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

Abusag Milad MD

First year fellow
Endorama 2/6/2014

HPI

- ❖ **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

Test/results	10/2012 (12pm)	2/2013 (4pm)	5/2013 (10am)	11/2013 (5pm)
CBC	Normal	normal	/	normal
Glucose	86	100	216	98
HbA1c	5.6	/	6.6	6.8
K	3.7	3.8	4.4	4.2
Carbon Dioxide	26	29	30	29
BUN	8	14	18	11
Cr	0.8	1	0.8	1.0
GFR (Calc)	72	63	72	58
ALT	36			
AST	25			
ALP	9			

Clinical Qs

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

Reference	Population	Odds ration (CI)
Gulliford et al (4), 2006	United Kingdom health improvement network	1.36 (1.10 – 1.69)
Gurwitz et al (5), 1994	New Jersey Medicaid database	2.23 (1.92 – 2.59)
Conn & Poynard (6), 1994	Meta-analysis	1.7 (1.12 – 2.16)
Blackburn et al (7), 2002	Ontario Drug Benefit Database	2.31 (2.11 – 2.54)

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

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 $\geq$40 mg of prednisone, $\geq$160 mg of hydrocortisone, $\geq$32 mg of methylprednisolone, or $\geq$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

Characteristic	All patients (n=50)		Pts without known DM (n=34)	
	Hyperglycemia at least once (n=32) 64%	Multiple episodes of hyperglycemia (n=26) >>52%	Hyperglycemia at least once (n=19) 56%	Multiple episodes of hyperglycemia (n=14) >> 41%
Male no	13	10	11	7
Known DM	4	12	0	0
Duration of GC therapy (days)	4.79 +/- 3.87	7.3 +/- 4.23	4.85 +/- 4.15	7.14 +/-3.76
Meds causing hyperglycemia	5	5	4	3
Length of hospital stay	8.58 +/- 6.07	18.42 +/- 12.88	8.25 +/- 6.04	19.86 +/- 13.13

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

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;

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.

Steroid doses	Fasting BS mmol/l		Fasting insulin (pmol/l)	
	Before	After	Before	After
Low dose	4.61 +/- 0.11	2.84 +/- 0.11	27.2 +/-3.4	47.4 +/- 5.2
High dose	4.57 +/- 0.12	5.08 +/- 0.12	24.9 +/- 2.4	57.1 +/- 5.8

