Norfolk and Norwich University Hospitals NHS
NHS Foundation Trust

Diabetes and Steroids – Where are we at the Moment?

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Before I Start – Something on DKA

Coming to an email inbox near you soon

Joint British Diabetes Societies Inpatient Care Group

Data collection tool for the Management of Diabetic Ketoacidosis (DKA) in Adults

(Admission to Discharge)

Patient Code:		Age:..... (years)	Gender: ☐ Male ☐ Female

1. Ethnicity ☐ Not stated

White	Mixed	Asian / British Asian	Black / Black British	Other
☐ a) British ☐ b) Irish ☐ c) Any other white background	☐ d) White /Black Caribbean ☐ e) White / Black African ☐ f) White and Asian ☐ g) Any other mixed background	☐ h) Indian ☐ i) Pakistani ☐ j) Bangladeshi ☐ k) Any other Asian	☐ l) Caribbean ☐ m) African ☐ n) Any other Black background	☐ o) Chinese ☐ p) Any other ethnic group

2. Date / time of Admission: .....dd/mm/yy ..... hh:mm

3. Date / time of Discharge: .....dd/mm/yy .....hh:mm

4. Date of death .....dd/mm/yy **5.** Cause of death:

.....

Diagnosis (Where appropriate put a √=yes , X = No N/A= not applicable, NR = not recorded)

6) Was the diagnosis confirmed according to diagnostic criteria? ☐ Yes ☐ No ☐ N/A

a) Blood ketones ..... mmol/L	**7. Seen by ICU or senior medical review within 12 hours?** ☐Yes ☐ No ☐ Not recorded ☐ N/A	**8. Was treatment area?**
b) Urine ketones		a) ☐ Level 1? (eg general ward area) b) ☐ Level 2? (eg high dependency area) c) ☐ Level 3? (eg ITU) d) ☐ Other? (please state)
c) Blood glucose .....mmol/L	**DIAGNOSIS of DKA:** Ketonaemia > 3.0mmol/L **or** significant ketonuria (more than 2+ on standard urine sticks) Blood glucose > 11.0mmol/L or known diabetes mellitus Bicarbonate (HCO_3^-) < 15.0mmol/L **and/or** venous pH < 7.3	.....
d) pH		
e) Bicarbonate .....mmol/L		

9. Date / time diagnosis confirmed: ..... / ..... hh:mm

10. In your opinion, was the patient's care delivered in an appropriate clinical area? ☐ Yes ☐ No ☐ Not recorded ☐ N/A

Joint British Diabetes Societies Inpatient Care Group

Institutional Standards for the Management of Diabetic Ketoacidosis (DKA) in Adults (Complete one per Institution)

Name of Hospital:		Date form completed:	
Form completed by		Grade	

(Put N/A= not applicable or NR = not recorded)

1. Guidelines	Yes	No	Don't know
a) Do you have a DKA treatment pathway?			
b) Do you have local guidelines for managing DKA?			
c) Do you have an Integrated Care Plan (ICP) for DKA?			
d) Are your guidelines current and valid?			
e) What are your guidelines based on? ☐ i) Joint British Diabetes Societies guidance? ☐ ii) Other..... (please state)			

2. Staffing	Yes	No	Don't know
a) In the clinical areas where patients with DKA are initially cared for, do you have trained health care professionals available to measure blood ketone levels 24 hours per day?			
b) Do you have dedicated inpatient diabetes specialist nurses at a staffing level of 1WTE per 300 beds? If the answer is NO – what is your current DSN staffing level per 300 beds?.....WTE			
c) Do you have a clinical lead responsible for the implementation & audit of DKA guidelines?			

3. Monitoring	Yes	No	Don't know
a) In the clinical areas where patients with DKA are initially cared for, do you have the facility to measure blood ketones in your Trust?			
b) Do you have blood glucose testing meters that are centrally connected in your Trust?			

4. Audit / Education	Yes	No	Don't know
a) Do you have a quality assurance scheme in place for both glucose and ketone meters?			
b) Have you audited the outcomes of your patients admitted with DKA the last past?			
c) Do you monitor against performance indicators eg those listed in the JBDS guideline?			
d) Do you have a rolling educational programme for medical staff?			
e) Do you have a rolling educational programme for nursing staff?			

5. Patients	Yes	No	Don't know
a) Do your patients have access to the specialist diabetes team within 24 hours of admission?			
b) Do your patients have the choice to self-manage their diabetes?			

