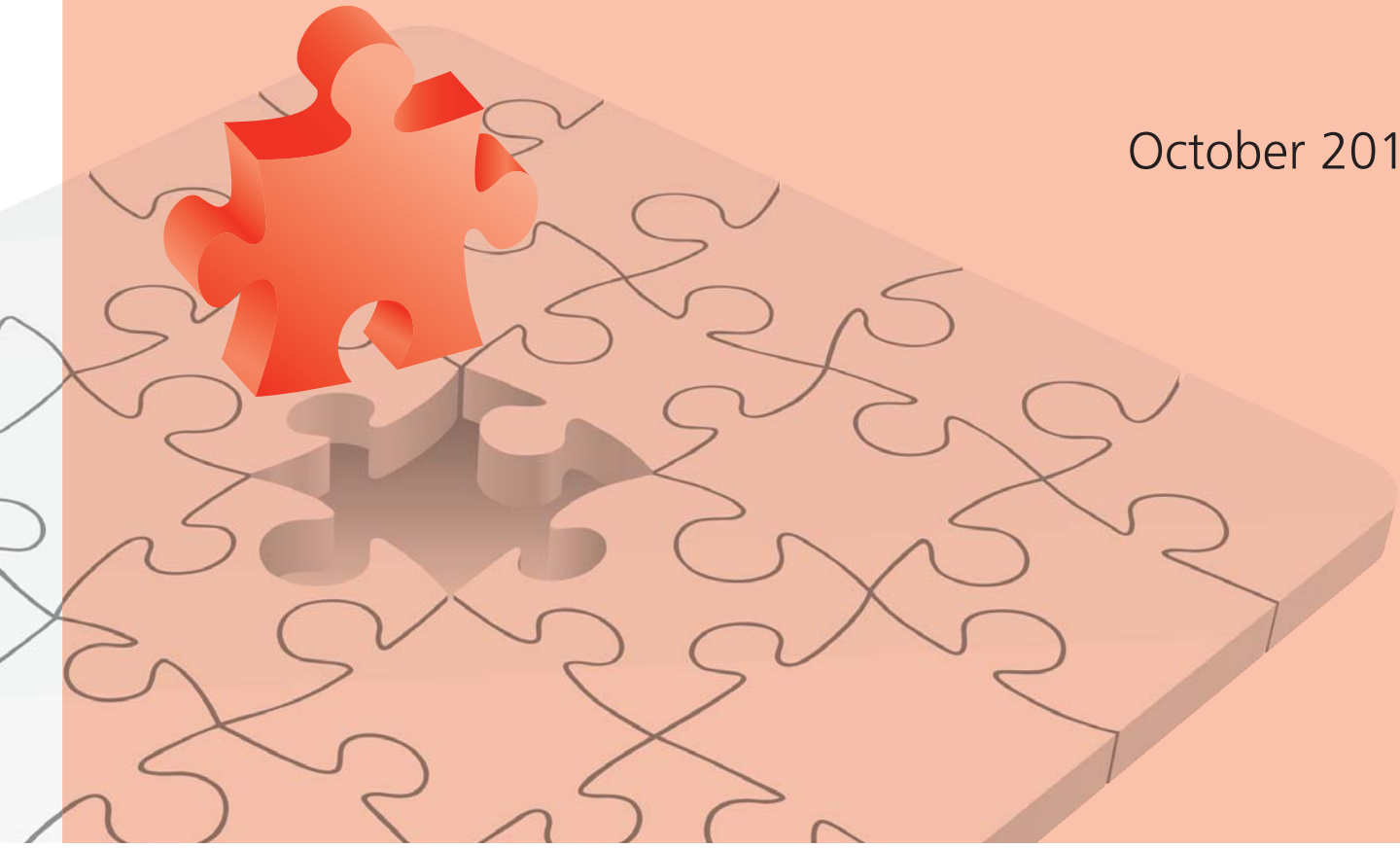
JBDS-IP Joint British Diabetes Societies for inpatient care

Management of Hyperglycaemia and Steroid (Glucocorticoid) Therapy



October 2014

DIABETES UK CARE. CONNECT. CAMPAIGN.

ABCD Association of British Clinical Diabetologists

DISN UK GROUP

WEDS welsh endocrine and diabetes society

ADC

trend UK TRAINING RESEARCH AND EDUCATION FOR NURSES IN DIABETES

Royal College of Nursing

diabetesFRAIL The emergence of a concept

This document is coded JBDS 08 in the series of JBDS documents

Other JBDS documents:

Admissions avoidance and diabetes: guidance for clinical commissioning groups and clinical team; December 2013, JBDS 07

The management of the hyperosmolar hyperglycaemic state (HHS) in adults with diabetes; August 2012, JBDS 06

Glycaemic management during the inpatient enteral feeding of stroke patients with diabetes; June 2012, JBDS 05

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The Management of Diabetic Ketoacidosis in Adults; revised September 2013, JBDS 02

The hospital management of hypoglycaemia in adults with diabetes mellitus; revised September 2013, JBDS 01

These documents are available to download from:
ABCD website: www.diabetologists-abcd.org.uk/JBDS/JBDS.htm
Diabetes UK website: www.diabetes.org.uk

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Foreword

This is the latest in the series of Joint British Diabetes Societies for Inpatient Care (JBDS-IP) guidelines, and focuses on steroid induced hyperglycaemia and steroid induced diabetes. They are evidence based where possible but are also drawn from accumulated professional knowledge and consensus agreement. The use of steroids in patients with established diabetes is a common clinical problem, with no generally accepted management strategy. Steroid induced diabetes may be frequently undiagnosed and only discovered on the emergence of symptoms or complications of acute hyperglycaemia.

