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

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PEDIATRIC NURSE PRACTITIONER

Disclosure

I have nothing to disclose

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
Cases: B-Cell ALL

<table>
<thead>
<tr>
<th></th>
<th>AL</th>
<th>RC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>7 years</td>
<td>20 years</td>
</tr>
<tr>
<td>Weight</td>
<td>25 Kg</td>
<td>102 kg</td>
</tr>
<tr>
<td>Gender</td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>Caucasian</td>
<td>Caucasian</td>
</tr>
<tr>
<td>Induction Steroid:</td>
<td>Dexamethasone 3mg BID</td>
<td>Prednisone 68 mg BID</td>
</tr>
<tr>
<td>Presentation:</td>
<td>day 10 of induction</td>
<td>day 4 of induction</td>
</tr>
<tr>
<td>Symptoms:</td>
<td>polydipsia, polyuria, fatigue</td>
<td>no symptoms, prior weight gain (over the past 12 months)</td>
</tr>
<tr>
<td>Relevant Past History:</td>
<td>Autism, ADHD</td>
<td>Asthma, MGMT2DM</td>
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Diagnostic Evaluation

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<thead>
<tr>
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<tr>
<td>Initial Glucose:</td>
<td>546 mg/dL</td>
<td>253 mg/dL</td>
</tr>
<tr>
<td>Urine Ketones:</td>
<td>Trace</td>
<td>Negative</td>
</tr>
<tr>
<td>HbA1c:</td>
<td>6.3%</td>
<td>6.5%</td>
</tr>
<tr>
<td>C-Peptide level:</td>
<td>4.1 ng/mL</td>
<td>not obtained</td>
</tr>
<tr>
<td>Insulin level:</td>
<td>41.2 uIU/mL</td>
<td>not obtained</td>
</tr>
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</table>

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
  - Over 5 year survival rate: 80% and 85% 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)
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)

ALL and Hyperglycemia

Prevalence: 4-27%
Risk factors:

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

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
ALL and Hyperglycemia

❖ Increased risk of complications
➢ Bacteremia
➢ Hospital Readmission

Sonabe et al., 2008

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

Steroid Potency

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

Management: General Dosing Recommendations

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

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: 0.1 units/kg for every 10 mg of prednisone prescribed, up to a max of 0.4/kg
Clinical Course: Hospital

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</tr>
<tr>
<td>wt</td>
<td>25kg</td>
<td>102kg</td>
</tr>
<tr>
<td>Insulin Regimen</td>
<td>70/30 insulin NPH &amp; Regular + Aspart ISF</td>
<td>70/30 insulin NPH &amp; Regular + Aspart ISF</td>
</tr>
<tr>
<td>Total units of insulin per kg/day</td>
<td>0.5 u/kg/day</td>
<td>2.4 u/kg/day</td>
</tr>
</tbody>
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Clinical Course: Outpatient

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<tr>
<td>wt</td>
<td>25kg</td>
<td>102kg</td>
</tr>
<tr>
<td>Discharged on steroids</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Blood glucose levels post discharge</td>
<td>Persistent hyperglycemia, requiring rapid escalation over 5 days</td>
<td>Euglycemia, followed by hyperglycemia, requiring de-escalation</td>
</tr>
<tr>
<td>Total u/kg/day 7 days post-discharge</td>
<td>5.5 u/kg/day</td>
<td>1.0 u/kg/day</td>
</tr>
<tr>
<td>Off of Insulin</td>
<td>Day 28 of therapy, upon discontinuation of steroid medication</td>
<td>Day 23 of therapy due to hypoglycemic seizure</td>
</tr>
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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
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

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

Oncology Nurse Education

❖ Sampayo et al., discusses how nursing education and intervention on “steroid induced algorithm” proved successful
Next Steps

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

Resources