50 Year Old Female recently diagnosed with IPF and Steroid Induced Diabetes

Abusag Milad MD
First year fellow
Endorama 2/6/2014
50 year old F with PMH of HTN, Afib, Obesity
Doing well until 2/2013
- c/o worsening SOB + dry cough and Dx with IPF
- Started on Prednisone 80 mg daily >> tapered slowly.
- HbA1c was 5.6 four months prior to steroid
- After steroid BS >200
- HbA1C (6.6) three months after started on steroid
- Started on Lantus and Novolog
ROS

• **Constitutional**: Negative
• **HENT**: negative for headache, blurred vision, No sore throat
• **Cardio/pulm**: No CP, +ve SOB on exertion no palpitation, no orthopnea or PND
• **GI**: No pain, + diarrhea, no vomiting, no melena or hematochezia
• **GU**: Negative
• **Skin/MSK**: no dry skin, no hair loss, no rash, no striae
• **Neuro**: no headache, no weakness, no numbness, no tingling,
• **Psych**: negative
PMH:
- HTN
- Obesity
- Afib

Family History:
- Hypothyroidism (maternal grandmother)
- DM (mother). Has 2 daughter no h/o DM
- CAD (father)

Surgical history:
- Non

Social history
- Never smoke, drink alcohol socially, no illicit drugs.

Home medications
- Spironolactone 25 mg po daily
- Bisoprolol 5 mg po daily
- Lantus 10 units daily
- Novolog 4 units with meals + LDSSI (1-5)
- Warfarin 5 mg po daily
- Prednisone 10 mg daily
- Bactrim (SS) 1 tab daily
On Examination

- **Vitals**: BP 134/77 | Pulse 85, no fever, RR 14. Wt 101.5kg, BMI 36.2
- **General**: Obese, awake alert, setting comfortable on exam table
- **HEENT**: normocephalic non traumatic, no plethora, no supraclavicular fullness, EOM normal
- **Neck**: supple, no LN enlargement, no thyromegaly, no acanthosis nigricans
- **CVS/Pulm**: inspiratory crackles bilateral mainly basally, S1 + S2, no murmur.
- **Abd**: soft lax, no organomegaly, no tenderness, audible bowel sounds.
- **Skin**: warm, no rash, no acanthosis nigricans, no striae
- **Neuro**: CN intact, sensation normal, normal reflexes
- **Psych**: normal mood, and affect
## General Labs

<table>
<thead>
<tr>
<th>Test/results</th>
<th>10/2012 (12pm)</th>
<th>2/2013 (4pm)</th>
<th>5/2013 (10am)</th>
<th>11/2013 (5pm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBC</td>
<td>Normal</td>
<td>normal</td>
<td>/</td>
<td>normal</td>
</tr>
<tr>
<td>Glucose</td>
<td>86</td>
<td>100</td>
<td>216</td>
<td>98</td>
</tr>
<tr>
<td>HbA1c</td>
<td>5.6</td>
<td>/</td>
<td>6.6</td>
<td>6.8</td>
</tr>
<tr>
<td>K</td>
<td>3.7</td>
<td>3.8</td>
<td>4.4</td>
<td>4.2</td>
</tr>
<tr>
<td>Carbon Dioxide</td>
<td>26</td>
<td>29</td>
<td>30</td>
<td>29</td>
</tr>
<tr>
<td>BUN</td>
<td>8</td>
<td>14</td>
<td>18</td>
<td>11</td>
</tr>
<tr>
<td>Cr</td>
<td>0.8</td>
<td>1</td>
<td>0.8</td>
<td>1.0</td>
</tr>
<tr>
<td>GFR (Calc)</td>
<td>72</td>
<td>63</td>
<td>72</td>
<td>58</td>
</tr>
<tr>
<td>ALT</td>
<td>36</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AST</td>
<td>25</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALP</td>
<td>9</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
1). How common is steroid-induced diabetes mellitus?
2). Is there a threshold dose of steroids that will induce diabetes in patients?
3) Is there any role for oral agents in treatment of SID?
4). How should we initiate insulin therapy in these patients and then adjust it with changing steroid dose?
Is it common?