This guideline constructs a framework for the recognition and management of steroid induced hyperglycaemia and steroid induced diabetes, and is designed for use by general physicians. Necessarily, the guideline includes recommendations for the management of patients when they leave hospital and thus, this guidance may also be utilised for those treated with steroids in the outpatient department or in General Practice.

As with all of the JBDS-IP documents, this document is dynamic and will be reviewed in response to feedback with a view to incorporating emerging evidence. This document has been produced by the Joint British Diabetes Societies for Inpatient Care on behalf of Diabetes UK, the Association of British Clinical Diabetologists (ABCD), the Diabetes Inpatient Specialist Nurse (DISN) UK Group and Training Research and Education for Nurses in Diabetes (TREND-UK), in collaboration with the Primary Care Diabetes Society (PCDS).

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Introduction

This document aims to guide the management of hyperglycaemia in people given steroids as a hospital inpatient, and following discharge. The prevalence of steroid use in hospital inpatients may be in excess of 10% (Swafe et al 2014), in the context of an up to 30% prevalence of diabetes in hospital inpatients, with a mean diabetes prevalence of 16% (NaDIA 2012). In the outpatient population, 40% of steroid use is for respiratory disease, with most of the rest being used in musculoskeletal and cutaneous diseases, and conditions requiring immunosuppression. Most steroid use is for less than 5 days, but 22% is for greater than 6 months and 4.3% for longer than 5 years (Fardet et al 2011).

The use of steroid treatment in people with pre-existing diabetes will undoubtedly result in worsening glucose control; this may be termed **steroid induced hyperglycaemia**. This will warrant temporary additional and more active glycaemic management. A rise in glucose, related to steroid therapy occurring in people without a known diagnosis of diabetes is termed **steroid induced diabetes**. This may or may not resolve when the steroids are withdrawn.

Steroid treatment may be administered as a single high dose for a defined period and titrated down slowly. Steroid treatment can also be used as a maintenance therapy for a prolonged period, and may be given in high dose when a malignant tumour is identified or at the end of life. This can be administered orally or intravenously. The management of adrenal suppression due to long-term steroid use is beyond the remit of this document and advice on how to manage this condition should be sought from local endocrine services.

There is little evidence to guide how patients with hyperglycaemia related to steroid use should be managed. Short courses of steroids resulting in minimal periods of hyperglycaemia may not warrant intervention. Higher dose steroids for longer periods may result in significant symptomatic hyperglycaemia including fatigue, polyuria and polydipsia with the potential for acute complications related to hyperglycaemia (Donihi AC et al 2006).

The control of hyperglycaemia in such circumstances will ameliorate symptoms, reduce the risk of acute complications, and lessen the increased risk of infections and other complications associated with hyperglycaemia. It is also important to note that acute illness may result in "stress hyperglycaemia" independent of steroid administration (Dungan et al, 2009).

This document is aspirational and the guidance outlined is a consensus based on best practice collated from around the United Kingdom. Where evidence is available, this is referenced. The entry point to the treatment algorithms indicated within this document would be any supraphysiological dose of steroid, approximating to a dose of prednisolone of greater than 5mg – or equivalent dose of the alternative synthetic glucocorticoids (See Table 1 page 9). Some patients may develop hyperglycaemia at a lower steroid dose, so clinical vigilance is therefore recommended with steroid therapy at any dose.

Steroids - mechanism of action

Synthetic glucocorticoids mimic the effect of the endogenous steroids, nuclear hormones that cross the cell membrane to bind to specific glucocorticoid receptors in the cytoplasm of target cells to form glucocorticoid-receptor (GR) complexes. The activated GR complex is translocated to the cell nucleus and modulates DNA transcription. This results in transactivation of anti-inflammatory proteins and transrepression of pro-inflammatory proteins (Geer et al 2014). Steroid administration also modulates carbohydrate metabolism via complex mechanisms, including effects on beta cell function as well as inducing insulin resistance by effects on insulin receptors in liver, muscle and adipose tissue. These effects promote hyperglycaemia in "at risk individuals".

Predisposing factors leading to increased risk of hyperglycaemia with steroid therapy

- Pre-existing type 1 or type 2 diabetes
- People at increased risk of diabetes (e.g. obesity, family history of diabetes, previous gestational diabetes, ethnic minorities, polycystic ovarian syndrome)
- Impaired fasting glucose or impaired glucose tolerance, HbA1c 42-47mmol/mol
- People previously hyperglycaemic with steroid therapy
- Those identified to be at risk utilising the University of Leicester/Diabetes UK diabetes risk calculator (riskscore.diabetes.org.uk)

Steroid therapy – impact on blood glucose

Steroids may be administered by various regimes and in variable doses. A single or short course of steroid (e.g. prednisolone) in the morning may be the commonest mode of administration. In susceptible patients, this will often result in a rise in blood glucose by late morning that continues into the evening. Overnight the blood glucose generally falls back, often to baseline levels the next morning. Thus treatment should be tailored to treating the hyperglycaemia, whilst avoiding nocturnal and early morning hypoglycaemia. In pregnancy and other situations, a single dose or short course of steroid may be administered. Many hospital inpatients will receive multiple daily doses of steroids.