P value <0.05

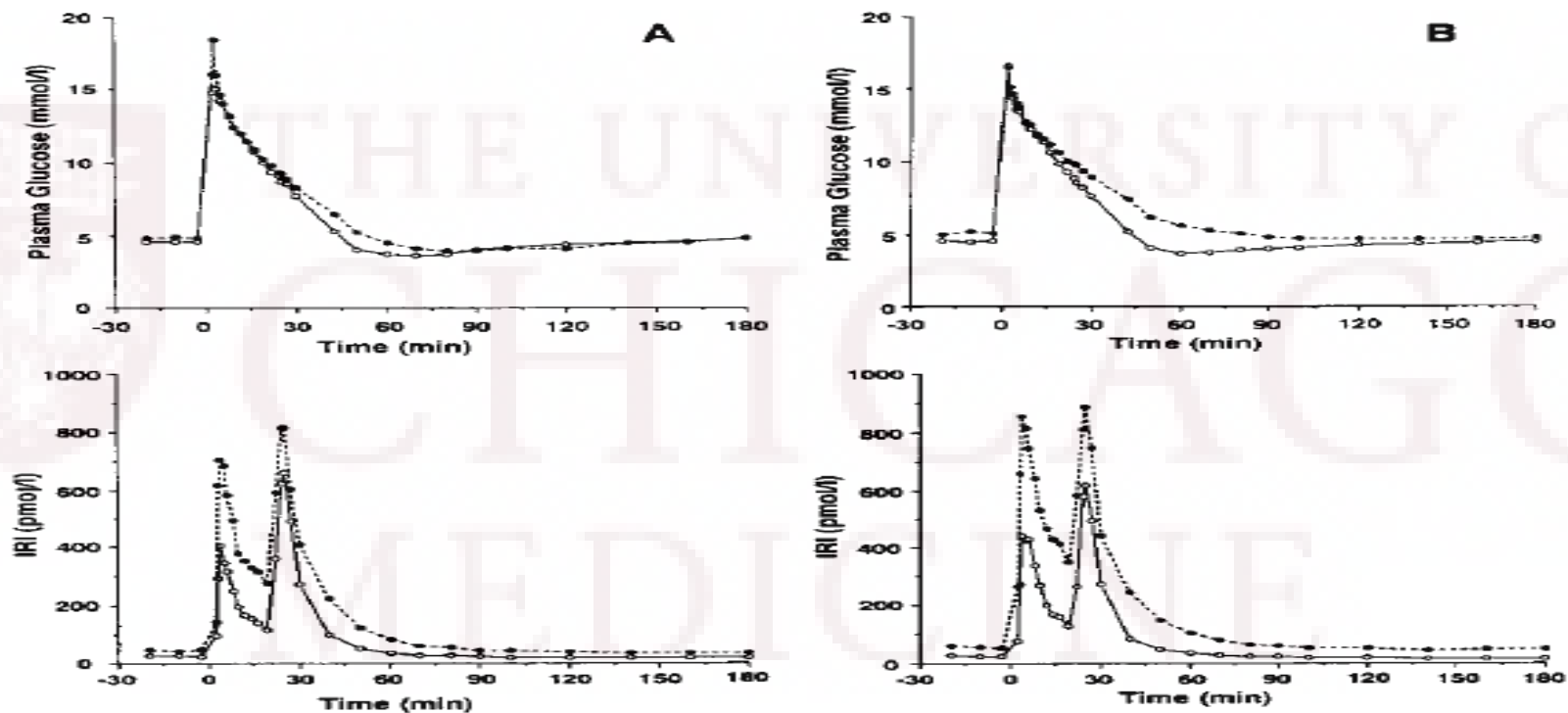# Glucose/Insulin level with different doses of steroid

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. Polonsky[3]

Department of Medicine, University of Chicago, Chicago, Illinois 60637; [2]Department of Electronics and Informatics,