Published Odds Ratios (and Confidence interval) for Occurrence of New onset DM with use of Glucocorticoid therapy

<table>
<thead>
<tr>
<th>Reference</th>
<th>Population</th>
<th>Odds ratio (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gulliford et al (4), 2006</td>
<td>United Kingdom health improvement network</td>
<td>1.36 (1.10 – 1.69)</td>
</tr>
<tr>
<td>Gurwitz et al (5), 1994</td>
<td>New Jersey Medicaid database</td>
<td>2.23 (1.92 – 2.59)</td>
</tr>
<tr>
<td>Conn &amp; Poynard (6), 1994</td>
<td>Meta-analysis</td>
<td>1.7 (1.12 – 2.16)</td>
</tr>
<tr>
<td>Blackburn et al (7), 2002</td>
<td>Ontario Drug Benefit Database</td>
<td>2.31 (2.11 – 2.54)</td>
</tr>
</tbody>
</table>

*** Most of studies showed incidence of DM with steroid therapy 10–20%

Endocr Pract. 2009;15(No. 5)
Prevalence of Corticosteroid related hyperglycemia in hospitalized patient

Amy Calabrese Donihi, PharmD, BCPS,1 Ditina Raval, PharmD,1 Melissa Saul, MS,2 Mary T. Korytkowski, MD,2,4 and Michael A. DeVita, MD.
UPMC 2006

✓ Retrospective review of electronic medical records of patients admitted to the general medicine service at UPMC during a 1-month period (June/1/03 – June/30/03)
✓ Patients receiving high-dose corticosteroid therapy, defined as ≥ 40 mg of prednisone, ≥ 160 mg of hydrocortisone, ≥ 32 mg of methylprednisolone, or ≥ 6 mg of dexamethasone per day for at least 2 days
✓ Total number of admission (617) and number of patients received high dose steroid (50 patients).
✓ 34 patients has no h/o DM in the past

Endocr Pract. 2006;12(No. 4)
## Conclusion

Hyperglycemia was documented in **32 of these 50 patients (64%)**, and multiple hyperglycemic episodes occurred in **26 (52%)**. Among patients without a history of diabetes, **19 of 34 (56%)** had hyperglycemia at least once.

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**Endocr Pract. 2006;12(No. 4)**
High-Dose But Not Low-Dose Dexamethasone Impairs Glucose Tolerance

KAZUNARI MATSUMOTO, HIRONORI YAMASAKI, SHOICHI AKAZAWA, HIROYUKI SAKAMAKI, MIWA ISHIBASHI, NOR10 ABIRU, SHIGEO UOTANI, HIROSHI MATSUO, YOSHIHIKO YAMAGUCHI, KUMPEI TOKUYAMA, AND SHIGENOBU NAGATAKI

Department of Internal Medicine, Nagasaki University School of Medicine (K.M., H.Y., S.A., H.S., M.Z., N.A., S.U., H.M., Y.Y., S.N.), Nagasaki 852, Japan;

JCEM . 1996 Vol81 . No 7
Fasting Glucose/Insulin level before and after different doses of steroid

- Sample size 20 young healthy men. BMI 20-22, age 20-31, no previous h/o DM and no FH of DM
- Ten subjects received a low dose of dexamethasone (2 mg/day) for 3 days, and the other 10 received a high dose of dexamethasone (6 mg/day) for 3 days.

<table>
<thead>
<tr>
<th>Steroid doses</th>
<th>Fasting BS mmol/l</th>
<th>Fasting insulin (pmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>Low dose</td>
<td>4.61 +/- 0.11</td>
<td>2.84 +/- 0.11</td>
</tr>
<tr>
<td>High dose</td>
<td>4.57 +/- 0.12</td>
<td>5.08 +/- 0.12</td>
</tr>
</tbody>
</table>

P value <0.05

JCEM . 1996 Vol81 . No 7
Glucose/Insulin level with different doses of steroid

Fig. 1. Time course of mean plasma glucose (top) and insulin (bottom) concentrations during frequently sampled intravenous glucose tolerance test before and after the administration of dexamethasone. A, Low-dose dexamethasone (2 mg/day for 3 days); B, high-dose dexamethasone (6 mg/day for 3 days). ○, Before dexamethasone; ●, after dexamethasone.
Impaired -cell compensation to dexamethasone-induced hyperglycemia in women with polycystic ovary syndrome

David A. Ehrmann,1 Elena Breda,2 Matthew C. Corcoran,1 Melissa K. Cavaghan,1 Jacqueline Imperial,1 Gianna Toffolo,2 Claudio Cobelli,2 and Kenneth S. Polonsky3

Department of Medicine, University of Chicago, Chicago, Illinois 60637; 2Department of Electronics and Informatics, University of Padua, Padua, 35131 Italy; and 3Department of Medicine, Washington University School of Medicine, St. Louis, Missouri 63110
Studied 10 PCOS and 6 control subjects with normal glucose tolerance

An oral glucose tolerance test (OGTT) and a graded glucose infusion protocol were performed at baseline and after subjects took 2.0 mg of dexamethasone orally