Glucose levels in most individuals can be predicted to rise approximately 4 to 8 hours following the administration of oral steroids and sooner following the administration of intravenous steroids. Capillary blood glucose (CBG) monitoring is paramount to guiding appropriate therapeutic interventions. Conversely, glucose levels may improve to pre-steroid levels 24 hours after intravenous steroids are discontinued. If oral steroids are weaned down over several weeks the glucose levels may decline in a dose dependent fashion. This may not always occur, particularly in those with pre-existing undiagnosed diabetes.

Table 1. Steroid dose equivalents

Steroid	Potency (Equivalent doses)	Duration of action (Half-life in hours)
Hydrocortisone	20mg	8
Prednisolone	5mg	16-36
Methylprednisolone	4mg	18-40
Dexamethasone	0.75mg	36-54
Betamethasone	0.75mg	26-54

N.B. potency relates to anti-inflammatory action, which may not equate to hyperglycaemic effect

Glucose targets

In line with other JBDS inpatient documents, the recommended target level for glucose in hospital inpatients is 6-10mmol/L, accepting a range of 4-12mmol/L. However, certain patient groups do not require such tight control, (e.g. those at the end of life) and those who may be severely disabled by a hypoglycaemic event such as:

- Patients with dementia
- The confused
- The frail older person
- People at risk of falling
- Those with variable appetite and dietary intake

Thus individualised targets and an appropriate care plan should be documented when hyperglycaemia is first identified, mindful of the symptoms associated with uncontrolled hyperglycaemia.

Glucose Monitoring

An HbA1c prior to the commencement of steroids in patients perceived to be at high risk of steroid induced diabetes and in those with known diabetes may be informative.

At the commencement of corticosteroid therapy in people considered at risk of steroid induced diabetes, capillary blood glucose (CBG) testing should be initiated once daily. This should be prior to or following lunch or evening meal when the hyperglycaemic effects of morning steroid dosing is likely to be greatest.

Monitoring Guidance

In people without a pre-existing diagnosis of diabetes

- Monitoring should occur at least once daily – preferably prior to lunch or evening meal, or alternatively 1-2 hours post lunch or evening meal. If the initial blood glucose is less than 12mmol/L continue to test once prior to or following lunch or evening meal
- If a subsequent capillary blood glucose is found to be greater than 12mmol/L, then the frequency of testing should be increased to four times daily (before meals and before bed)
- If the capillary glucose is found to be consistently greater than 12mmol/L i.e. on two occasions during 24 hours, then the patient should enter the treatment algorithm (See Appendix 1 – Steroid induced diabetes)

In people with a pre-existing diagnosis of diabetes

- Test four times a day, before or after meals, and before bed, irrespective of background diabetes control
- If the capillary glucose is found to be consistently greater than 12mmol/L i.e. on two occasions during 24 hours, then the patient should enter the treatment algorithm (See Appendix 2 – Steroid induced hyperglycaemia)

Diabetes treatment options

All those experiencing hyperglycaemia should receive appropriate education from trained individuals including:

- Diabetes management
- Healthy lifestyle choices
- The risk of hypoglycaemia with non insulin and insulin therapies

Medication options for people taking once daily steroid therapy

Non insulin therapies

Sulphonylureas promote insulin release from the pancreatic beta cell. By consensus, a short acting sulphonylurea, such as gliclazide, taken once daily may best manage the glucose excursion associated with a once daily oral steroid treatment. Whilst monitoring for hypoglycaemia the gliclazide may be titrated to a maximum of 240mg in the morning. An evening dose of gliclazide may also be initiated to achieve a maximum daily dose of 320mg.

Intuitively, pioglitazone may seem an appropriate choice for the management of steroid induced hyperglycaemia. The evidence base for the use of pioglitazone above other treatments described within this guideline is weak (Willi et al 2002). Pioglitazone may also take a number of weeks to achieve maximal effect. However, once daily pioglitazone is an option providing there are no contraindications (e.g. heart failure and fluid retention, particularly when used in conjunction with insulin, macular oedema, risk of fractures, unexplained macroscopic haematuria).

Despite their potentially attractive modes of action, there is currently no evidence to support the use of DPP-IV inhibitors, GLP-1, or SGLT-2 inhibitors in the management of steroid induced diabetes/ hyperglycaemia (See Appendices 1 and 2).

Insulin therapies

Morning administration of basal human insulin (Humulin I, Insuman Basal, Insulatard) may closely fit the glucose excursion induced by a single dose of oral steroid in the morning.

We advocate the commencement of 10 units of basal human insulin with a daily dose increase of between 10% and 20%, titrated to the blood glucose level, although dose increments of up to 40% have been shown to be required in some individuals (Dashora et al 2004).

Basal analogue insulin may be appropriate if hyperglycaemia is present throughout the day and into the evening. In this context, basal insulin may best be administered in the morning.

Care should be taken to identify and protect against nocturnal and early morning hypoglycaemia if insulin glargine, insulin detemir or insulin degludec are used in this context.

Medication options for people taking multiple daily doses of steroid

Multiple daily doses of steroid such as intravenous hydrocortisone or oral dexamethasone can cause hyperglycaemic effects throughout the 24 hour period.