University of Padua, Padua, 35131 Italy; and [3]Department 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**
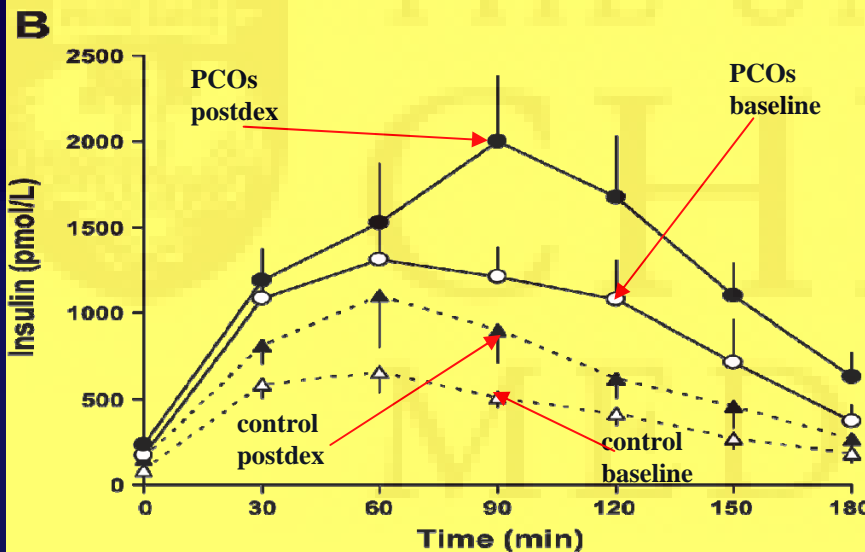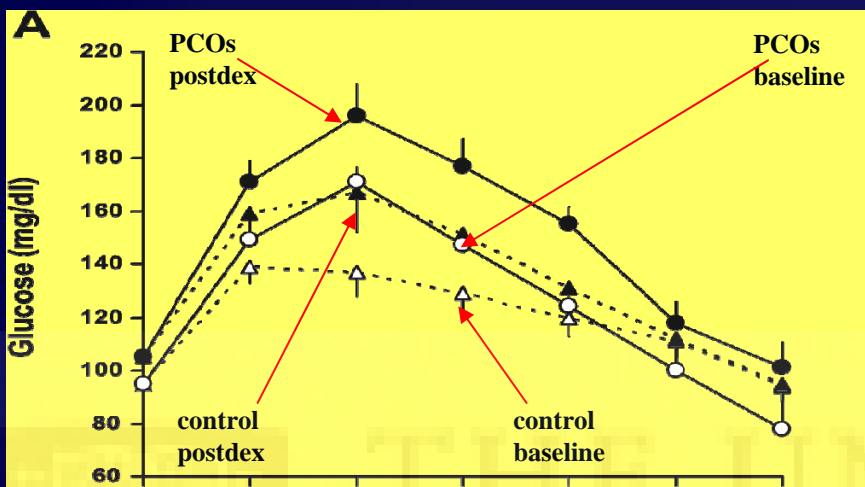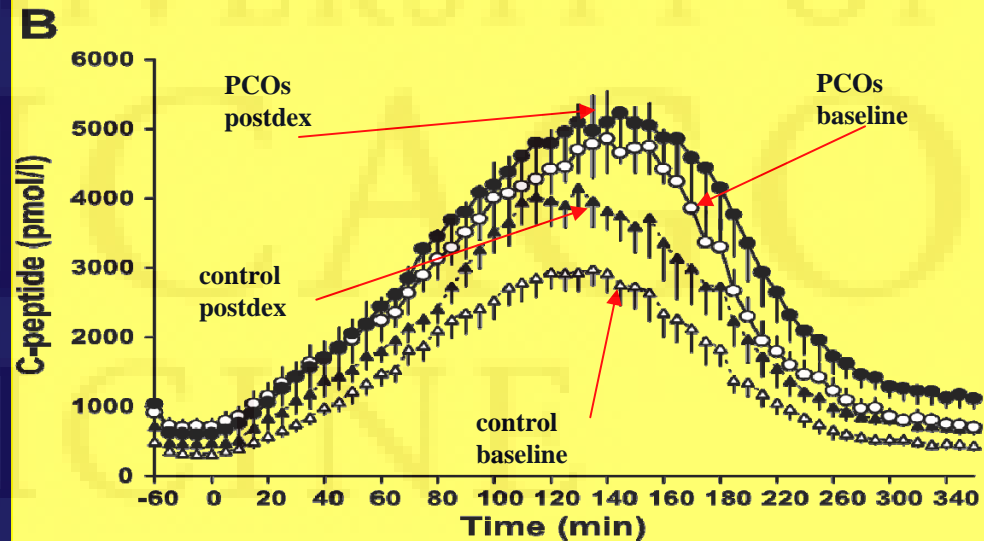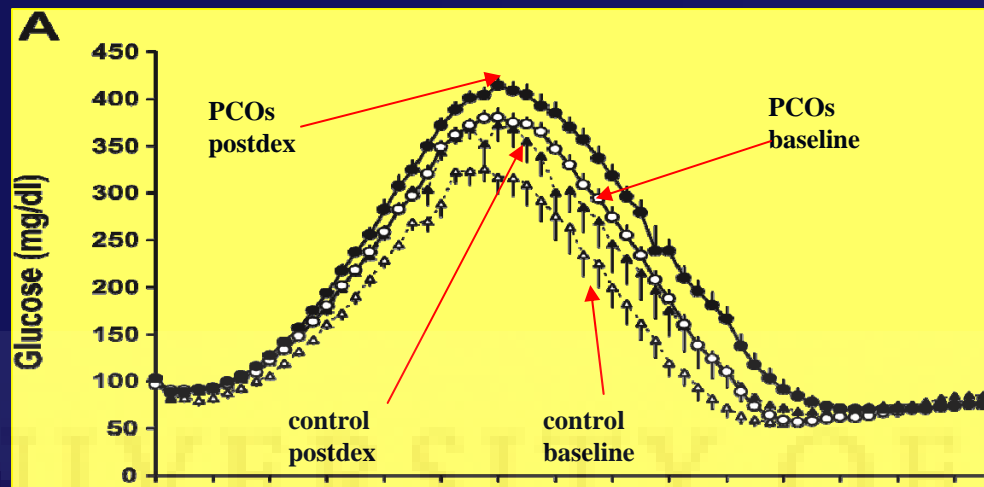
OGTT / **GGT**

