060

GENDER DIFFFERENCES AFTER LPS-INDUCED CHORIOAMNIONITIS IN FETAL SHEEP

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Background and aims: Several studies have demonstrated survival advantage for female preterm infants. However the reason for this phenomenon is not completely understood. It is well known that lung development, an important determinant of survival of preterm infants, is gender specific and that an exposure to intra-amniotic infection improves lung volumes. We hypothesized that female fetuses would have improved lung maturational responses to chorioamnionitis compared to males.

Methods: Time-pregnant ewes received intra-amniotic injections with saline (n=60) or LPS at 2days (n=30) and 7days (n=45) before caesarean-section at 124-125 days of gestation (term is~147d). The experiments were performed with the same batch of LPS in the period of 2003-2010. We assessed the inflammatory response in bronchalveolar lavage fluid and cord blood, and the lung maturation with pressure-volume(PV) curves.

Results: In cord blood, leukocyte and thrombocytes concentrations were comparable for males and females. Furthermore, no gender differences in pulmonary inflammatory responses were noticed in our study. However, the PV-curve at 40cmH_2O pressure showed significant differences in lung volume between male and female lambs at 2d LPS (male 4.5±0.3ml/kg body weight [BW]; female 6.7±1ml/kgBW; p=0.02) and 7d LPS (male 20.5±2.2ml/kgBW; female 27.0±1.4ml/kgBW; p=0.01), indicating that female lungs were more mature than male lungs after chorioamnionitis.

Conclusions: Compared to males, female fetuses exposed to intra-amniotic LPS have increased lunggas volumes without differences in fetal inflammation. These results highlight important sex differences in response to chorioamnionitis. Given the high incidence of chorioamnionitis in preterm infants this may in part explain the female advantage in outcome.