Non-insulin therapies

Administration of oral non-insulin therapies is unlikely to be effective in controlling the resultant hyperglycaemia. A trial of gliclazide 40mg twice daily (BD) may be indicated and titrated daily to a maximum of 160mg BD. Metformin and pioglitazone are unlikely to be of significant benefit and there is no evidence to support the use of GLP-1, DPP-4 inhibitors or SGLT-2 inhibitors in these circumstances.

Insulin therapies

Subcutaneous insulin using a basal or multiple daily injection regimen will be the most appropriate choice of treatment to achieve glycaemic control for the majority of patients, although it is recommended that you involve the local inpatient or community diabetes team.

It may be that a twice daily premixed, basal bolus, or more complex insulin regimen will be required if oral medication, or once daily insulin proves insufficient to control hyperglycaemia. Close attention will need to be paid to blood glucose monitoring and early intervention may be necessary to prevent prolonged symptomatic hyperglycaemia. Consequent titration of the insulin dose will allow maintenance of glucose control in the face of increasing or decreasing steroid dose.

In acutely unwell hospital inpatients with significant hyperglycaemia, oral non insulin therapies are unlikely to achieve glucose control. In this situation, temporary use of a variable rate intravenous insulin infusion (VRIII) with urgent review by the diabetes inpatient team would be appropriate.

Treatment of steroid induced hyperglycaemia (see Appendix 2)

Type 2 diabetes – non-insulin therapy

If patients are treated with gliclazide, increase the morning dose in 40mg increments to a maximum of 240mg, with a total daily dose not exceeding 320mg. Titration of metformin may also be beneficial. There is little experience or evidence to suggest benefit of DPP-4 inhibitors, GLP-1 analogues or SGLT-2 inhibitors in this situation so temporary addition of basal human insulin may be indicated.

Type 2 diabetes – insulin therapy

Pre-mixed insulin regimen

- An increase in the morning insulin dose may be effective in reducing steroid induced hyperglycaemia.

Basal-bolus

- An increase in the lunch and evening meal short acting boluses may be appropriate.
- If on basal insulin consider switching to morning administration and increase dose in 2-4 unit increments (or by 10-20%) every 24-48 hours, in line with results of capillary blood glucose monitoring.
- Monitor closely for early morning hypoglycaemia if basal analogue insulin utilised.
- Diabetes teams should be involved should hyperglycaemia persist, as a change to a more complex insulin regimen may be required.

Type 2 diabetes and steroid treatment – General Guidance

1. Set target for Capillary Blood Glucose (CBG) e.g. 6-10mmol/L
2. Consider increasing monitoring to 4 times daily
3. Refresh diabetes education with patient

If hyperglycaemia on non-insulin therapies

- Gliclazide – titrate to maximum of 320mg daily, with maximum 240mg in the morning
- Metformin – titrate to maximum of 1g BD

If hyperglycaemia on insulin therapies

- If on evening once daily human insulin consider switch to morning dosing
- If uncontrolled hyperglycaemia or multiple daily dosing of steroid consider switch to basal analogue insulin (or alternative regimen) and involve diabetes team in hospital or community
- Beware of nocturnal and early morning hypoglycaemia

Type 1 diabetes

Insulin doses can be titrated in at least 2 unit increments every 24-48 hours, to achieve target glucose levels, though evidence suggests that significant increases in the insulin dose of up to 40% may be required to normalise the steroid induced hyperglycaemia (Dashora et al 2004).

Diabetes Specialist Nurses (DSN) or community diabetes teams should be involved.

An increase in lunch and evening meal short acting bolus insulin dose may be warranted if a basal-bolus regimen is utilised. Alternatively a switch of insulin regimen may be required, for example from twice daily premixed insulin to a basal-bolus regimen.

Hospital Discharge in patients without a previous diagnosis of diabetes

When a patient is discharged from hospital on steroid therapy a clear strategy for the management of hyperglycaemia or potential hyperglycaemia should be in place. The titration of therapy to address the hyperglycaemia should be communicated to the community diabetes team, GP or community DSNs. (See discharge letter- Appendix 4).

Patients commenced on steroids as an inpatient and discharged after a short stay with the intention of continuing high dose steroids should receive standard education including:

- Diabetes management
- Lifestyle advice
- Risks associated with hyperglycaemia and hypoglycaemia
- Blood glucose monitoring and the need to test once daily in the late afternoon or evening

If a reading is in excess of 12mmol/L, then testing should be increased to four times daily.

If two readings exceed 12mmol/L in a 24 hour period then follow the algorithm in Appendix 1 (see following summary).

Post hospital discharge:

- If the steroid dose remains above 5mg prednisolone or equivalent, for a protracted period, and the patient is insulin treated then the blood glucose should be checked at least once daily and prior to driving.
- If the steroid dose is being titrated upwards, then test at least once daily.
- If a reading exceeds 12mmol/L increase testing to four times daily, including post prandially.
- If two readings exceed 12mmol/L in a 24-hour period then follow the algorithm in Appendix 1 (see following summary).
- As the steroid dose decreases, the treatment of hyperglycaemia will similarly need to be titrated down. e.g. a weekly 5mg reduction of prednisolone from 20mg may require a 20-25% reduction in insulin dose, or a 40mg reduction in gliclazide.
- If steroids were discontinued prior to discharge and hyperglycaemia persists, then blood glucose monitoring should be continued post discharge until normoglycaemia returns or until a definitive test for diabetes is undertaken (fasting glucose, OGTT or HbA1c).
- If steroid treatment is ceased in hospital and blood glucose tests are in the normal range, then post-discharge blood glucose testing is **not** recommended. A definitive test for diabetes should still be undertaken (p.17).