If you have any further comments please feel free to use the other side of this piece of paper

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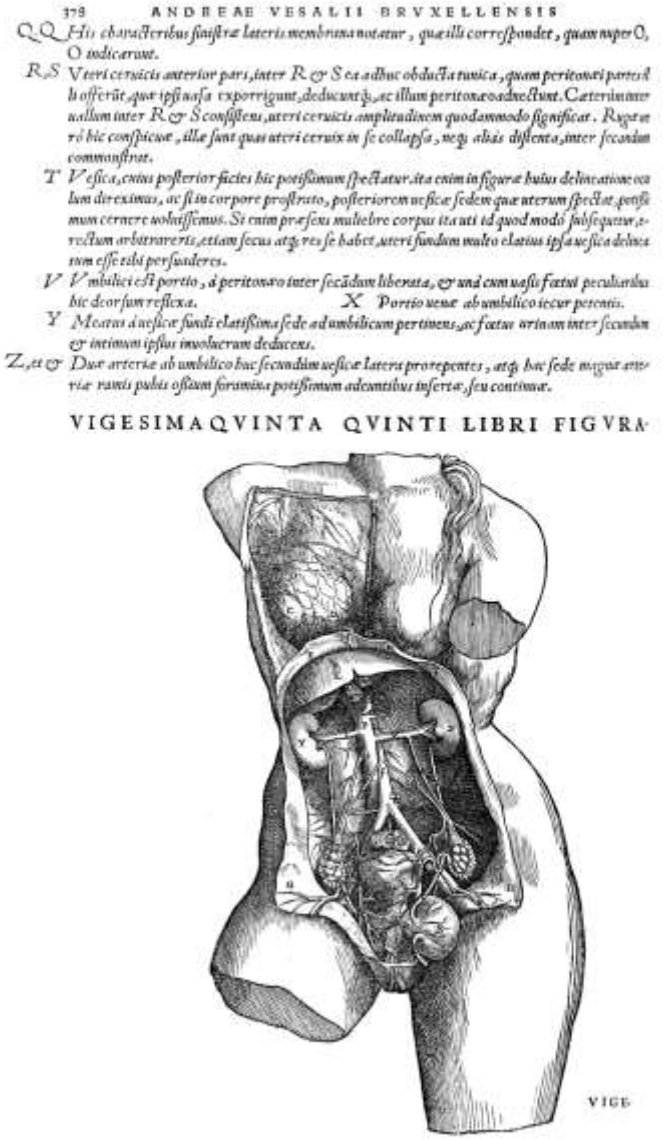
Glucocorticoids and Diabetes ?Issues

- Is it a problem?
- How to control hyperglycaemia associated with glucocorticoid use?



A Bit Of Background

- At any one time, ~0.75% of the UK population is on oral glucocorticoids (0.2% in 20-29 year olds, 2.5% in 70-79 year olds)
- 40% of glucocorticoid use is for respiratory disease, with most of the rest being musculoskeletal and cutaneous diseases and conditions requiring immunosuppression
- Most use is for <5 days, but 22% is for > 6 months and 4.3% for > 5 years

Royal College of Physicians Glucocorticoid guidelines 2002
www.nos.org.uk/NetCommunity/Document.Doc?id=422
Fardet L et al Rheumatology 2011;50(11):1982-1990

NNUH Prevalence Data (January 2014)

- All adult wards (excluding A+E, CCU, ITU/HDU)
- 120 out of 940 (12.8%) patients were receiving glucocorticoids – of whom 16 had pre-existing diabetes
- Only 25 (13 with diabetes) had their BG checked regularly
- 3 people with diabetes on glucocorticoids had no BG checked
- 95 patients had no evidence of BG checking

Narwani V et al Clinical Medicine in press

NNUH Prevalence Data (January 2014)

- 99 patients were on prednisolone
  - Mean daily dose 25mg ± 12.5 (range 0.5-60)
- 16 patients were on dexamthasone
  - Mean daily dose 9.2mg ± 6.5 (range 0.5-20)
- 4 patients on hydrocortisone
  - Mean daily dose 107.5mg ± 106.9 (range 20-200)

Narwani V et al Clinical Medicine in press

How do Glucocorticoids Affect Carbohydrate Metabolism?

- They promote visceral adipose tissue deposition
- Enhance lipolysis
- Alter levels of adipose tissue derived hormones and cytokines
- Acutely increases hepatic glucose production
- Complex effects on β-cell function

How do Glucocorticoids Affect Carbohydrate Metabolism?

- In the longer term induces insulin resistance
  - Diminished ability of insulin to initiate intracellular signalling mechanisms - in the liver, adipose, muscle
- Inhibits glucose uptake into muscle and reduced oxidative phosphorylation
- Induction of hyperinsulinaemia, dyslipidaemia and the metabolic syndrome

Saltiel AR et al Nature 2001;414:799-806
Hollingdal M et al Diabetologia 2002;45:49-55
Boyle PJ Diabetes Reviews 1993;1:301
Lambillotte C et al J Clin Invest 1997;99:414-423
Petersons CJ et al Diabetes Care 2013;36:2822-2829

Inhibition of Glucose Uptake

- Starts very early after glucocorticoid ingestion
- In (previously well controlled) inpatients the earliest manifestation of this is postprandial hyperglycaemia

Schacke H et al Pharmacol Ther 2002;96:23-43
Dimitriadis G et al Biochem J 1997;321:707–712
Petersons CJ et al Diabetes Care 2013;36:2822-2829

Spectrum of Disease

- The hyperglycaemia may be a transient rise of blood glucose levels or may result in HHS
- The best predictors of glucocorticoid-induced diabetes are family history of diabetes, increasing age, and glucocorticoid dose

Clement S Diabetes Care 2004;27(2):553-591

Some Evidence of Harm

- 433 patients admitted with an exacerbation of COPD from St George's in Tooting in 01/02
- Absolute risk of adverse outcomes (death or prolonged stay) increased ~15% per 1 mmol/L increase in glucose

Glucose level (mmol/L)	<6.0	6.0 - 6.9	7.0 - 8.9	>9.0
Mortality (%)	11.6	15.9	21.3	31.0

Baker EH et al Thorax 2006;61(4):284-289

Now We Know the Cause, What's the Treatment?