❖ 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
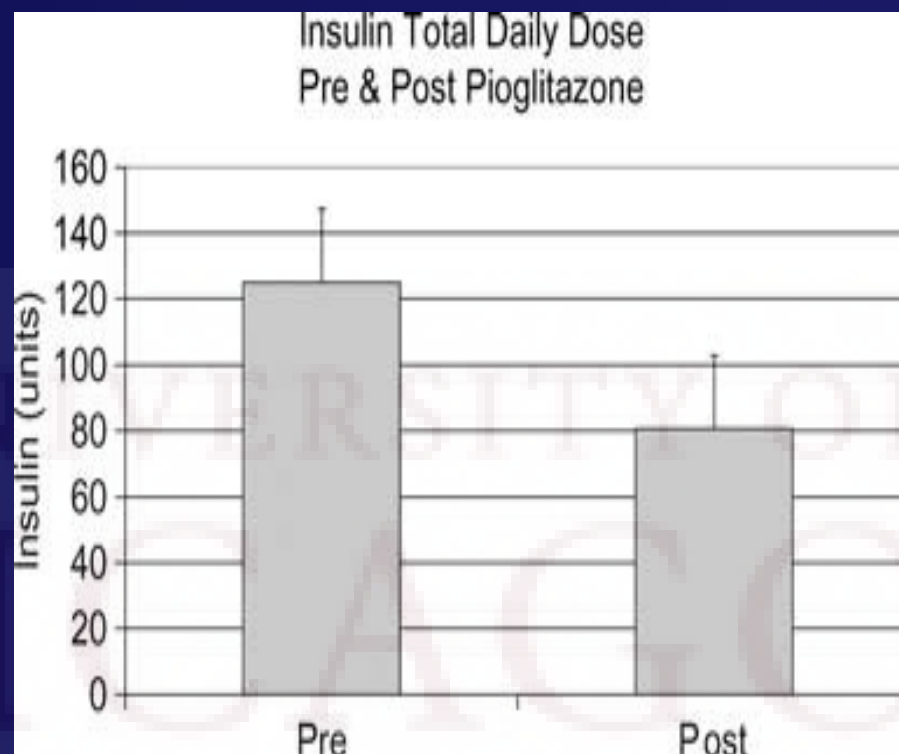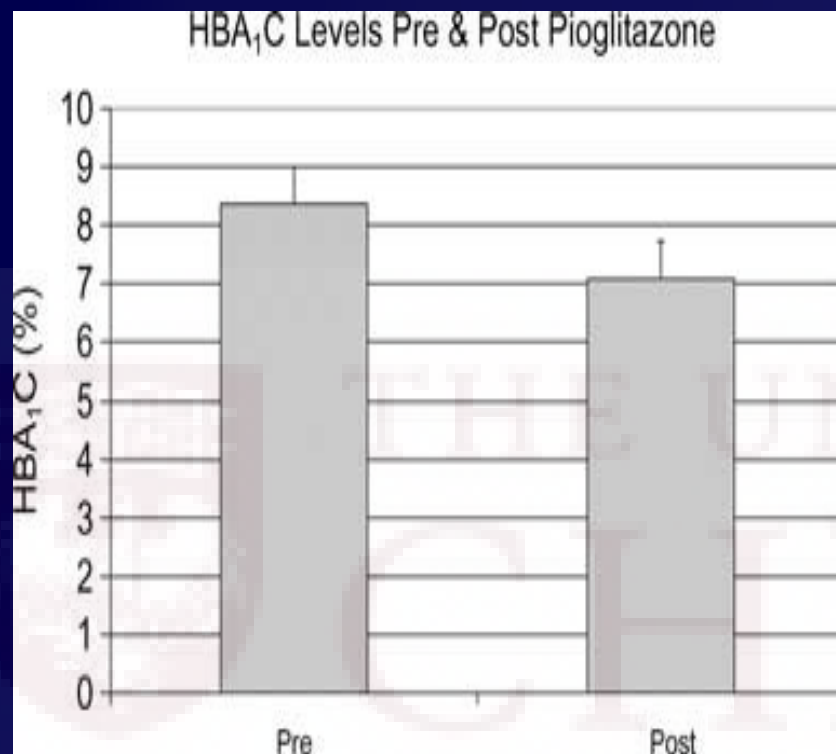
Pioglitazone