Hospital discharge of patients at risk of steroid induced diabetes/hyperglycaemia

Steroids commenced and patient discharged

- Standard education for patient and carer
- Blood glucose testing once daily (pre or post lunch or evening meal)
- If blood glucose readings greater than 12mmol/L increase frequency of testing to four times daily
- If two consecutive blood glucose readings greater than 12mmol/L in a 24 hour period follow algorithm for management of steroid induced diabetes

Patient discharged on decreasing dose of steroid above 5mg od

- Standard education for patient and carer including advice on hypoglycaemia
- Continue CBG monitoring until blood glucose normalises (4-7mmol/L)
- Review by agreed individual (e.g. GP, diabetologist, diabetes specialist nurse, etc.) at an appropriate juncture to consider down-titration of antihyperglycaemic therapy if necessary

Patient discharged following steroid cessation

If hyperglycaemia persists

- CBG testing until return to normoglycaemia (4-7mmol/L)
- OR until a definitive diagnosis of diabetes is undertaken

If hyperglycaemia resolved stop CBG testing and arrange definitive test for diabetes

Screening post discharge

After stopping steroid therapy in people without pre-existing diabetes who experienced steroid induced hyperglycaemia there should be screening for a diagnosis of diabetes. This should be at least 6 weeks following stopping steroid treatment.

Given the recent hyperglycaemia the use of HbA1c as a screening tool, should be delayed until 3 months following steroid cessation. A fasting glucose or OGTT may be advantageous if a diagnosis of diabetes is clinically suspected prior to 3 months elapsing. Where present, practitioners should adhere to local guidelines for diabetes screening. It is anticipated that general practices will provide the majority of follow up of diabetes for the patients described in this guideline. This will require robust lines of communication between hospital and community settings and the local diabetes team.

Outpatient management and high dose steroid therapy

Outpatient departments and general practices may commence a course of steroid for use in the community setting. It is advised that patients treated in this context be screened for the potential emergence of steroid induced diabetes or hyperglycaemia.

It is advised that those who are expected to remain on steroids for a protracted period, and who are "at risk" of hyperglycaemia with steroid therapy (see page 8), be provided with a glucose meter and instructed on how to check their CBG.

Initially it is recommended that patients check the CBG once daily prior to or 1-2 hours following lunch or evening meal. If a CBG is recorded greater than 12mmol/L, then blood glucose monitoring should be increased to a maximum of four times daily. If blood glucose is greater than 12mmol/L on two occasions in 24 hours then the patient should consult the clinician who commenced the steroid, or if agreed locally, the general practitioner. The clinician should then consider the algorithm for the management of hyperglycaemia with steroid use, and potentially commence a sulphonylurea or optimise existing non-insulin or insulin therapy.

Steroid treatment in pregnancy

Steroid administration in pregnancy may cause transient hyperglycaemia or result in increased levels of hyperglycaemia in those with gestational diabetes mellitus or pre-existent diabetes. The majority of steroid use in pregnancy will be two single doses of betamethasone administered intramuscularly to promote foetal lung maturity at birth.

- In people with pre-existing diabetes or gestational diabetes, blood glucose monitoring will already be required at least four times a day.
- If the blood glucose is greater than 12mmol/L on two occasions in 24 hours, consider titrating therapy to manage the hyperglycaemia.
- If the patient is already on insulin, the doses may need to be increased significantly by 40% or more at the time of the first steroid injection, for a period of 24-72 hours. The diabetes team should always be involved in the management of such patients.
- Some units prefer to admit patients for a VRIII to cover the hyperglycaemia associated with the administration of betamethasone in people on insulin treatment.
- As the steroid dose is reduced, any diabetes treatment given may need to be titrated down in keeping with blood glucose results.

Two doses of steroid are unlikely to reveal significant hyperglycaemia for a prolonged period in those without diabetes. Therefore in pregnant women without a pre-existing diagnosis of gestational diabetes or known to have diabetes prior to conception the advice would be not to monitor in this particular circumstance.

Steroid treatment in end of life care

People with diabetes at the end stages of life have a unique set of clinical needs.

Steroid therapy is frequently used in palliative care for symptom control, usually as dexamethasone or prednisolone. Regardless of the indication, the impact of steroids on glucose control can cause additional hyperglycaemic symptoms.

Once daily steroid therapy

This can be managed by morning administration of a sulphonylurea, (e.g. gliclazide) or morning isophane insulin (e.g. Insulatard, Humulin I or Insuman Basal). See Appendix 3 for guidance produced by Diabetes UK on end of life clinical care (Diabetes UK 2013).

Twice daily steroid therapy

This may include splitting higher doses of dexamethasone. If so consider an alternative approach to setting times for testing glucose levels, and for managing the impact on blood glucose.

Twice daily gliclazide or isophane insulin

This can be effective but there is a risk of early morning hypoglycaemia and care must be taken in adjusting doses with that risk in mind.

