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ROCK2 Gene Single Nucleotide Polymorphisms and Association with Bronchopulmonary Dysplasia in Extremely Low Birth Weight Infants

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Background

Bronchopulmonary dysplasia (BPD) leads to significant morbidity in ELBW infants.

- In intron; MAF (Minor Allele Frequency), C= 0.30
- G allele and GC genotype more in RDS

ROCK-2 SNP rs2290156

- In intron; MAF, A = 0.35
- TC genotype more in RDS compared to controls

ROCK-2 SNP rs726843

- In intron; MAF, C = 0.39
- Affects ROCK2 expression by interfering with microRNA-1183 binding
- Association with stiffer arteries and with high altitude essential hypertension

Hypothesis

We hypothesize that ROCK2 gene SNP variants rs2290156, rs726843 and rs978906 are associated with development of BPD in ELBW infants.

Methods

Inclusion criteria

- ELBW infants (birth weight < 1kg)
- Informed parental consent

SNP Analysis

DNA was isolated from buccal swabs of 137 ELBW infants and analyzed via real-time PCR using Taqman probes for ROCK2 gene SNP variants rs2290156, rs726843 and rs978906.

Statistics

Chi-square test, Fisher’s exact test, Mann-Whitney Rank Sum test and t-test were performed for statistical analysis; p <0.05 was considered significant.

Results

Demographic Characteristics

<table>
<thead>
<tr>
<th>No BPD (n = 57)</th>
<th>BPD (n = 80)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age, wks, median (IQR) 26 (24, 27) 25 (24, 26) 0.22</td>
<td></td>
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<tr>
<td>Birth weight, g, mean (SD) 792.9 (123.8) 752.0 (147.3) 0.09</td>
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<tr>
<td>Female Gender, n (%) 32 (56) 48 (60) 0.78</td>
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<tr>
<td>Race, n (%) Non Hispanic White 18 (33) 29 (38) 0.78 Non Hispanic Black 16 (29) 20 (26) 0.89 Hispanic 16 (29) 23 (30) Other 5 (9) 5 (6) Antenatal steroids, n (%) 43 (81) 68 (91) 0.18</td>
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Conclusions

- ROCK2 gene SNP rs978906 shows association with BPD
- We speculate that this variant may play a role in the development of BPD by influencing smooth muscle tone in the pulmonary vasculature

References


Bronchopulmonary dysplasia (BPD) leads to significant morbidity in ELBW infants.

Fig 1. Pathogenesis of BPD

Rho associated coiled-coil containing protein kinase 2 (ROCK-2) gene
- On chromosome 2p24
- ROCK: Serine/threonine protein kinase

Fig 2.  ROCK-2 functional domains

Fig 3. ROCK pathways (eNOS, endothelial Nitric Oxide Synthase; ERM, ezrin/radixin/moesin; MLCP; Myosin Light Chain Phosphatase)