Glucose Supplementation in Hypoglycemic Mice Following Roux-en-Y Gastric Bypass Surgery

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Background
- Roux-en-Y gastric bypass (RYGB) surgery is an effective treatment for obesity and diabetes in humans.
- Mouse models of RYGB surgeries aid in the investigation of energy homeostasis and the mechanisms of obesity and diabetes.
- At the Mouse Biology Program (MBP), RYGB mortality rates have reached >60%.
- Mice are profoundly hypoglycemic 24 to 48 hours following surgery.
- Literature reports intensive peri-operative glycemetic control has been shown to reduce surgical site infection, morbidity, and mortality.
- Although glucose homeostasis is extensively studied in mice, the influence of hypoglycemia in the post-operative period is not well documented.

Hypothesis
Subcutaneous (SQ) glucose administration in mice provides more sustained systemic glucose levels than oral/transmucosal (OTM) administration, causing decreased morbidity and mortality following Roux-en-Y gastric bypass (RYGB) surgery.

Results

![Average Blood Glucose Measurements](image)

**Figure 1.** Blood glucose measurements vs time. Results are expressed as means ± SD. Significant differences for *p* < 0.05.

**Table 1.** Causes of death in post-operative mice as determined by necropsy.

<table>
<thead>
<tr>
<th>Cause of Death</th>
<th>Mouse #</th>
<th>Dose Group</th>
<th>Days Post-Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspiration Pneumonia</td>
<td>#14</td>
<td>No Dose</td>
<td>2</td>
</tr>
<tr>
<td>#15 Dose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bedding Impaction</td>
<td>#7</td>
<td>Dose</td>
<td>4</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>#10</td>
<td>Dose</td>
<td>2</td>
</tr>
<tr>
<td>#11 No Dose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgery Site Leakage</td>
<td>#2</td>
<td>No Dose</td>
<td>10</td>
</tr>
<tr>
<td>#6 Dose</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Discussion

**Phase 1:**
- Sustainability of BG over time was the original criteria for determining dosing route. OTM was anticipated to have an early spike and drop whereas SQ was expected to increase slowly and sustain longer. The contrary results that occurred may have been from difficult OTM dosing into the mouse’s small mouth.
- SQ and OTM routes showed similar kinetic profiles after 60 minutes, therefore SQ was chosen for phase 2 due to ease and reliability of administration.

**Phase 2:**
- There was no significant difference in mortality between D and ND groups. Although not statistically significant, grimace scale assessment anecdotally showed greater discomfort in the ND group. Literature also shows that hypoglycemia causes depressive-like behaviors in mice, reduced movement, and social withdrawal.
- This cohort’s mortality rate of 44% is lower than the MBP’s previous 70%. Due to procedural changes including lowered opiate dosages and smaller suture, it is not discernible what is responsible. However, it is documented that prolonged hypoglycemia leads to inefficient energy for wound healing. Since these mice models are labor and financially intensive, including glucose supplementation in the RYGB protocol is recommended.

Ideas for Future Studies
- Raise threshold for definition of hypoglycemia from ≤60 mg/dL to ≤80 mg/dL or administer prophylactically. Severe hypoglycemia can cause seizures, coma, and death, so early detection should increase recoverability, animal welfare, and overall survivability.
- Increase number of blood glucose measurements per day from 3x/day to 4x/day. More intensive glycemetic control will minimize large fluctuations.

References and Acknowledgements

**References:**

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