**Effect of Intrauterine Growth Restriction on Retinopathy of Prematurity**

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**Purpose**

- Postnatal infant growth is important to reduce the risk of developing severe retinopathy of prematurity (ROP). We predicted that intrauterine growth restriction (IUGR) would increase the severity of ROP. In this study, we sought to develop a model of IUGR and ROP.

**Introduction**

- Retinopathy of prematurity (ROP) is a leading cause of childhood blindness and is associated with abnormal retinal vascular development in premature infants.

- Risk factors include low birth weight, young gestational age, oxygen stresses, and poor postnatal weight gain.

- Intrauterine growth restriction (IUGR) causes low birth weight, but its effects on ROP remain incompletely understood. We, therefore, sought to study the role of IUGR in ROP. We developed a model in which rat pups with IUGR were placed into a model of human ROP.

**Methods**

- IUGR in rat pups was created with a well-established protocol in which pregnant rat dams underwent prenatal bilateral uterine artery ligation 2 or 3 days before pup birth. IUGR pups had weights ≤6g. Control pups received anesthesia only and were >6g (control).

- Newborn IUGR or control pups were placed into the 50/10 rat model of oxygen-induced retinopathy (OIR), in which oxygen levels fluctuated between 50% and 10% every 24 hours, or were allowed to develop in room air conditions (RA). The 50/10 OIR model is the most representative model of human ROP.

- At postnatal day (p)18, retinas were prepared as flat mounts and stained with lectin to visualize the vasculature. Flat mounts were analyzed for areas of abnormal intravitreal neovascularization (IVNV) and avascular retina (AVA), both normalized to total retinal area and reported as percentages.

- Statistics were performed by One-way ANOVA

**Results**

![Figure 2.](image)

**Figure 2.** IUGR+OIR, Control+OIR, IUGR+RA and Control+RA birth weight and weight gain at p18. (A) Birth weight at p0 (p=NS); (B) Weight gain of pups at p18 were 31.6±0.2 g in IUGR+RA and 14.5±0.6 g in IUGR+OIR.

![Figure 3.](image)

**Figure 3.** IUGR+OIR, Control+OIR, IUGR+RA and Control+RA birth weight and weight gain at p18. (A) Birth weight at p0 (p=NS); (B) Weight gain of pups at p18 were 31.6±0.2 g in IUGR+RA and 14.5±0.6 g in IUGR+OIR. Males pups (A) and Females pups (B and D).

![Figure 4.](image)

**Figure 4.** Lectin Stained Retinal Flat Mounts at Postnatal Day (p) 18. (A) IUGR+OIR; (B) IUGR+RA; (C) Control+OIR; (D) Control+RA. Arrow shows IVNV and star AVA.

**Conclusions**

- Pup weight gain was greater in the IUGR+RA group than in the IUGR+OIR group.

- In this experiment, fluctuations in oxygen in the OIR model were associated with reduced body weight gain and with increased IVNV and reduced AVA in both IUGR and control pups.

**References**


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**Table 1. Analyses of Avascular Retinal Areas and Area of Intravitreal Neovascularization in Lectin Stained Retinal Flat Mounts at Postnatal Day (p) 18.**

<table>
<thead>
<tr>
<th>Groups</th>
<th>%IVNV</th>
<th>P-Value</th>
<th>%AVA</th>
<th>P-Value</th>
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<tbody>
<tr>
<td>A. IUGR+OIR</td>
<td>3.77</td>
<td>No</td>
<td>22.81</td>
<td>P&lt;0.001</td>
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<td>B. IUGR+RA</td>
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<td>0</td>
<td>0</td>
<td>0</td>
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<td>C. Control+OIR</td>
<td>0.28</td>
<td>No</td>
<td>50.54</td>
<td>P&lt;0.0001</td>
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<tr>
<td>D. Control+RA</td>
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<td>0</td>
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