- Education and pre-empting the (almost) inevitable
- Letting teams know that when someone starts glucocorticoid treatment that blood glucose levels are very likely to rise and to watch for it
- When it happens, treat early

This is likely to meet with quite a lot of resistance – so be prepared!

Apart From That, What's the Treatment?

- There is work to shown that the hyperglycaemia associated with long term glucocorticoid use is amenable to treatment with glitazones
- There is a complex interaction between glucocorticoids and PPAR signalling pathways – these are the therapeutic targets for the glitazones

Willi SM et al Diabetes Res & Clin Pract 2002;58(2):87-96

But…..

- They work very slowly – so may have been useful in an outpatient setting
- Several controversies abound regarding the use of glitazones, thus their use is declining
  - Increased CV death rates
  - Increased fracture rates
  - Increased rates of macular oedema
  - Bladder cancer

Nissen SE NEJM 2007;356(24):2457-2471
Loke YK et al CMAJ 2009;180(1):32-39
Ryan EH et al Retina 2006; 26(5):562-70
Ferwana M et al Diabetic Med 2013;30(9):1026-1032

Sulphonylureas

- Little published evidence but widely used
- We asked for examples of guidelines used at different hospitals – and we got lots!
- All variations around a theme with some minor differences
- Most often used first line

Don't Incretins Prevent Postprandial Hyperglycaemia?

- They do, but GLP-1 use is limited by
  - Little experience in this setting
  - It makes people who are already unwell feel nauseated
  - Not appropriate for people who are NBM (??)
  - Safety concerns
- There are limited published data on the use of DPP-IV antagonists in this situation
  - e.g. Umpierrez using sitagliptin in 90 hospitalised patients

Umpierrez GE et al Diabetes Care 2013;36(11):3430-3435

The Best Treatment?

- Insulin is recommended in the US as the drug of choice for the treatment of glucocorticoid-induced hyperglycaemia
- Theoretically, prandial insulin should minimise the effects of the postprandial rise in glucose
- For patients receiving high-dose intravenous glucocorticoids, an intravenous insulin infusion may be appropriate

Hirsch IB et al Endocr Metab Clin North Am 1997;26:631–645

No Surprises There Then

- The dose needed is difficult to predict
- Intravenous infusions tend to achieve acceptable blood glucose concentrations quicker than MDI
- An insulin infusion allows appropriate tapering of insulin infusion rates
  - Glycaemic control is not compromised
  - Hypoglycaemic risks can be minimised – especially with pulsed high dose glucocorticoids

What About Subcutaneous Insulin?

- Clearly iv insulin is not the answer for everyone – but is if the blood glucose is consistently above ~12 mmol/L
- Subcutaneous insulin needs higher prandial doses than basal
- No work has been done to compare human with analogue insulin

Some Guidelines

- The ADA says…
- Glucose monitoring [with a prescription] for correction insulin should be initiated in any patient not known to have diabetes who receives therapy associated with high risk for hyperglycaemia, including high-dose glucocorticoid therapy

Standards of Medical Care in Diabetes — Diabetes Care 2014;37:S18-S80

ADA Guidelines Continued….

- If hyperglycaemia is documented and persistent, initiation of basal/bolus insulin therapy may be necessary
- Such patients should be treated to the same glycaemic goals as patients with known diabetes

Standards of Medical Care in Diabetes — Diabetes Care 2014;37:S18-S80

Where's the Evidence?

- Naturally, there isn't any
- But there is evidence that hyperglycaemia in a hospital setting (for any cause) is associated with poor mortality, morbidity, and health economic outcomes
- Improving glycaemic control improves these outcomes

Umpierrez GE et al J Clin Endocrinol Metab 2002; 87:978–982
Bruno A et al Diabetes Care 2008;31(11):2209-2210
Dhatariya K BMJ 2013;346:f134

What Should the Targets Be?

- Targets similar to those of outpatients are unrealistic in hospital due to the effects of
  - Stress hyperglycaemia
  - Altered nutritional intake
  - Multiple interruptions to medical care
- Aiming for a range of 6.0 – 10.0 mmol/L with an acceptable range of 4.0 – 12.0 mmol/L if they can be safely achieved
- For end of life care, a range of 6.0 – 15.0 mmol/L is acceptable

The Future

- JBDS is launching a guideline on the management of glucocorticoid induced hyperglycaemia in hospitalised patients
- Watch this space!

A Quote to Sum it Up

- If an inpatient is on glucocorticoids… “the design of insulin therapy depends on the timing of the glucocorticoids and challenges the creativity of the caregiver”

Thompson CL et al Diabetes Spectrum 2005; 18:20-27

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