Steroid Induced Hyperglycemia: An Unexpected and Diverging Insulin Therapy Course in Two patients with the same Oncologic Diagnosis

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Disclosure

I have nothing to disclose

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Objectives

- At the completion of this session, the learner will be able to:
  - Explain the diagnosis and treatment of steroid induced diabetes as a secondary diagnosis
  - Identify techniques to safely escalate insulin doses as an outpatient endocrine nurse practitioner

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Cases: B-Cell ALL

	AL	RC
Age	7 years old	20 years old
Weight	25 Kg	102 kg
Gender	Female	Male
Ethnicity	Caucasian	Caucasian
Induction Steroid:	Dexamethasone 3mg BID	Prednisone 68 mg BID
Presentation:	day 10 of induction	day 4 of induction
symptoms:	polydipsia, polyuria, fatigue	no symptoms, prior weight gain (over the past 12 months)
Relevant Past History:	Autism, ADHD	Asthma, MGM T2DM

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Diagnostic Evaluation

	AL	RC
Initial Glucose:	546 mg/dL	253 mg/dL
Urine Ketones:	+ Trace	Negative
Hba1c:	6.3%	6.5%
C-Peptide level:	4.1 ng/mL	not obtained
insulin level:	41.2 uIU/mL	not obtained

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Acute Lymphoblastic Leukemia

ALL is the most common childhood malignancy

- 2500-3500 new cases diagnosed each year in the United States
- Incidence is increasing
- Survival improved dramatically since the 1980's
  - overall 5 year survival rate > 85% and >93% for low risk groups
  - survival rate is due to standardized research protocols
- Goals of research protocols are to:
  - improve clinical outcomes
  - reduce toxicities
  - reduce late occurring adverse events (uptodate)

SEER Cancer Statistic Review, 2016.
UptoDate

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Treatment of ALL

- **Induction therapy involves :**
  Three to four weeks of daily:
  - Vincristine
  - Asparaginase (uptodate) 200 IU/Kg/day IV X 28 days
  - **Corticosteroids:** Prednisone (40mg/m2), Prednisolone, Dexamethasone (6mg/m2)

sonabend et al., 2008

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ALL and Hyperglycemia

Prevalence: 4-27%

Risk factors:

- > age 10 years
- Increased BMI
- Family history of diabetes
- Down syndrome

Valentina et al. 2018

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ALL and Hyperglycemia

- **Diagnosis:** elevated levels of c-peptide, insulin and glucose
  - HbA1C ?
- **Impact:**
  - Transient hyperglycemia has been associated with:
    - Poorer survival of relapse
    - Poor overall survival
    - Increased risk of developing metabolic disorders later on in life

Gatziouta, et al. 2016; Yoshida et al. 2015

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ALL and Hyperglycemia

- Increased risk of complications
  - Bacteremia
  - Hospital Readmission

Sonabed et al., 2008

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Corticosteroid Effects on Glucose Metabolism: Insulin Resistance

- Impairing glucose tolerance, mainly by **inducing insulin resistance**- the effects seem to be dose-dependent
- Decreasing the expression of insulin receptor substrate causing a down regulation of glucose transport in the muscle
- Requiring more insulin for cellular glucose uptake
- Stimulating the liver to secrete glycogen stores, which results in a **surge of circulating glucose**

Chikani et al. 2017; Tamez-Perez et al. 2015; Powers, 2015

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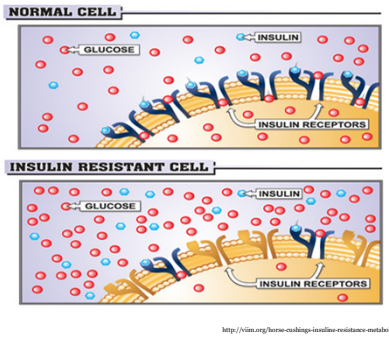

http://vim.org/horse-cushings-insuline-resistance-metabolic-syndrome.php

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Steroid Potency

- Hydrocortisone 1
- Prednisone 4
- Prednisolone 4
- Methylprednisolone 5
- Dexamethasone 25

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Management: General Dosing Recommendations

- Daily dose of 0.3-0.5 u/kg
- Daily dose of 0.1-0.4 u/kg

Fattorusso et al, 2018 ; Umpierrez et al, 2012

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Management: Regimen Recommendations

- **Basal/Bolus**: Hyperglycemia induced by glucocorticoids should be treated first with basal insulin, in order to fight insulin resistance and normalize fasting blood glucose
- **Single dose of NPH:** A single daily dose of isophane based on weight and prednisone dose: 0.1units/kg for every 10 mg of prednisone prescribed, up to a max of 0.4/kg

Dhital, et al. 2012; Clore et al. 2009

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Clinical Course: Hospital

	AL	RC
Age	7 years old	20 years old
wt	25kg	102kg
Insulin Regimen	70/30 insulin NPH & Regular + Aspart ISF	70/30 insulin NPH & Regular + Aspart ISF
Total units of insulin per/ kg/day	0.5 u/kg/day	2.4 u/kg/day

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Clinical Course: Outpatient

	AL	RC
Age	7 years old	20 years old
Weight	25 kg	102 kg
Discharged on steroids	yes	yes
Blood glucose levels post discharge	persistent hyperglycemia, requiring rapid escalation over 5 days	euglycemia, followed by hypoglycemia, requiring de-escalation
Total u/kg/day 7 days post-discharge	5.5 u/kg/day	1u/kg/day
Off of Insulin	day 28 of therapy, upon discontinuation of steroid medication	day 23 of therapy due to hypoglycemic seizure

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Discussion

- 2 patients with identical oncology diagnosis requiring steroid treatment
- Initially, similar insulin requirements for hyperglycemia
- Ultimately insulin escalation in one, and de-escalation in the other
- Insulin dosing requirements did not correlate with patient age or weight

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Safety Concerns

- Rapid dose adjustments through telephone communication
  - Potential for severe hyper- and hypoglycemia at home
- Educational barriers
- Technology barriers
- Frequency of Blood glucose monitoring
- Risk for hospital-acquired infections

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Issues to be Addressed

- Should we routinely screen? How do we ?
- Limited research in children with hyperglycemia and ALL
- No pediatric guidelines: lack of agreement re: management
- Impact of secondary diagnosis on the child and family

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Oncology Nurse Education

- Sampayo et al., discusses how nursing education and intervention on "steroid induced algorithm" proved successful

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Next Steps

- **More evidenced-based research:**
  - Related to hyperglycemia secondary to steroid therapy
  - Impact of steroid induced hyperglycemia
  - Validated protocols for managing this condition

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Resources

1. SEER Cancer Statistics Review, National Cancer Institute. Bethesda, MD. Available at: http://seer.cancer.gov/faststats/selections.php?#Output (Accessed on April 04, 2016).
2. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, revised 4th edition, Swerdlow SH, Campo E, Harris NL, et al. (Eds), International Agency for Research on Cancer (IARC), Lyon 2017.

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