

Androgens and glucocorticoids in the developing lung: Gender specific delay in synthesis between male and female

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A male prevalence is observed in respiratory distress of the neonate (RDS) related with surfactant deficiency. RDS occurs when alveolar Type II pneumocyte (PTII) maturation is incomplete at the time of delivery and depend of the presence of androgens in male lung. Pulmonary maturation occurs late in pregnancy and depends of an epithelial-fibroblast communication. This maturation ends with surfactant production by PTII. Positive and negative regulators control the epithelium proliferation and differentiation and ultimately surfactant production. This negative effect of androgens has been also reproduced in the mouse model. Among steroids, glucocorticoids stimulate biochemical development of the lung and reduce the risk of RDS by stimulating production of fibroblast paracrine factors that accelerate PTII maturation, the latter leading to surfactant synthesis whereas androgens exert opposing effects by delaying lung maturation and surfactant production. A good understanding of how these steroids control lung function is essential before introducing interventions that could alter natural processes. To clarify this, we performed an ontogeny study in mouse fetal lung of androgen- and glucocorticoid-producing enzyme genes expression during the gestation window that overlaps the surge of surfactant. We showed an up regulation of androgen-synthesizing gene expression with the emergence of mature PTII cells in male and female developing lung suggesting that during this period androgens exert a positive role in cell reprogramming. In addition, a strong and narrow peak of expression of all genes involved in glucocorticoid synthesis from cholesterol occur two days before PTII maturation which is stimulated by glucocorticoid. Finally, these actions are delayed in male and female fetal lung. Supported by NSERC and CIHR.