If hypoglycaemia is a concern, once daily insulin glargine or insulin detemir given in the morning may be a safer, less complex regimen, especially for those new to insulin. Early discussions with the diabetes specialist team can assist in choosing the most appropriate diabetes treatment regimens for the steroid utilised.

Short-term courses (less than 3 days) of steroids

This may only require closer blood glucose monitoring but longer courses will require a review of glucose-lowering therapy and may result in a switch from oral agents to insulin. In this situation, an insulin regimen (e.g. Humulin I, Insulatard, or Insuman Basal) given once daily could be considered.

In those without a pre-existing diagnosis of diabetes prior to the commencement of steroids, blood glucose monitoring, and patient and carer education should be undertaken in alignment with principles outlined within this document. Liaison with a community dietitian may assist in meal planning.

Blood glucose targets at the end of life may differ from those traditionally given. Glucose levels should be targeted between 6mmol/L and 15mmol/L, though targets should be individualised (see Appendix 3).

Audit Standards

- Patients treated with steroids appropriately screened for hyperglycaemia with blood glucose monitoring – 90%
- Patients with steroid induced hyperglycaemia with adequate glucose control (blood glucose of not greater than 12mmol/L on 2 occasions within 24 hours) – 75%
- Patients with steroid induced diabetes with appropriate glucose control (blood glucose of not greater than 12mmol/L on 2 consecutive occasions) during the course of steroid treatment – 75%
- Patients discharged from hospital with an appropriate diabetes discharge plan – 100%
- Patients with steroid induced diabetes, appropriately screened for diabetes – 75%
- Patients at end of life managed appropriately on end of life steroid induced diabetes pathway – 75%

Controversial Areas

Assessment of hyperglycaemia following cessation of steroids

Steroid treatment may be ceased precipitously following a short course, or the dose reduced slowly over days or weeks. Those patients who have received high dose steroids for two weeks or longer may be at risk of adrenal suppression and clinicians should be aware of this when assessing such patients. As previously indicated, the management of adrenal suppression due to long term steroid use is beyond the remit of this document and advice on how to do this correctly should be sought from the local endocrine service.

Steroid induced diabetes should resolve as the steroid dose reduces and stops. However, a proportion of people found to be hyperglycaemic on steroid therapy will have had pre-existing type 2 diabetes. Steroids may reveal a propensity to type 2 diabetes, and diabetes may persist following cessation of steroid therapy. A fasting glucose or OGTT 6 weeks after cessation of steroid therapy may indicate the continued presence of diabetes. Utilising HbA1c in this context will be confounded by the recent hyperglycaemia. Should an HbA1c be used to confirm the diagnosis of diabetes following an episode of steroid induced diabetes, the HbA1c should be assessed at least three months following steroid cessation.

Hospital Discharges

Currently there is little planning for the discharge of patients commenced on steroids with no history of hyperglycaemia. This document sets out an aspirational framework, based on best practice, which ensures that steroid induced diabetes is identified, monitored and treated. Whilst this involves resource to educate patients and carers and the use of monitors and test strips, the benefits of reduced crisis management and potentially hospital admission and outpatient referral, we believe offsets the initial investment in resource.

Patients on steroids with diabetes who are discharged from hospital require co-ordinated and pragmatic discharge planning and an ongoing care plan. GP practices should be informed of the discharge and the care plan communicated.

Where present the community diabetes team may facilitate the discharge and provide input into ongoing diabetes care. Alternatively the GP surgery may take responsibility for the patient and ongoing diabetes care, with support from the hospital or community diabetes nursing team.

The patient and carers should be actively involved in the preparation of the care plan. They should be provided with written instructions and educational material regarding the management of hypoglycaemia, capillary blood glucose testing and actions in the event of hyperglycaemia. If necessary a "hot review" in a hospital or community based diabetes clinic one to two weeks following hospital discharge, should be considered.

Newer Agents

There is little evidence for the use of glucagon like peptide-1 (GLP-1) mimetics or sodium glucose transporters 2 (SGLT-2) inhibitors in the management of steroid related diabetes. DPP-IV inhibitors have been studied in the hospital inpatient setting (Umpierrez et al 2013), though not specifically for use in patients with steroid induced diabetes.

Given the relative lack of evidence to assure the efficacy and safety of the newer pharmacotherapies in hospital inpatients, we do not recommend their use within this guideline. We welcome emerging evidence that may lead to a change in practice in this area.

We recommend human insulin within this guideline because its pharmacokinetic profile may be best suited to the profile of hyperglycaemia associated with once daily steroid administration. If steroids are administered in multiple doses then hyperglycaemia may persist throughout the day and basal analogue insulin may be most appropriate. Changes in insulin regimens should be discussed with the diabetes inpatient specialist team or responsible diabetes clinician in the community.

