

Steroid Induced Diabetes



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Outline

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Introduction

- **Glucocorticoids are frequently prescribed to patients with a wide range of inflammatory and autoimmune diseases.**
- **They are associated with a number of side effects, including new-onset hyperglycemia in patients without a history of diabetes or severely uncontrolled hyperglycemia in patients with known DM**
- **Steroid induced hyperglycemia leads to longer hospital stays, delayed wound healing and increased infections**
- **Screening for SIDM should be considered in all patients (especially in those with risk factors) treated with medium to high doses of glucocorticoids.**

- **Low dose** ≤ 7.5 mg
- **Medium dose** > 7.5 mg but ≤ 30 mg
- **High dose** > 30 mg but ≤ 100 mg
- **Very high dose** > 100 mg
- **Pulse therapy** ≥ 250 mg prednisone equivalent a day for one or a few days.
(Prednisolone equivalence a day)

Definition

Steroid induced diabetes

A rise in glucose, related to steroid therapy occurring in people without a known diagnosis of diabetes. This may or may not resolve when the steroids are withdrawn. (JBDS)

Steroid induced hyperglycaemia

The use of steroid treatment in people with pre- existing diabetes resulting in worsening glucose control (JBDS)

Predisposing factors leading to increased risk of hyperglycaemia with steroid therapy

- Pre-existing Type 1 or Type 2 diabetes
- A family history of Type 2 diabetes
- Previous gestational diabetes
- Previous impaired fasting glucose or impaired glucose tolerance
- Polycystic ovarian disease/and or obesity
- Ethnic minority groups
- History of hyperglycaemia with steroid use
- Higher dose of glucocorticoid treatment (prednisolone >20 mg, hydrocortisone >50 mg, dexamethasone >4 mg)
- Longer duration of glucocorticoid treatment
- Advanced age

Prevalence

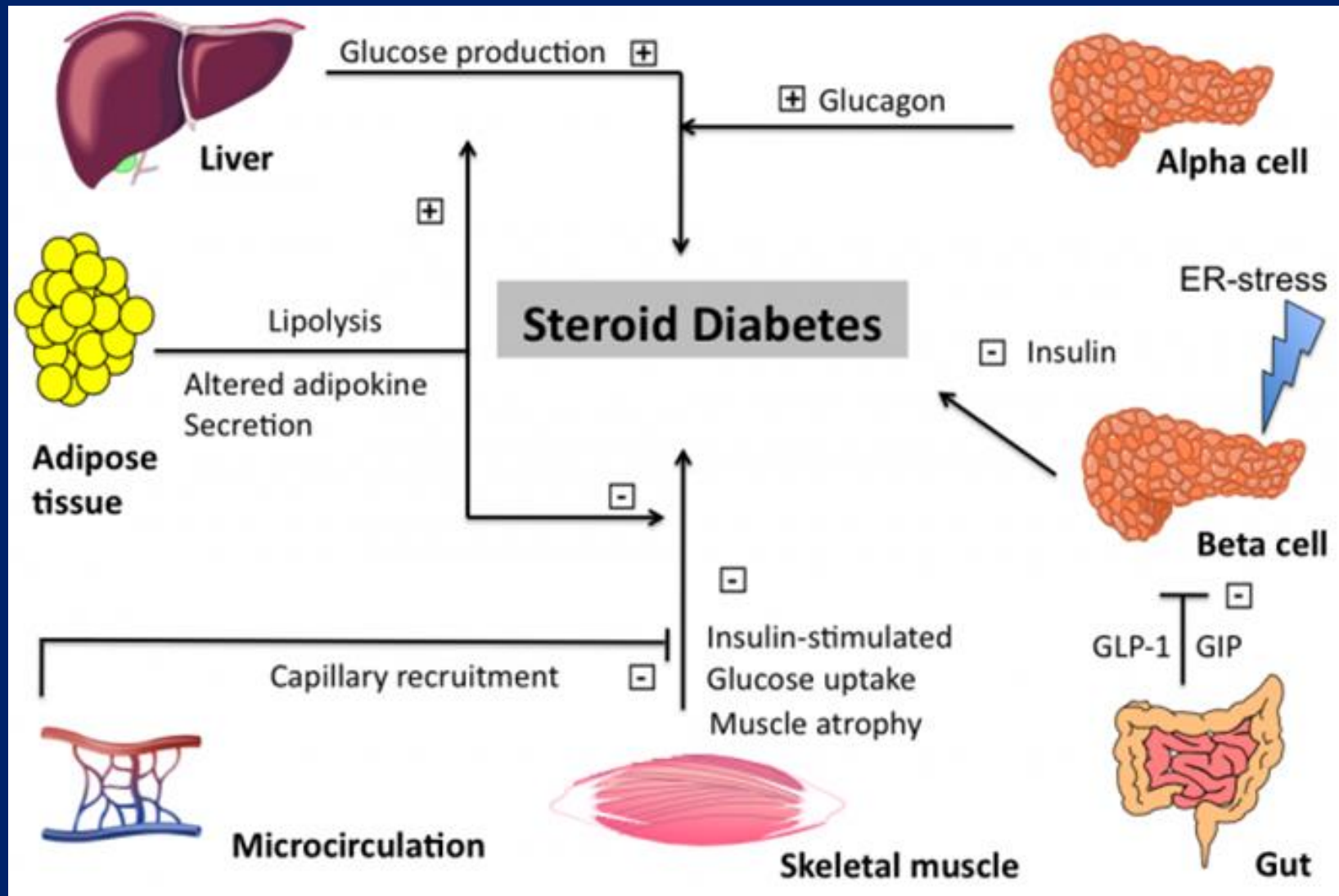
Steroid induced hyperglycemia

- 20%

Incidence of Steroid induced DM

- 30%

Glucocorticoid-induced Hyperglycemia: Mechanisms



Impact of steroid on blood glucose

- A single or short course of steroid (e.g. prednisolone) in the morning → 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.
- Glucose levels rise approximately **4 to 8 hours** following the administration of oral steroids and sooner following the administration of intravenous steroids
- 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.