Those with normal glucose tolerance had a graded glucose infusion (GGI) procedure 2–3 days after the OGTT. One and two weeks later, respectively, the OGTT and GGI were repeated after oral administration of dexamethasone, 1 mg at 11 PM on the night before study and 1 mg at 8 AM on the morning of study
women with PCOS and normal glucose tolerance would be less able than control subjects to maintain normoglycemia in response to augmentation of insulin resistance induced by low doses of dexamethasone.
Oral agents for treatment of steroid induced diabetes
Pioglitazone in the Management of Diabetes Mellitus after Kidney/Liver Transplantation

Priya Luther and David Baldwin Jr,
Section of Endocrinology, Department of Internal Medicine, Rush University Medical Center, Chicago, IL

American Journal of Transplantation 2004; 4: 2135–2138
<table>
<thead>
<tr>
<th>Pt</th>
<th>DM (pre/post)</th>
<th>BMI</th>
<th>Age/sex</th>
<th>Ethnicity</th>
<th>Transplant</th>
<th>Tacrolimus dose</th>
<th>Prednisone dose</th>
<th>DM Rx</th>
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<tbody>
<tr>
<td>1</td>
<td>Post</td>
<td>33</td>
<td>48 M</td>
<td>cauc</td>
<td>Kidney</td>
<td>2</td>
<td>5</td>
<td>insulin</td>
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<tr>
<td>2</td>
<td>pre</td>
<td>34</td>
<td>68 F</td>
<td>AA</td>
<td>Kidney</td>
<td>4</td>
<td>5</td>
<td>insulin</td>
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<td>3</td>
<td>pre</td>
<td>27</td>
<td>57 M</td>
<td>Hisp</td>
<td>Kidney</td>
<td>2</td>
<td>5</td>
<td>insulin</td>
</tr>
<tr>
<td>4</td>
<td>pre</td>
<td>32</td>
<td>54 M</td>
<td>Asian</td>
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<td>5</td>
<td>4</td>
<td>insulin</td>
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<tr>
<td>5</td>
<td>pre</td>
<td>29</td>
<td>43 F</td>
<td>Cauc</td>
<td>Liver</td>
<td>5</td>
<td>20</td>
<td>insulin</td>
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<td>6</td>
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<td>31</td>
<td>47 M</td>
<td>Asian</td>
<td>Kidney</td>
<td>1</td>
<td>5</td>
<td>insulin</td>
</tr>
<tr>
<td>7</td>
<td>post</td>
<td>31</td>
<td>49 F</td>
<td>Hisp</td>
<td>Kidney</td>
<td>5</td>
<td>15</td>
<td>insulin</td>
</tr>
<tr>
<td>8</td>
<td>pre</td>
<td>34</td>
<td>49 M</td>
<td>Cauc</td>
<td>Kidney</td>
<td>3</td>
<td>5</td>
<td>insulin</td>
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<tr>
<td>9</td>
<td>pre</td>
<td>29</td>
<td>55 M</td>
<td>AA</td>
<td>Liver</td>
<td>5</td>
<td>5</td>
<td>insulin</td>
</tr>
<tr>
<td>10</td>
<td>post</td>
<td>32</td>
<td>57 M</td>
<td>Cauc</td>
<td>Kidney</td>
<td>2</td>
<td>5</td>
<td>insulin</td>
</tr>
</tbody>
</table>

Patients were followed for mean of 242 days (range: 104–431 days) after the initiation of pioglitazone

*American Journal of Transplantation 2004; 4: 2135–2138*
- Mean HBA1C 8.36% ± 1.5% pre-pioglitazone, 7.08% ± 1.5% post-pioglitazone.
- Benefit was equally present in patients with pre-existing diabetes mellitus and in those with PTDM
- Total daily insulin dose 125.1 ± 28.1 units pre-pioglitazone, 80.6±22.8 units post-pioglitazone, p=0.002

*American Journal of Transplantation 2004; 4: 2135–2138*
Glucagon-Like Peptide-1 Receptor Agonist Treatment Prevents Glucocorticoid-Induced Glucose Intolerance and Islet-Cell Dysfunction in Humans

DANIEL H. VAN RAALTE MD, RENATE E. VAN GENUGTEN MD, MARGOT M.L. LINSSSEN MSC2
Department of Internal Medicine, VU University Medical Center, Amsterdam, 2011

- Eight healthy men were included.
- Age 18–35 years, BMI=22.0–28.0 kg/m2
- Exclusion criteria were h/o DM, use of any medication cause insulin resistance, first-degree relative with type 2 diabetes, smoking, shift work, a history of GC use, and recent changes in weight or physical activity.
- 80 mg Prednisone + (placebo vs Exenatide)
- The meal contained 905 kcal (50 g fat, 75 g carbohydrates, 35 g protein)
The effect of PRED with or without concomitant EXE infusion on plasma glucose (A), insulin (B), C-peptide (C), and glucagon (D) levels during the meal challenge

