Steroids and Diabetes

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Case

• 33-year-old female
• Referred to Diabetes Clinic from Hepatology Clinic, BMC on December 2011 because of “steroid-induced diabetes”
• In 2004 she was diagnosed with autoimmune hepatitis
• Started then on 40mg prednisolone once daily
• Developed steroid-induced diabetes
• Treated with insulin
• In 2008 steroids were withdrawn
• Her blood glucose returned to normal and insulin was stopped
Case

• On December 17\textsuperscript{th} 2011 she presented to Hepatology Clinic, BMC with elevated liver enzymes while on 50mg azathioprine
• Started on prednisolone 30mg once daily
• Her FBG before prednisolone initiation was 77mg/dl
• Ten days later she presented with FBG of 197mg/dl and referred to Diabetes Clinic, BMC
Case

• On December 28\textsuperscript{th}, 2011 she was seen in Diabetes Clinic
  – asymptomatic
  – her father has diabetes (? Type)
  – BMI 21.9 kg/m\textsuperscript{2}
  – her FPG was 197mg/dl and PPG 312mg/dl
  – started on pre-mixed insulin 15 units AM and 10 units PM

• One week later
  – FPG 116mg/dl, PPG 216mg/dl
  – No dose change was made as she starts the tapering of steroid
Case

• January 30\textsuperscript{th}, 2012
  – She was on 20mg prednisolone
  – FPG 62 mg/dl
  – PPG 172 mg/dl
  – pre-mixed insulin decreased to 12 units AM and 10 units PM

• March 2012
  – Prednisolone increased to 40mg/dl
  – FPG 262mg/dl, PPG >500mg/dl
  – Pre-mixed insulin increased to 22units AM and 16 units PM
Case

- **April 2012**
  - Started prednisolone tapering
  - Advised to adjust insulin dose according to self-monitored BG
- **July 2012**
  - Prednisolone 5mg/day
  - FPG < 100mg/dl
  - No hypoglycemia
  - Pre-mixed insulin 12units AM and 12units PM
  - She is advised to monitor PPG
Steroids and endocrinopathies

- Diabetes and worsening of hyperglycemia in pre-existing diabetes
- Cushing’s syndrome
- Adrenal suppression
- Osteoporosis
- Dyslipidemia
Steroid-induced hyperglycemia
Pathophysiology

- Increased hepatic glucose production
- Decreased muscle and fat glucose uptake
- Decreased insulin production and secretion
Typical pattern

Normal or minimally elevated fasting glucose (FBG)
Exaggeration of the postprandial glucose (PPG) rise

• FBG is likely to increases if:
  – Dose $\geq 40$ mg prednisolone equivalent
  – Steroids are given twice daily

• Blood glucose start to rise 6 hours after dose administration
Steroid-induced hyperglycemia

• How common?
• Can it be predicted?
• How to screen for it?
• When and how to treat it?
Steroid-induced hyperglycemia
Prevalence

• Steroids are the most common cause of drug-induced hyperglycemia
• Steroids are commonly used and misused drugs
Steroid-induced hyperglycemia
Prevalence

Use of systemic steroids in medical ward (Benghazi)
9% of hospitalized patients received systemic steroids

<table>
<thead>
<tr>
<th>Indication</th>
<th>Frequency</th>
</tr>
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<tbody>
<tr>
<td>Bronchial asthma</td>
<td>34.6%</td>
</tr>
<tr>
<td>Stroke</td>
<td>23%</td>
</tr>
<tr>
<td>COPD</td>
<td>15.5%</td>
</tr>
<tr>
<td>Multiple sclerosis</td>
<td>7.7%</td>
</tr>
<tr>
<td>Brain tumour</td>
<td>5.7%</td>
</tr>
<tr>
<td>Myositis</td>
<td>5.7%</td>
</tr>
</tbody>
</table>

Elmehdawi RR. Jamahiriya Med J, 2006. 6 (2); 145-147.
Steroid-induced hyperglycemia Prevalence

• Exact prevalence is unknown
• Virtually all patients with pre-existing diabetes will have exacerbation of hyperglycemia when steroids are given
• Prevalence of new-onset diabetes in steroid-treated patients varies between 10-50%
• The odds ratio for developing new-onset diabetes in patients treated with steroids is 1.5-2.5
Steroid-induced hyperglycemia
Predictors

- Age
- Body weight
- Family history of type 2 diabetes
- Personal history of gestational diabetes
- Dose of steroid
- Route of steroid administration
- ? Duration of steroid therapy
- Type of glucocorticoid does not seem to influence risk of hyperglycemia
Steroid-induced hyperglycemia

Predictors

- Risk of steroid-induced diabetes according to dose prescribed

<table>
<thead>
<tr>
<th>Dose (prednisolone equivalent)</th>
<th>OR</th>
</tr>
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<tbody>
<tr>
<td>&lt; 10 mg/day</td>
<td>1.77</td>
</tr>
<tr>
<td>10-20 mg/day</td>
<td>3.02</td>
</tr>
<tr>
<td>20-30 mg/day</td>
<td>5.82</td>
</tr>
<tr>
<td>&gt;30 mg/day</td>
<td>10.34</td>
</tr>
</tbody>
</table>

