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) 1,2
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.


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What If…

Bedtime

Most recent meal

Procedure Time

17 hours of fasting

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

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.

Table 1. Summary characteristics of the study group patients

<table>
<thead>
<tr>
<th></th>
<th>Hypoglycemia group (BS &lt; 60 mg/dL)</th>
<th>Normoglycemia group (BS ≥ 60 mg/dL)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (patients)</td>
<td>45 (52.3%)</td>
<td>41 (47.7%)</td>
<td>86</td>
</tr>
<tr>
<td>Males</td>
<td>29 (59.2%)</td>
<td>16 (40.8%)</td>
<td>45</td>
</tr>
<tr>
<td>Females</td>
<td>16 (61.3%)</td>
<td>25 (38.7%)</td>
<td>41</td>
</tr>
<tr>
<td>Mean age at time of diagnosis (years)</td>
<td>4.07 ± 3.69 [3.23 - 5.98]</td>
<td>7.27 ± 6.89 [5.70 - 8.84]</td>
<td>6.05 ± 4.48 [5.09 - 7.01]</td>
</tr>
<tr>
<td>Mean age at start of maintenance therapy (years)</td>
<td>5.60 ± 3.47 [3.87 - 7.00]</td>
<td>9.10 ± 3.31 [7.16 - 10.86]</td>
<td>6.83 ± 4.56 [5.20 - 8.06]</td>
</tr>
<tr>
<td>Proportion of patients in maintenance therapy</td>
<td>35 (77.8%)</td>
<td>19 (46.3%)</td>
<td>54</td>
</tr>
<tr>
<td>Proportion of patients not in maintenance therapy</td>
<td>10 (22.2%)</td>
<td>22 (53.8%)</td>
<td>32</td>
</tr>
<tr>
<td>Proportion of patients with normal TPMT level</td>
<td>20 (55.3%)</td>
<td>20 (51.2%)</td>
<td>40</td>
</tr>
<tr>
<td>Proportion of patients with abnormal TPMT level</td>
<td>4 (44.4%)</td>
<td>5 (55.6%)</td>
<td>9</td>
</tr>
<tr>
<td>Proportion of patients with missing TPMT level</td>
<td>13 (28.8%)</td>
<td>16 (38.8%)</td>
<td>29</td>
</tr>
<tr>
<td>Total number of hypoglycemic episodes (&lt;60 mg/dL)</td>
<td>103 (100%)</td>
<td>0</td>
<td>103</td>
</tr>
<tr>
<td>Mean number of hypoglycemic episodes per patient</td>
<td>2.29 ± 2.02 [1.70 - 2.88]</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
Table 2. Distribution of BS level during hypoglycemia episodes

<table>
<thead>
<tr>
<th>Hypoglycemia severity</th>
<th>Number of episodes</th>
<th>Percent</th>
<th>Cumulative %</th>
</tr>
</thead>
<tbody>
<tr>
<td>60-69 mg/dL</td>
<td>255</td>
<td>71.2</td>
<td>71.2</td>
</tr>
<tr>
<td>50-59 mg/dL</td>
<td>76</td>
<td>21.2</td>
<td>92.5</td>
</tr>
<tr>
<td>40-49 mg/dL</td>
<td>25</td>
<td>7.0</td>
<td>99.4</td>
</tr>
<tr>
<td>30-39 mg/dL</td>
<td>2</td>
<td>0.6</td>
<td>100.0</td>
</tr>
<tr>
<td>Total</td>
<td>358</td>
<td>100.0</td>
<td></td>
</tr>
</tbody>
</table>

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

Thank you for attending this Webinar session.

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