- Several studies have reported that **transient increases in serum glucose** are associated with **acute inflammatory processes and endothelial dysfunction** in both **diabetic and non-diabetic** patients.
- **transplant population** → steroid hyperglycemia represents a strong predictor of **graft failure** with a **2-3 fold increased risk of fatal and non-fatal cardiovascular events** as compared with non-diabetic patients

Steroids and Diabetes: To Treat or Not?

- **Short courses of GC + minimal hyperglycaemia** = *may not warrant intervention.*
- **Higher dose steroids + longer periods** = *significant symptomatic hyperglycaemia with the potential for acute complications related to hyperglycaemia.*
- **Aims of control of hyperglycaemia:**
 - *ameliorates symptoms*
 - *reduce risk of acute complications*
 - *lessen the increased risk of infections*
 - *Reduces other complications of hyperglycaemia.*

Initial Monitoring and Action Plan:

No pre-existing diagnosis of diabetes

- Monitor once daily. – preferably 1-2 hours post lunch or evening meal.
- Action:
- If the initial CBG >200 mg/dl continue to test once prior to or following lunch or evening meals
- If a subsequent CBG >200 mg/dl → **increased to four times daily** (before meals & bed)
- If the CBG is found to be consistently >200 mg/dl **Treat**

Pre-existing diagnosis of diabetes

- Test four times a day, before or after meals, and before bed, irrespective of background diabetes control
- Action:
- If the CBG consistently >200mg/dl i.e. on two occasions during 24 hours **Treat**

Monitoring in outpatients setting

- capillary blood glucose (CBG) test
 - once or twice weekly, with a 2-hour post-lunch in patients without known diabetes, but who are at risk of steroid-induced diabetes
- HbA1c
 - Before starting steroid
 - Patients treated with corticosteroids for >2 months

Diagnosis

- Similar to the current criteria established by the American Association of Diabetes:
- Fasting blood glucose level of ≥ 126 mg/dL,
- HbA1c $> 6.5\%$ or
- blood glucose > 200 mg/dL 2 h after an oral glucose tolerance test or
- glycemia at any time ≥ 200 mg/dL

TREATMENT

Medication options for people taking once daily steroid therapy

Gliclazide (Best)

- taken once daily
- a maximum of 240mg in the morning (maximum daily dose of 320mg)

Insulin therapies

- Morning administration of **basal human insulin** (Insulatard, Insunova N, Wosulin N)
- Starting dose - 10 units
- increase 10% to 20%, titrated to the blood glucose level (s/t dose increments of up to 40%)
- **Basal analogue insulin** may be appropriate if hyperglycaemia is present throughout the day and into the evening.

Medication options for people taking multiple daily doses of steroid

• **Non-Insulin therapies**

- 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
- GLP-1, DPP-4 inhibitors or SGLT-2 inhibitors - no evidence to support the use

Insulin therapies

- Most appropriate choice
- twice daily premixed, basal bolus, or more complex insulin regimen
- In acutely unwell hospital inpatients with significant hyperglycaemia → variable rate intravenous insulin infusion (VRIII)

Treatment of steroid induced hyperglycemia

Type 2 diabetes – non-insulin therapy

- On gliclazide → increase the morning dose in 40mg increments to a maximum of 240mg, with a total daily dose not exceeding 320mg.
- On metformin → dose titration may be beneficial.
- On DPP-4 inhibitors, GLP-1 analogues or SGLT-2 inhibitors → temporary addition of basal human insulin

Treatment of steroid induced hyperglycemia

Type 2 diabetes – Insulin therapy

Pre-mixed insulin regimen

- Increase the morning insulin dose

Basal-bolus

- Increase the lunch and evening meal short acting boluses

Basal insulin

- switching to morning administration and increase dose in 2-4 unit increments (or by 10-20%) every 24-48 hours
- Monitor closely for early morning hypoglycaemia if basal analogue insulin is used.
- Diabetes teams should be involved if hyperglycaemia persist

After discharge

- **Diagnosis of diabetes should be at least 6 weeks following stopping steroid treatment.**
- **HbA1c as a screening tool, should be delayed until 3 months following steroid cessation**

Outpatient management

High dose steroid

- Same as inpatient management

Chronic low dose steroid

- Metformin is first line
- Pioglitazone
- DPP4 inhibitors

PATIENT EDUCATION

- **Blood glucose monitoring → to prevent the development of hyperglycemic emergencies**
- **Typical hyperglycemic symptoms → check their capillary blood glucose.**
- **Follow-up → an HbA1c test 12 weeks following completion of glucocorticoid therapy to re-assess their diabetes status**
- **On agents that can cause hypoglycemia need to check their blood glucose levels more frequently than usual 1 to 3 days after a glucocorticoid dose reduction**

Summary

- **Steroid induced hyperglycemia/diabetes is common**
- **Steroid induced hyperglycemia leads to longer hospital stays, delayed wound healing, increased infections and acute inflammatory processes and endothelial dysfunction**
- **Screening should be considered in all patients (especially in those with risk factors) treated with medium to high doses of glucocorticoids.**
- **Monitoring**
 - No pre-existing DM – once daily**
 - Pre-existing DM – four times a day**
- **Treatment**
 - once daily steroid therapy – gliclazide, Basal human insulin**
 - Multiple dose steroid - Insulin**

References

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THANK YOU