Hyperglycemia During the First Three Days of Life Increases the Risk of Retinopathy of Prematurity in Extremely Low Birth Weight Infants

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Background
- The association between hyperglycemia and ROP has been inconsistent in previous studies.
- Extremely low birth weight (ELBW) infants are at high risk for ROP. They often experience hypoglycemia initially and hyperglycemia while receiving IV glucose infusion.
- The effect of initial hypoglycemia on hyperglycemia associated ROP risk is unknown.

Objective
To study the effect of initial hypoglycemia and subsequent hyperglycemia during the first three days of life on the incidence of ROP and severe ROP in ELBW (birth weight ≤1000g) infants.

Methods
Clinical and demographic data were collected from 224 ELBW infants born during the years 2017-2019 at the Regional One Health NICU, Memphis, TN.

All blood glucose determinations done during the first 72 hours were collected from these infants along with maternal and neonatal demographic and clinical information.

The infants were divided into four groups based on hypoglycemia at birth and subsequent hyperglycemia during the first 72 hours:
- Group I: All the blood glucose levels were between 47-125mg/dl (euglycemia group);
- Group II: Initial hypoglycemia (<47mg/dl) and with treatment became euglycemic;
- Group III: Initial hypoglycemia (<47mg/dl) and at least one episode of hyperglycemia (>125mg/dl) subsequently;
- Group IV: Initial euglycemia followed by at least one episode of hyperglycemia.

Incidence of ROP and severe ROP (stage III or greater) was compared between the groups after adjusting for gestational age.

Results
- ROP incidence was lowest in infants who were euglycemic throughout the first 72 hours of life and no severe ROP was seen in this group.
- Infants who were hypoglycemic initially without experiencing hyperglycemia later appear to have higher incidence of ROP though it was not statistically different after adjusting for gestational age.
- Infants who were euglycemic at birth and became hyperglycemic later had increased incidence of ROP even after adjusting for gestational age; they also had the highest incidence of severe ROP.
- Comparing combined groups 1 & 2 vs. 3 & 4 showed no difference in ROP [aOR 1.5 (0.82-2.84)].
- Groups 1&2 vs 3&4 showed no difference in severe ROP [aOR 3.13 (0.69-14.16)].
- Mortality did not statistically differ between the groups.

Conclusions
- Hyperglycemia during the first three days of life without hypoglycemia at birth increases the risk for ROP.
- Hypoglycemia at birth appears to modify the risk of hyperglycemia associated ROP in ELBW infants.

<table>
<thead>
<tr>
<th>Max Glucose level in first 72 hours</th>
<th>ROP</th>
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<tbody>
<tr>
<td>Mean ± SD (mg/dL)</td>
<td>Median (Range)</td>
</tr>
<tr>
<td>Group 1 (28)</td>
<td>26.6 ± 2.3 *</td>
</tr>
<tr>
<td>Group 2 (33)</td>
<td>27.5 ± 2.5 §</td>
</tr>
<tr>
<td>Group 3 (78)</td>
<td>26.5 ± 2.5 †</td>
</tr>
<tr>
<td>Group 4 (85)</td>
<td>25.3 ± 1.9 †</td>
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</tbody>
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ANOVA: *p=0.04, § p=0.0001, † p = 0.0043. ROP aOR adjusted for gestational age.