

Concise advice on Inpatient Diabetes (COVID:Diabetes):

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DEXAMETHASONE THERAPY IN COVID-19 PATIENTS: IMPLICATIONS AND GUIDANCE FOR THE MANAGEMENT OF BLOOD GLUCOSE IN PEOPLE WITH AND WITHOUT DIABETES

NATIONAL INPATIENT DIABETES COVID-19 RESPONSE GROUP*

- i** This guidance is for use in **ALL** patients with COVID-19 who are treated with dexamethasone in a ward setting
It is **NOT** intended for Critical Care Units but may be adapted for this use
It differs from the previous COVID: Diabetes GUIDANCE FOR MANAGING INPATIENT HYPERGLYCAEMIA as it targets the greater insulin resistance in dexamethasone treated patients and should **ONLY** be used in this context

✓ Key Facts

- > Dexamethasone reduces mortality in people with COVID-19 who require ventilation or oxygen therapy
- > Corticosteroid therapy impairs glucose metabolism and is the commonest cause of life threatening inpatient Hyperglycaemic Hyperosmolar Syndrome (HHS)
- > COVID-19 increases insulin resistance and impairs insulin production from the pancreatic beta cells; this can precipitate hyperglycaemia and life threatening Diabetic Ketoacidosis (DKA) in people with diabetes and even in people not known to have diabetes
- > Glucose levels above 10.0 mmol/L have been linked to increased mortality in people with COVID-19
- > The recommended dexamethasone dose of 6mg/day (oral or IV) for 10 days, equivalent to 40mg of prednisolone/day, will undoubtedly affect glucose metabolism
- > Thus, the **triple whammy** of dexamethasone induced impaired glucose metabolism, COVID-19 induced insulin resistance and COVID-19 related impaired insulin production could result in significant hyperglycaemia, HHS and DKA in people with and without diabetes, increasing both morbidity and mortality
- > Sulphonylureas are **NOT** recommended in this context as beta cell function may be impaired and insulin resistance is likely to be severe. For this reason, these recommendations differ from those in the JBDS guideline on the Management of Hyperglycaemia and Steroid (Glucocorticoid) Therapy

AIMS

- i** To ensure **ALL** patients on dexamethasone receive appropriate glucose surveillance and appropriate management of hyperglycaemia

GLUCOSE MONITORING

Target glucose 6.0 -10.0 mmol/L (up to 12.0 mmol/L is acceptable)

Frequency of monitoring

> People not known to have diabetes

Check the glucose at least 6 hourly ideally at fasting periods (e.g. before meals and at bedtime). If after 48 hours all fasting glucose results are <10.0 mmol/L reduce frequency to once daily at 17.00-18.00 hrs. Continue until dexamethasone is stopped

If any fasting glucose is above 10.0 mmol/L continue 6 hourly monitoring and follow the guidance below to correct hyperglycaemia i.e. glucose above 12.0 mmol/L

> People with diabetes

Throughout the admission, check fasting glucose at least 6 hourly, or more frequently if the glucose is outside the 6.0 -10.0 mmol/L range



MANAGING DEXAMETHASONE RELATED HYPERGLYCAEMIA

First, exclude Diabetic Ketoacidosis and Hyperglycaemia Hyperosmolar Syndrome by checking blood glucose, ketones, venous pH, bicarbonate and U&Es and if DKA/HHS diagnosed follow specific guidelines for their management

⚠ If DKA/HHS have been excluded, follow the guidance below but note, this advice is conservative. If after initial treatment hyperglycaemia persists, do not hesitate to escalate to the next treatment step and involve the diabetes team as early as possible

ADVICE FOR CORRECTING INITIAL HYPERGLYCAEMIA – GLUCOSE ABOVE 12.0 MMOL/L

Use **subcutaneous** rapid acting insulin analogue (Novorapid®/Humalog®/Apidra®) as described below. Note these are conservative doses and depending on response in individual patients, as previously stated, may need to be increased rapidly (or where more insulin sensitive, decreased)

Recheck glucose at 4 hrs to determine response and whether a further correction dose is needed

> Insulin naïve

Follow the weight-based tables below in those people:

- » not known to have diabetes
- » with type 2 diabetes treated with diet alone or with oral hypoglycaemic agents

> Insulin treated

Where the total daily dose (TDD) of insulin is known follow the guidance in the table based on TDD. If the TDD is unknown, follow guidance according to the person's weight

CORRECTION DOSES OF RAPID ACTING INSULIN

GLUCOSE (MMOL/L)	• TDD = <50 UNITS PER DAY • OR WEIGHT < 50 KG	• TDD = 50 -100 UNITS PER DAY • OR WEIGHT 50 -100 KG	• TDD = >100 UNITS PER DAY • OR WEIGHT >100 KG	←
12.0-14.9	2 units	2 units	4 units	• Please check KETONES if glucose >12.0mmol/L ⚠ If KETONE >1.5mmol/L, for doctor review ⚠ If KETONE >3.0mmol/L Exclude DKA-Venous pH, bicarbonate, lab glucose, U&E. Refer to diabetes team
15.0-16.9	2 units	3 units	5 units	
17.0-18.9	3 units	4 units	5 units	
19.0-20.9	3 units	5 units	6 units	
21.0-22.9	4 units	6 units	7 units	
23.0-24.9	4 units	7 units	8 units	
25.0-27.0	5 units	8 units	9 units	
Over 27	6 units	9 units	10 units	

