Unit IV Insulin Prescription Chart

Insulin syringes: Insulin for infusion should be administered using pre-filled syringes of 50 units in 50ml, prepared by the pharmacy department. The preparation of insulin syringes on the unit is no longer considered appropriate practice. A record of patient name and batch number should be made on the insulin record sheet in the pharmacy room.	**Patient name:** **Hospital Number:** **Date of birth:** **Ward: Critical Care E5-NOT TO BE USED ON ANY WARD OTHER THAN ITU**

Prescribing IV Insulin Infusion

1) Prescribe intravenous insulin infusion on the Critical Care CIS prescription chart under Insulin soluble (human) pre-filled syringe. A trained DCCQ nurse can then administer according to these directions.
   - Where patient's blood glucose readings remain out of range for >70% of readings prescription should be reviewed every 6 hours and an individualized prescription should be considered to achieve this –refer to trust IV insulin guideline for advice
   - Do NOT use this chart for the treatment of DKA or HHS-seek advice from the duty consultant.
2) Fluids: Prescribe fluids on CIS. Ensure patients always have a source of glucose to oppose IV insulin infusion-the exceptions to this may be DKA or HHS.

Target blood glucose range for patient:……							
Indicate (circle) which regime is to be used and delete other columns							
Non-diabetic patients/ non-insulin dependent diabetics		Insulin dependent diabetics		Individualized regimen		Individualized regimen	
Blood glucose (mmol/L)	Insulin infusion rate (units/hr)	Blood glucose (mmol/L)	Insulin infusion rate (units/hr)	Blood glucose (mmol/L)	Insulin infusion rate (units/hr)	Blood glucose (mmol/L)	Insulin infusion rate (units/hr)
<2.5	No insulin. Give glucose	<2.5	No insulin. Monitor BMs every 30 mins. Give glucose				
2.5-3.4		2.5-3.4					
3.5-4.5	No insulin	3.5-4.5	0.5 units/hr				
4.6-10.0	No insulin	4.6-10.0	1 unit/hr				
10.1-12.0	1 unit/hr	10.1-12.0	2 units/hr				
12.1-15.0	2 units/hr	12.1-15.0					
15.1-18.0	3 units/hr	15.1-18.0	3 units/hr				
18.1-22.0	4 units/hr	18.1-22.0	4 units/hr				
>22.1	6 units/hr	>22.1	6 units/hr				
Prescribed by signature							
Name Date							

3) Monitoring: Monitor blood sugars hourly for first two hours, then 2 hourly for four hours then move to 4 hourly monitoring thereafter assuming sugars remain stable.
4) Restarting long-acting insulins: For insulin dependent diabetics consider restarting long-acting insulins (Lantus, Levemir, Degludec) when the patient enters the convalescent stage of their illness.
5) Discontinuing IV insulin: See main guideline for more information

Further to the DCCQ guideline additional information can be found in the trust's Glucose, Insulin and Potassium (GIK) drug therapy guideline.