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Appendix 1

Steroid (glucocorticoid) Induced Diabetes

NO KNOWN DIABETES

- Check HbA1c prior to the commencement of steroids in patients perceived to be at high risk
- On commencement of steroid, recommend CBG once daily pre or post lunch or evening meal, in those at "high risk" or with symptoms suggestive of "hyperglycaemia"
- If the capillary blood glucose (CBG) is below 12mmol/L consider the patient to be at low risk and record the CBG daily post breakfast or post lunch
- If CBG consistently <10mmol/L consider cessation of CBG testing
- If a capillary blood glucose is found to be greater than 12mmol/L the frequency of testing should be increased to four (4x) times a day
- If a capillary blood glucose is found to be consistently greater than 12mmol/L (i.e. on 2 occasions during a 24hr period), then the patient should enter the treatment algorithm below

CBG readings above desired target (6 - 10mmol/L - acceptable range 4 - 12mmol/L)

- Add in gliclazide 40mg with breakfast and increase the dose by 40mg increments daily if targets are not reached

If no symptoms of hypoglycaemia are experienced by the patient despite being on 160mg of gliclazide in the morning, consider titration to 240mg in the morning. (You may wish to seek specialist advice on dose titration at this stage)

If still no improvement on maximum dosage consider

- Adding an evening dose of gliclazide or add morning human NPH insulin e.g. Humulin I / Insulatard / Insuman Basal
- For NPH - commence 10 units daily in the morning and titrate every 24 hours by 10-20% to achieve desired CBG target

Discharge - Monitoring will need to be continued in patients remaining on glucocorticoids post discharge

- If steroid treatment is ceased in hospital and hyperglycaemia has resolved CBG can be discontinued post discharge
- If steroids are discontinued prior to discharge and hyperglycaemia persists then continue with monitoring until normal glycaemia returns or until a definitive test for diabetes is undertaken (fasting blood glucose, OGTT or HbA1c)

If steroids are reduced or discontinued:

- Continue CBG testing if CBG >12mmol/L in 24 hours
- Any changes made should be reviewed and consideration given to reverting to previous therapy or doses

If unsure at any stage about next steps or want specific advice on how to meet with patients needs or expectations please discuss with the team who usually looks after their diabetes (GP/Specialist Team).

Glycaemic targets:

- **Aim for 6 - 10mmol/L (acceptable range 4 - 12mmol/L)**
- **End of life care: Aim for 6 - 15mmol/L and symptom relief**

[Version 1.0] 13/08/2014
Design by S.Jamal UHL

Appendix 2

Managing Glucose Control in People with Known Diabetes On Once Daily Steroids (glucocorticoids)

KNOWN DIABETES, reassess glucose control and current therapy

- Set target blood glucose e.g. 6-10mmol/L (see glycaemic targets box below)
- Check capillary blood glucose (CBG) 4 times a day and use this flowchart to adjust diabetes medication accordingly
- In Type 1 diabetes also check daily for ketones if CBG> 12mmol/L

Type 2 diet control OHA +/- GLP1

If no 'hypo' symptoms and NOT on an SU:

- Commence gliclazide 40mg a.m., titrate daily until a maximum dose of 240mg a.m. or glycaemic targets are reached
- Seek specialist advice if you are concerned about dose titration in those taking 160mg with no improvement in glycaemic control
- If on twice daily gliclazide and targets not reached consider referral to specialist care for titration to 240mg morning dose plus 80mg p.m.

If no 'hypo' symptoms and taking maximum dose (320mg/day)

- Add Insuman Basal, Humulin I or Human Insulatard
- Aim for CBG appropriate to patients' needs

If CBG remains above desired target before the evening meal

- Increase insulin by 4 units or 10 - 20%
- Review daily
- If remains above target titrate daily by 10 - 20% until glycaemic target reached

Insulin controlled (Type 1 and Type 2). In Type 1 diabetes always test for ketones, if blood ketones more than 3mmol/L or urinary ketones >++ assess for DKA In Type 2 diabetes check for ketones if CBG levels >12mmol/L and the patient has osmotic symptoms

Once daily night time insulin, transfer this injection to the morning:

- Titrate by 10 - 20% daily according to pre-evening meal CBG readings
- If targets not achieved consider BD, or basal bolus regimen

Twice daily insulin:

- Morning dose will need to increase 10 - 20% daily according to pre-evening meal CBG readings
- Aim for CBGs to individual needs as stated above, unless patient experiences 'hypo' despite snacks

Basal bolus insulin:

- Consider transferring evening basal dose insulin to the morning and increase short/fast acting insulin by 10 - 20% daily until glycaemic target reached
- Aim for agreed CBGs target to patients needs pre-meal, unless patient has hypo despite snacks or has long gaps between meals

If steroids are reduced or discontinued:

- Blood glucose monitoring may need to be continued in inpatients and, in discharged patients assessed by their GP
- Any changes made should be reviewed and consideration given to reverting to previous therapy or doses

If unsure at any stage about next steps or want specific advice on how to meet with patients needs or expectations please discuss with the team who usually looks after their diabetes (GP/Specialist Team).