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

Pt	DM (pre/post)	BMI	Age/sex	Ethnicity	Transplant	Tacrolimus dose	Prednisone dose	DM Rx
1	Post	33	48 M	cauc	Kidney	2	5	insulin
2	pre	34	68 F	AA	Kidney	4	5	insulin
3	pre	27	57 M	Hisp	Kidney	2	5	insulin
4	pre	32	54 M	Asian	Kidney	5	4	insulin
5	pre	29	43 F	Cauc	Liver	5	20	insulin
6	Post	31	47 M	Asian	Kidney	1	5	insulin
7	post	31	49 F	Hisp	Kidney	5	15	insulin
8	pre	34	49 M	Cauc	Kidney	3	5	insulin
9	pre	29	55 M	AA	Liver	5	5	insulin
10	post	32	57 M	Cauc	Kidney	2	5	insulin

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

HBA₁C Levels Pre & Post Pioglitazone / Insulin Total Daily Dose Pre & Post Pioglitazone

- 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

Glucagon-Like Peptide-1 Receptor Agonist Treatment Prevents Glucocorticoid-Induced Glucose Intolerance and Islet-Cell Dysfunction in Humans

DANIËL H. VAN RAALTE MD,RENATE E. VAN GENUGTEN MD, MARGOT M.L. LINSSEN MSC2

Department of Internal Medicine, VU University Medical Center, Amsterdam, 2011

- ❖ Eight healthy men were included.