MAINTAINING GLYCAEMIC CONTROL

> People NOT on an intermediate acting (NPH) or long acting insulin:

Where glucose has risen above 12.0 mmol/L due to dexamethasone treatment, start NPH insulin which has an intermediate duration of action (e.g. Humulin I®, Insulatard®) – total dose 0.3 units/kg/day. Give 2/3 of the total daily dose in the morning (07.00 – 08.00) and the remaining 1/3 in the early evening (17.00-18.00). e.g. 0.3 x 80kg = 24 units/d i.e. 16 units a.m. and 8 units p.m.). NOTE- there should be a low threshold for dose escalation (see table below) and referral to the diabetes team

NPH insulin twice daily is recommended as this gives more flexibility with dose adjustment. However, the metabolic effects of dexamethasone can persist for up to 36 hours, thus a longer acting basal analogue insulin may also be considered. See tables below for dose adjustment of long acting insulin and twice daily intermediate and long acting insulins

⚠ ALERT NOTE – if:

- > Older (>70 yrs) or frail
- > Serum creatinine >175 umol/L (eGFR <30 ml/min)

Use a reduced NPH insulin dose of 0.15 units/kg (e.g. 0.15 x 80kg = 12 units i.e. 8 units a.m. and 4 units p.m.) NOTE- there should be a low threshold for dose escalation and referral to the diabetes team

> People already using once or twice daily long-acting insulin or twice daily NPH including those on basal-bolus regimens

Increase the long acting basal or NPH insulin by 20% but this may need rapid escalation by as much as 40% depending on response. Titrate the dose using the tables below. Patients on basal-bolus regimens may not require 'mealtime' insulin boluses if not eating, however, if hyperglycaemia persists during adjustment of basal insulin then use corrective rapid acting insulin doses according to total daily insulin dose (TDD) or weight given in the table for correction doses of rapid acting insulin



› **People on twice-daily pre-mix insulin**

e.g. NovoMix 30®/Humulin M3®/Humalog Mix 25®/Humalog Mix 50®

Continue mixed insulin and adjust dose (follow dose adjustment for long-acting insulin table below). Consider increasing the morning dose by 20% but this may need rapid escalation by as much as 40% each day depending on the response. There should be a low threshold for referral to the diabetes team

DOSE ADJUSTMENT FOR LONG-ACTING INSULIN

Doses can be titrated daily, although longer-acting insulins may take 48-72 hours to reach steady state. Dose adjustments will affect blood glucose throughout the day

ONCE daily long-acting insulin

GLUCOSE LEVEL JUST BEFORE INSULIN DOSE	
<4mmol/L	Reduce insulin by 20%
4.1-6mmol/L	Reduce insulin by 10%
6.1-12mmol/L	No change
12.1-18mmol/L	Increase insulin by 10%
>18mmol/L	Increase insulin by 20%

TWICE daily NPH or long-acting insulin

GLUCOSE LEVEL	JUST BEFORE MORNING INSULIN DOSE	JUST BEFORE EVENING INSULIN DOSE
<4mmol/L	Reduce evening insulin by 20%	Reduce morning insulin by 20%
4.1-6mmol/L	Reduce evening insulin by 10%	Reduce morning insulin by 10%
6.1-12mmol/L	No change	No change
12.1-18mmol/L	Increase evening insulin 10%	Increase morning insulin by 10%
>18mmol/L	Increase evening insulin by 20%	Increase morning insulin by 20%

› **People using a personal insulin infusion pump**

If the person is too unwell to manage their pump, transfer to a Variable Rate Intravenous Insulin Infusion (VRIII) with a basal insulin given alongside – seek the advice of the diabetes team. If the pump is removed, give the pump to a relative for safekeeping or label with the patients details and safely store

Those people well enough to manage their subcutaneous insulin infusion pump should be recommended to initially increase the basal rates by 20% and be made aware that this may need to be increased further on a daily basis. Refer all people using a personal insulin pump to the diabetes team

END OF DEXAMETHASONE THERAPY- DAY 10

Insulin resistance will begin to fall when the dexamethasone has been stopped but may take a number of days. Continue to monitor glucose 6 hourly and down titrate using the guidance table above

DISCHARGE AND FOLLOW-UP

› **Diabetes precipitated by COVID-19 infection and dexamethasone treatment**

Normoglycaemia may be established after stopping dexamethasone without the need for ongoing diabetes therapy. However, up to a third of people may later develop diabetes therefore alert the GP that the patient will need a yearly HbA1c measurement

› **People with known diabetes**

These patients will require close support following discharge. The discharge guidelines and patient information leaflet produced by this group are available to facilitate this. The leaflet can be accessed here: <https://www.diabetes.org.uk/professionals/resources/shared-practice/inpatient-and-hospital-care#patients>

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