High risk of Fasting Hypoglycemia Among Children During Acute Lymphoblastic Leukemia (ALL) Therapy

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Faculty Disclosure

• Nothing to disclose

• This data was previously presented by Ashraf Mohamed MD, at the Multinational Association of Supportive Care in Cancer (MASCC) Annual Meeting

Learning Objective

• Identify factors that may increase the risk of hypoglycemia in ALL patients.

• Estimate prevalence of hypoglycemia during ALL treatment
Outline

• Background
• Introduction to Research
• Methods of Study
• Results
• Conclusions

Background

• Recurrent symptomatic and asymptomatic hypoglycemia has been noticed in children receiving ALL chemotherapy. Only few and small studies looked at this therapy related complication.

• Factors that may increase risk of hypoglycemia in ALL patients:
  1. Accelerated starvation
  2. Adrenal suppression
  3. Mercaptopurine therapy (6MP)
  4. Chemotherapy-Induced Nausea and Vomiting (CINV)
  5. Prolonged fasting

COG agent monograph changed for mercaptopurine in December 2016 with version 9:

• Previous statement from monograph 7/22/2015:
  Do not give oral mercaptopurine with food or milk. Concurrent milk products can decrease absorption and mercaptopurine effect is enhanced if given at bedtime on an empty stomach.

• Current statement from 12/12/2016: Mercaptopurine should be taken consistently at the same time every day.
**What If…**

**Bedtime**

**Most recent meal**

**Procedure Time**

*17 hours of fasting*

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**Symptoms of hypoglycemia in children**

*are easy to be confused with chemotherapy side effects*

- shakiness
- dizziness
- hunger
- irritability
- sudden moodiness or behavior changes
- clumsy
- difficulty paying attention, or confusion
- pallor

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**Primary Aim**

- To study the prevalence and risk factors for hypoglycemia during ALL therapy
Methods

• Charts for children (up to 18 years old) treated for ALL between 2011-2016 (86 patients) were studied for evidence of hypoglycemia. Hypoglycemia was defined as blood sugar (BS) < 70 mg/dL. We restricted further analysis for risk factors to BS < 60 mg/dL.

• Statistical mean differences between the subgroups were analyzed with SPSS (v23) using a nonparametric Mann-Whitney U test.

Study Limitations

• Retrospective
• Relatively small number
• Thiopurine methyltransferase (TPMT) genotype was not available for almost 50% of the patients
• Data was only collected during routine appointments for chemotherapy or procedures. This may have underestimated the true prevalence of hypoglycemia.

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<thead>
<tr>
<th>Table 1. Summary characteristics of the study group patients</th>
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<td>n (patients)</td>
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<tr>
<td>Males</td>
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<td>Females</td>
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<td>Mean age at time of diagnosis (years)</td>
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<td>Mean age at start of maintenance therapy (years)</td>
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<td>Proportion of patients in maintenance therapy</td>
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<td>Proportion of patients not in maintenance therapy</td>
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<td>Proportion of patients with normal TPMT level</td>
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<td>Proportion of patients with low TPMT level</td>
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<td>Proportion of patients with raising TPMT level</td>
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<td>Total number of hypoglycemic episodes (&gt;60 mg/dL)</td>
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<td>Mean number of hypoglycemic episodes per patient</td>
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Results

- 45 out of 86 patients (52%) developed hypoglycemia during treatment.
- Majority of hypoglycemic episodes (N = 80/103, 78.2%) occurred on the day of procedure when patients were fasting overnight.
- 51 of the 103 hypoglycemic episodes (48.5%) occurred in children ≤3 years.
- 78 of the 103 hypoglycemic episodes (75.8%) occurred in children < 6 years.
- 6% of hypoglycemic children—all <3 years of age—presented with life threatening hypoglycemia symptoms including seizure and loss of consciousness.
- No statistically significant difference was found regarding hypoglycemic events and sex, TPMT genotype, duration or phase of therapy.
Conclusion

- This study showed high prevalence of hypoglycemia during childhood ALL therapy.
- Younger age, especially < 6 years, is associated with higher risk of hypoglycemia as well as life-threatening episodes.
- Based on results of this study, new education efforts to both the medical staff and patients have been implemented.
  - We piloted a survey to staff and patients over 6MP administration and over half are still following the outdated guidelines.
  - Mass education concerning new administration guidelines for 6MP is urgently needed – both for healthcare workers and patient families.

Future Research Endeavors

- Guidelines have been updated to decrease the duration of fasting with medication administration.
- Our clinic is participating in an American Society of Clinical Oncology Quality Improvement Project (ASCO QI) to identify the barriers to preventing hypoglycemia.
  - Patient caregiver/knowledge of hypoglycemia risk
  - Length of fasting
  - Timing of 6MP administration

Which of the following is associated with an increased risk of hypoglycemia during ALL treatment?

A. Gender
B. <6 years of age
C. TPMT genotype
D. Duration of therapy