Diabetes care, volume 34, Feb 2011
DPP-4 inhibitors in the treatment of hyperglycemia induced by chronic use of steroids

Tamez AL, Quintanilla DL, Cisneros-Franco JM, Hernández-Coria MI, González-González JG

Januvia 100 mg po daily was given to 19 patient with SIH for 6 months

<table>
<thead>
<tr>
<th>No of pt with SIH</th>
<th>19</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Male (14), Female (5)</td>
</tr>
<tr>
<td>Mean age</td>
<td>42 +/- 7</td>
</tr>
<tr>
<td>Mean BMI</td>
<td>31 +/- 1.37</td>
</tr>
<tr>
<td></td>
<td><strong>Before</strong></td>
</tr>
<tr>
<td>Mean BS (P&lt; 0.001)</td>
<td>184 +/- 16</td>
</tr>
<tr>
<td>Mean HbA1c (P&lt; 0.001)</td>
<td>8.1 +/- 0.84</td>
</tr>
</tbody>
</table>

*Journal Endocrinology and Nutrition 2011, Issue 3, Spain*
Nateglinide (Starlix)

Glucocorticoid-Induced Diabetes Mellitus: Prevalence and Risk Factors in Primary Renal Diseases

Department of Medicine, Shiga University of Medical Science. Division of Nephrology
Japan

Nephron Clin Pract 2007;105:c54–c57
✓ Study period: April 2002 and June 2005.
✓ Total number of patients 42
✓ Patients with previous diagnosis of DM, impaired fasting before the corticosteroid therapy were excluded from the study.
✓ DM Dx with **2hrs post prandial >200**
✓ Oral prednisolone (PSL) at an initial dose of **0.8–1.0 mg/kg/day** for at least 4 weeks.
✓ All patients were treated without any other immunosuppressant such as cyclosporine.
- 17 out of 42 (40%) developed DM (2 hrs BS >200)
- In 7 patients marked hyperglycemia (>250), was found after lunch, but not after either breakfast or dinner
- All of the 7 patients with marked postprandial hyperglycemia were given nateglinide 10 min before lunch (90 mg daily).

The diabetes states in 7 patients who developed marked hyperglycemia (250 mg/dl) before (open circle) and after (close triangle) the treatment with nateglinide (10 min before lunch, 90 mg daily).
**Insulin**

**Glucocorticoid -Induced Hyperglycemia**

John N. Clore, MD, MS; Linda Thurby-Hay, MS, RN, ACNS-BC  
Division of Endocrinology and Metabolism, Virginia Commonwealth University, Richmond, Virginia.

- Electronic (MEDLINE) and a library review of the existing pertinent literature published from 1950 to March 2009.
- Recommended insulin types and Wt based starting dose.
## Suggested Dosages of NPH Insulin for Tapering Dosages of Glucocorticoids

<table>
<thead>
<tr>
<th>Prednisone dose (mg/day)</th>
<th>NPH Insulin dose (U/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;40</td>
<td>0.4 u/kg</td>
</tr>
<tr>
<td>30</td>
<td>0.3 u/kg</td>
</tr>
<tr>
<td>20</td>
<td>0.2 u/kg</td>
</tr>
<tr>
<td>10</td>
<td>0.1 u/kg</td>
</tr>
</tbody>
</table>

- NPH peak 6-8hrs and last for 12-14hrs
- Lantus preferred if Dexamethasone used or prednisone given twice a day

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Diabetes care, volume 34, Feb 2011
Dose adjustment for patient on insulin

- Increase TDD by 20-40% with start of high dose steroid.
- Increase correctional insulin by one step (low to moderate dose)
- Adjust insulin dose as needed
Back to my patient

- Current insulin regimen ((Lantus 10 Units daily + Novolog 4 units with meals + Low dose SSI)). Still on prednisone 10mg daily.

Plan:
- Will try Januvia 100 mg daily
- ? Add Starlix (Nateglinide) 60 mg po daily if BS still high
Incidence of SID about 10-20% but prevalence can be as high as 50-60% with high dose steroid.

PCOS and normal glucose tolerance would be less able than control subjects to maintain normoglycemia in response to augmentation of insulin resistance induced by low doses of dexamethasone.

Pioglitazone can be use to decrease insulin requirement and improve HbA1c in absence of contraindication.

GLP-1 agonist, DPP-4 inhibitors and meglitinide showed benefit in SID.

Wt based insulin dose recommended in pt never been on insulin before.
References


Thank You

Milad Abusag, MD
Endorama 2/6/2014