Glycaemic targets:

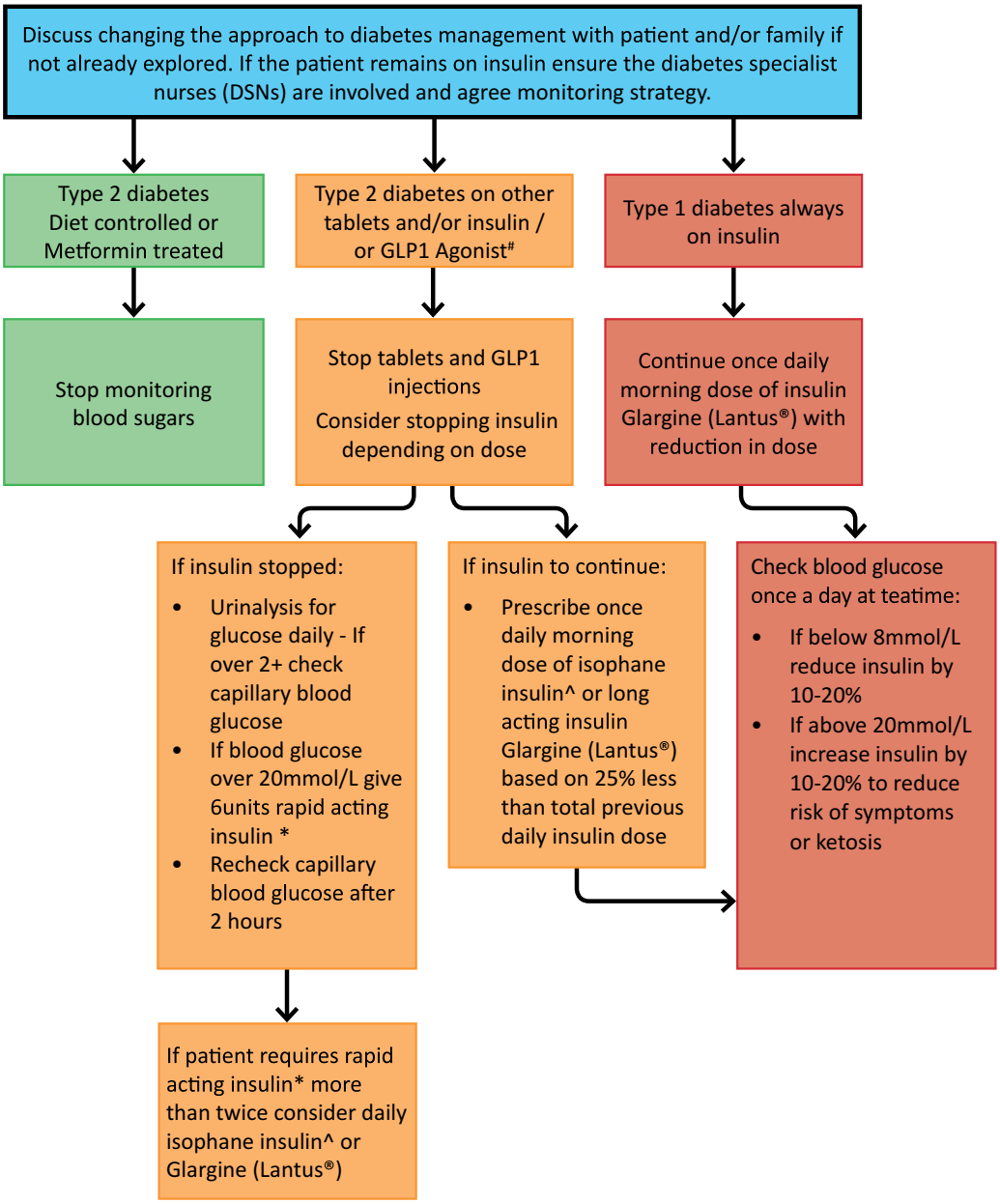
- **Aim for 6 - 10mmol/L (acceptable range 4 - 12mmol/L)**
- **End of life care: Aim for 6 - 15mmol/L and symptom relief**

[Version 2.0] 25/09/2014
Design by S.Jamal UHL

Appendix 3

Algorithm to show End of life Steroid Management

End of Life Diabetes Management



Key

Bydureon (Exenatide ER), Byetta (Exenatide) / Victoza, (Liraglutide), Lyxumia (Lixisenatide)

* Humalog/Novorapid/Apidra
^ Humulin I /Insulatard/ Insuman Basal

- Keep tests to a minimum. It may be necessary to perform some tests to ensure unpleasant symptoms do not occur due to low or high blood glucose
- It is difficult to identify symptoms due to "hypo" or hyperglycaemia in a dying patient
- If symptoms are observed it could be due to abnormal blood glucose levels
- Test urine or blood for glucose if the patient is symptomatic
- Observe for symptoms in previously insulin treated patient where insulin has been discontinued

For queries relating to the diabetes flowchart please contact the Diabetes Specialist Nurses
For queries relating to palliative care please contact the Palliative Care Team

Appendix 4

Patient Letter – Glucose Monitoring and Steroid use

Dear……

Prior to starting steroid medication a routine Blood Sugar or Capillary Blood Glucose (CBG) test was taken which was found to be higher than normal.

This does not mean you have diabetes

However, taking steroid medication can lead to a rise in blood glucose levels which may need to be treated. Therefore, it is important that you regularly monitor your CBG levels at home using the monitor provided by the hospital.

Please measure your CBG once daily before or after lunch or evening meal for the first 48 hours after starting steroid medication and complete the table below

Start Date:…….

Before breakfast	2 hours after breakfast	Before lunch	2 hours after lunch	Before evening meal	2 hours after evening meal	Before bed

- If your CBG is greater than 12mmol/L on 2 consecutive occasions please contact your GP for further advice.
- If your CBGs are all less than 10mmol/L after 48 hours you can stop intensive monitoring but continue to check CBG once a week whilst taking the steroid medication.
- If your CBG is more than 20mmol/L and you feel unwell please urgently contact your GP for advice or visit your local A+E department.