- ❖ Age 18–35years, 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)
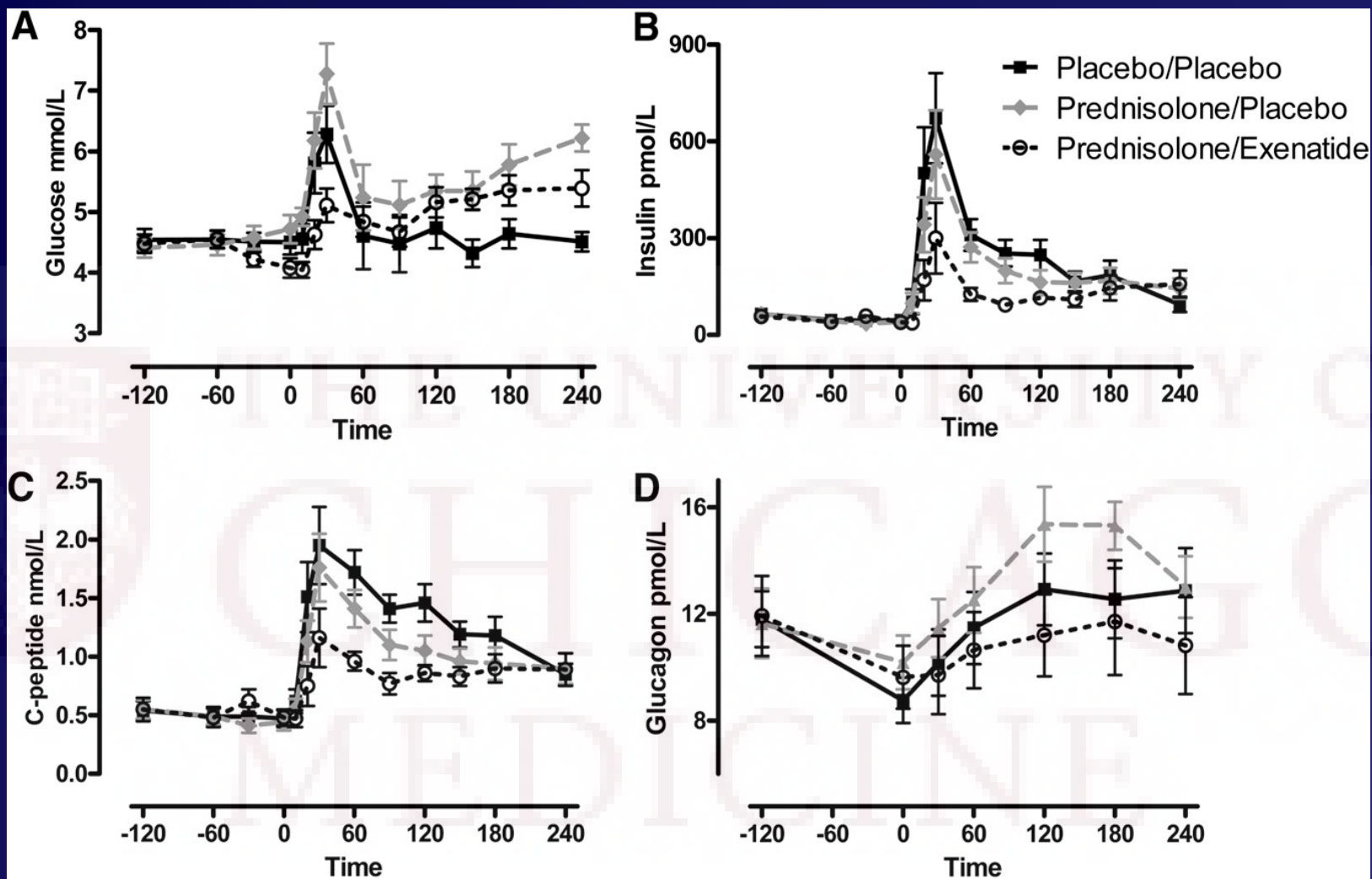
The effect of PRED with or without concomitant EXE infusion on plasma glucose (**A**), insulin (**B**), C-peptide (**C**), and glucagon (**D**) levels during the meal challenge

DPP-4 inhibitor

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

| No of pt with SIH	19	
Gender	Male (14), Female (5)	
Mean age	42 +/- 7	
Mean BMI	31 +/- 1.37	
	Before	**After**
Mean BS (P< 0.001)	184 +/- 16	124 +/- 13
Mean HbA1c (P< 0.001)	8.1 +/- 0.84	6.1 +/- 0.18

Nateglinide (Starlix)

