NEUROENDOCRINE REGULATION OF RETINOIC ACID RECEPTORS DURING LUNG BRANCHING IN NORMAL AND HYPOPLASTIC LUNGS

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The pathogenesis of pulmonary hypoplasia and congenital diaphragmatic hernia (CDH) is unknown. CDH represents a spectrum of lung hypoplasia and consequent pulmonary hypertension (PH) that leads to high morbidity and mortality of patients. We studied neuroendocrine factors and retinoic acid in order to achieve the relation underlying them.

At 13.5 days post-conception normal and CDH lungs were cultured in vitro during four days with DMSO, retinoic acid, bombesin, ghrelin, bombesin antagonist and ghrelin antagonist. Morphometric analysis were done after the culture and Western Blot (WB) was performed to quantify the protein levels of retinoic acid receptors (RAR). Immunohistochemistry (IHC) was performed as well on normal, nitrofen and CDH E17.5 lungs.

When compared with controls, CDH lungs presented higher expression of RAR in IHC and WB. Moreover in normal lungs after the administration of bombesin and ghrelin the expression of RAR also increases and in case of retinoic acid administration it decreases. Regarding bombesin and ghrelin antagonists administration, RAR expression decreases as it was expected. In terms of morphometry, treated groups showed an increase in branching, perimeter and area. This study, shows for the first time that retinoic acid deficit on CDH lungs is associated with neuroendocrine factors overexpression. Furthermore, neuroendocrine factors such as ghrelin and bombesin sensitis for RAR expression.

IN VIVO MIR-200B AS A POTENTIAL THERAPY FOR CONGENITAL DIAPHRAGMATIC HERNIA

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Congenital diaphragmatic hernia (CDH) is associated with lung hypoplasia and pulmonary hypertension (PH) leading to a high morbidity and mortality. MicroRNAs, affect gene expression and miR-200b is involved in epithelial-mesenchymal transition in cancer and is downregulated in rat nitrofen lungs.

We hypothesised that miR-200b regulates lung branching. Therefore, we aimed to evaluate whether in vivo administration of miR-200b influences lung development and branching morphogenesis.

Timed-pregnant dams were treated with nitrofen (CDH group) or olive oil (control group) on E9 and received a tail vein injection of miR-200b mimics (5 mg/kg) or saline, respectively. At E21.5 and P0, we dissected the lungs and evaluated the presence or absence of CDH. We estimated the lung hypoplasia and we did histological studies to determine radial alveolar count (RAC) and medial arterial thickness.

Nitrofen lungs treated with miR-200 b mimics, in vivo display improved development and larger size. These embryos were also bigger than the embryos of the nitrofen group plus saline. Their size was similar to control embryos. After RAC analysis revealed that nitrogen treated lungs have larger alveolar spaces than nitrogen lungs. In terms of arteries we did not observe any differences.

Administration of miR-200b in vivo decreases lung hypoplasia and increases the size of the lungs as well as alveolar airspaces. These data show promising results for miR-200b as a potential therapeutic target in CDH patients.

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CRICOID PRESSURE AS AN ADJUNCT TO NEONATAL INTUBATION: A NATIONAL SURVEY

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Background and aims Although widely documented for use in adult intubation, there is paucity of literature available on the application of cricoid pressure (CP) during neonatal intubation. It is briefly mentioned in the NRP guideline, as a possible adjunct measure. This study was mounted to determine how widely the technique is used by paediatricians and neonatologists in clinical practice.

Methods A questionnaire was devised, consisting of eight questions. The questionnaire was distributed nationally to 40 consultant paediatricians/neonatologists, 31 specialist registrars, 40 neonatal nurses, midwives and ANNPs.

Results The overall response rate was 76% (n = 84). Findings summarised in table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>No. Respondents (n = 84) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perform intubation</td>
<td>54 (64.3)</td>
</tr>
<tr>
<td>Assist in intubation</td>
<td>29 (34.5)</td>
</tr>
<tr>
<td>Familiar with CP</td>
<td>82 (97.6)</td>
</tr>
<tr>
<td>Feel that CP improves visualisation of the glottis</td>
<td>70 (83.3)</td>
</tr>
<tr>
<td>Feel that CP aids opening of the vocal cords</td>
<td>16 (19)</td>
</tr>
<tr>
<td>Feel that CP facilitates intubation</td>
<td>40 (47.6)</td>
</tr>
<tr>
<td>Aware of CP complications</td>
<td>63 (75)</td>
</tr>
</tbody>
</table>

Conclusions · Almost all the healthcare professionals surveyed were aware of the cricoid pressure technique.

· The majority felt that cricoid pressure has a role in improving glottis visualisation.

· One half found that it facilitated intubation.

· A minority felt that it helped to open the vocal cords during intubation.

· The high response rate provides an accurate reflection of neonatal intubation practice in Ireland.

PERINATAL FACTORS IN THE DEVELOPMENT OF BRONCHOPULMONARY DYSPLASIA

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Background and aims Aetiology of BPD is multifactorial with prenatal and postnatal factors being involved. First, we aimed to evaluate the association between chorioamnionitis and BPD. Secondly, the effect of other perinatal factors on the risk of developing BPD were analysed.

Methods Retrospective analysis of all infants with GA <32 weeks or BW <1500 g. admitted into our hospital between 2002–2010. 120 patients who died before 36 weeks of PMA were excluded.

Results The average GA was: 29.7 ± 3 s; 217/432 (50%) had any type of chorioamnionitis (histological or clinical); 75/432 (17.4%) met diagnostic criteria for BPD at 36 weeks.

Univariate analysis: lower GA, any type of chorioamnionitis, DAP and duration of mechanical ventilation (MV) were associated with an increased risk of BPD (p < 0.05).

Multivariate analysis: administration of antenatal corticosteroids or chorioamnionitis did not independently modify the risk of BPD. But adding both, the effect became statistically significant protective for BPD (OR 0.52, 95% CI 0.03 to 0.79).

Days in MV is the only factor that independently increased the risk of BPD. Neither a lower GA nor the presence of PDA had significantance; but, the risk of BPD was higher in the presence of PDA and MV together: every day in MV increased the risk of BPD (OR 1.130, 95% CI 1.001- 1.27).

Conclusions Chorioamnionitis in coexistence with antenatal corticosteroids decreases the risk of BPD. Mechanical ventilation is the main risk factor for BPD. In the presence of DAP, ventilation increases the risk of BPD.