Steroid-induced hyperglycemia Screening

The only published guidelines are the 2003

*International consensus guidelines on new-onset diabetes after transplantation:*

- Recommendation: screen with **FBG**
  - once a week for first 4 weeks post-transplant
  - at 3, 6 and 12 months post-transplant
  - annually after the first year

Steroid-induced hyperglycemia Screening

- In a study of non-diabetic patients with primary renal disease receiving 0.75mg/kg/day of prednisolone:
  - 40.5% found to have post-lunch glucose > 200mg/dl but normal FBG levels

Steroid-induced hyperglycemia Screening

• An experts opinion:
  – Warn patients of typical hyperglycemic symptoms
  – Screen with 1- or 2-hr post-lunch glucose weekly until steroids tapering starts then reduce the frequency of testing accordingly
  – PPG ≥ 200mg/dl indicates development of steroid-induced diabetes
  – PPG 140-199mg/dl indicates impaired glucose tolerance
  – HbA1c is not useful to screen for steroid-induced diabetes
  – Screen high risk patients for pre-existing diabetes with FBG before starting steroid therapy
Steroid-induced hyperglycemia
Treatment

• Decision on when to treat and how to treat depends on:
  – Duration of steroid therapy
  – Degree of hyperglycemia
  – Underlying conditions and comorbidities
Steroid-induced hyperglycemia
Treatment

When to treat?

• Outpatients patients receiving short courses of steroids:
  – No need for therapy if they are asymptomatic or mildly symptomatic

• Hospitalized patients for 3 days or more with a FBG > 110 mg/dl or a PPG > 140 mg/dl would be candidates for therapy

• All patients on long-term steroid therapy (>4 weeks) should be treated if hyperglycemia develops
Steroid-induced hyperglycemia Treatment

How to treat?

• 2003 International consensus guidelines on new-onset diabetes after transplantation: “treatment steroid-induced diabetes is similar to that of type 2 diabetes”

• 2012 Endocrine Society Clinical Practice Guideline on Management of Hyperglycemia in Hospitalized Patients in Non-Critical Care Setting “we recommend that insulin therapy be initiated for patients with persistent hyperglycemia while receiving glucocorticoid therapy”
Steroid-induced hyperglycemia

Treatment

How to treat?

• An experts opinion
  – If PPG <300 mg/dl: treat with an oral hypoglycemic drug, with or without insulin
  – If PPG>300 mg/dl or hospitalized patient: treat with insulin

Steroid-induced hyperglycemia
Treatment

How to treat?

• Diet and exercise
  – Not practical

• Oral hypoglycemic agents
  – Almost all agents can be used
  – Limitations: may not target PPG, inflexible, slow onset of action, risk of drug, a lot of contraindications and side effects

• Insulin
  – Most appropriate agent
  – Prandial insulin is the best drug to target PPG, suitable in multiple medical illnesses, unlimited dosing
Steroid-induced hyperglycemia
Treatment

How to treat?

• Starting insulin
  – Total daily dose (TDD): 0.1-0.4 units/kg
  – The main need is prandial insulin
  – If only PPG is elevated and FBG is normal:
    • NPH
    • Premixed (NPH and regular)  
      – A pre-lunch or pre-dinner prandial insulin can be added
  – If both PPG and FBG are elevated
    • Regimens similar to those used in type 1 and type 2 diabetes
      with the exception of increasing the ratio of prandial insulin
      to 50-70% of TDD
Steroid-induced hyperglycemia
Treatment

How to treat?

• Adjusting insulin
  – Insulin should be adjusted to achieve the following targets
    • FBG 70-130 mg/dl
    • PPG< 180 mg/dl
  – When tapering steroid:
    • Reduce or stop the basal insulin first
    • Reduce or stop the evening doses first
Steroid-induced hyperglycemia
Treatment

How to treat?

• In a patient with pre-existing diabetes
  – If on diet alone, may need starting an oral hypoglycemic agent
  – If on oral hypoglycemic therapy, increasing the dose, adding another agent or starting insulin may be necessary
  – If on insulin, doses could increase by up to 30-100%
Steroid-induced hyperglycemia

**Will it resolve when steroids are stopped?**

- Resolution of hyperglycemia is expected in patients with normal glucose tolerance before starting steroid therapy.
- When both FBG and PPG in the lower target range and the steroid dose is less than 7.5mg prednisolone equivalent, anti-hyperglycemic therapy is stopped for 3-7 days to check for diabetes resolution.
- However there is no way to predict whether glucose will return to normal upon steroid withdrawal since steroid therapy may have only unmasked a pre-existing diabetes.
Key Messages

- Steroid-induced diabetes is a common side effect of steroid therapy.
- High risk patients should be screened for undiagnosed diabetes before starting steroid therapy.
- The primary effect of steroids is on PPG.
- Screening for steroid-induced diabetes by PPG is recommended for all patients treated with steroids.
- Oral agents can be used for mild cases but insulin is the most appropriate therapy.
- Hyperglycemia usually normalises after steroid withdrawal unless there is a pre-existing diabetes.
Thank You