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

T. Uzu, T. Harada, M. Sakaguchi, M. Kanasaki, K. Isshiki, S. Araki, T. Sugiomoto, D. Koya, M. Haneda
Department of Medicine, Shiga University of Medical Science. Division of Nephrology
Japan

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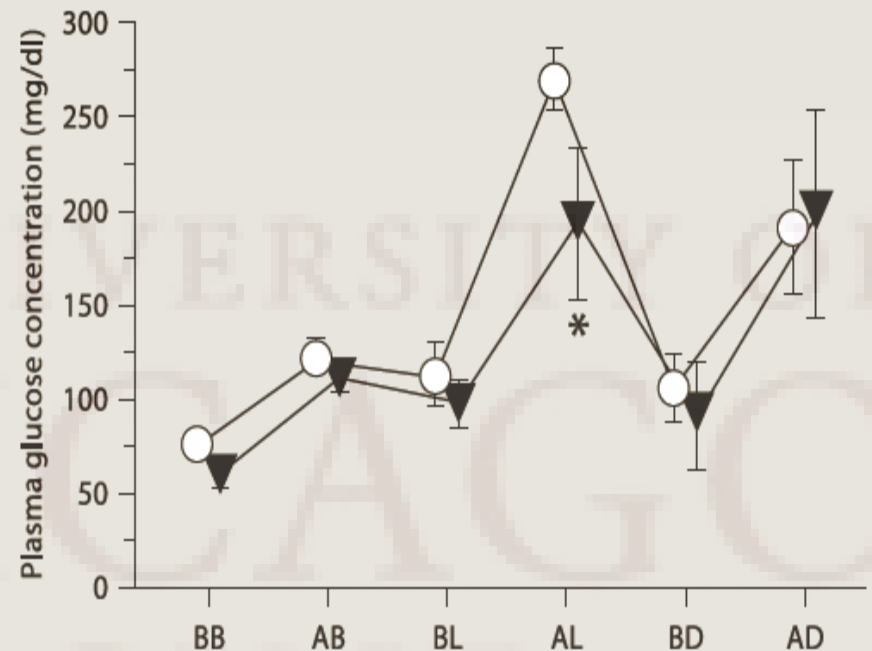
The diabetes states in 7 patients who developed marked hyperglycemia (250 mg/dl) before (open circle) and **after (close triangle)** the treatment with nateglinide (10 min before lunch, 90 mg daily).

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.

o Electronic (MEDLINE) and a library review of the existing pertinent literature published from 1950 to March 2009.

o Recommended insulin types and Wt based starting dose.

Patient not on insulin before

Suggested Dosages of NPH Insulin for Tapering Dosages of Glucocorticoids	
Prednisone dose (mg/day)	NPH Insulin dose (U/kg)
>40	0.4 u/kg
30	0.3 u/kg
20	0.2 u/kg
10	0.1 u/kg

➢ NPH peak 6-8hrs and last for12-14hrs
➢ Lantus preferred if Dexamethasone used or prednisone given twice a day

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**

AACE website

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**

summary

➤ **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

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2) Owen OE, Cahill Gf Jr. Metabolic effects of exogenous glucocorticoids in fasted man. J Clin Invest.1973;52: 2596-2605.

3) Clement S, Braithwaite SS, Magee Mf, et al (American Diabetes Association Diabetes in Hospital Writing Committee). Management of diabetes and hyperglycemia in hospitals [published corrections appear in Diabetes Care. 2004;27:856 and Diabetes Care. 2004;27:1255]. Diabetes Care. 2004;27:553-591.

4) Gulliford MC, Charlton J, latinovic R. Risk of diabetes associated with prescribed glucocorticoids in a large popu- lation. Diabetes Care. 2006;29:2728-2729.

5) Gurwitz JH, Bohn RI, Glynn RJ, Monane M, Mogun H, Avorn J. Glucocorticoids and the risk initiation of hypoglycemic therapy. Arch Intern Med. 1994;154:97-101.