Acta Biomed 2012; 83; Supplement 1: 9-11 © Mattioli 1885

Original article

Pregnancy and neonatal respiratory outcome

M. Colnaghi, P. Cognizzoli, F. Ciuffini, M. Fumagalli, F. Mosca
NICU, Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico - Università degli Studi di Milano, Italy

Abstract. Preterm labor is the final common pathway of different complications of pregnancy and despite substantial progress in antenatal care, preterm birth remains a major health issue across the globe. Preterm deliveries in the larger group of spontaneous preterm labor or preterm prelabor rupture of membranes (PPROM) are often associated with intrauterine chorioamnionitis. Current evidence underlines the role of "inflammatory" and "placental dysfunction" disorders in pregnancy on prematurity-associated morbidity, particularly respiratory outcome. (www.actabiomedica.it)

Key words: Preterm infant, placental dysfunction, chorioamnionitis, respiratory outcome

Introduction

Preterm labor is the final common pathway of different complications of pregnancy and despite substantial progress in antenatal care, preterm birth remains a major health issue across the globe.

The preterm birth accounts for 5 to 13% of all live births, 75% of perinatal mortalities and more than 50% of long-term infant morbidities. Pregnancy disorders that lead to preterm delivery may be separated into two groups: those associated with placental dysfunction and those associated with intrauterine inflammation. In the former group, the indicated preterm birth may relate to fetal or maternal indications for intervention such as intrauterine growth restriction (IUGR), maternal pre-eclampsia or HELLP (haemolysis, elevated liver enzymes and low platelets) syndrome. Preterm deliveries in the larger group of spontaneous preterm labor or preterm prelabor rupture of membranes (PPROM) are often associated with intrauterine chorioamnionitis (1, 2).

Intrauterine growth restriction

The regulation of normal foetal growth is based on maternal, placental and foetal interactions; abnormalities in any of these compartments results in IUGR, a multisystem disorder and a major cause of perinatal mortality and morbidity . IUGR is intended as the failure of the fetus to reach its growth potential and it is not synonymous with small for gestational age (SGA) which is a size limit which cannot differentiate between physiological and pathological smallness . The most common cause of IUGR (80-90% of all cases) is a compromised supply of nutrients and oxygen through the placenta to the foetus. Other causes of IUGR , secondary to fetal factors, usually result from an early-onset insult leading to cellular hypoplasia (3). The lung is an organ that can be detrimentally affected by adverse conditions during its early development. Experimental studies showed that placental restriction of fetal growth would alter lung structure , with subsequent impaired lung function in a variety of ways depending on the

timing, severity, duration, and type of stress imposed . The pulmonary structural changes could be explained by arrested development of the acinus with a more simplified structure, an increase in relative airspace volume and a reduction in gas exchange surface density (4). Moreover experimental IUGR causes a significant reduction vessel density indicating decreased vascularization in the fetal lung (5). Early studies indicated the possibility that IUGR infants demonstrate accelerated surfactant maturation; other studies have shown no evidence that infants have been stressed by placental insufficiency or showed that IUGR results in decreased surfactant proteins expression (6). Also the potential adverse effects of antenatal steroids (AS) in growth-restricted fetuses continue to be debated. Severe IUGR is associated with reduced 11b-hydroxysteroid dehydrogenase type 2 (11b-HSD 2) activity in the placenta,with reduced cortisol to cortisone conversion favoring excessive fetal exposure to maternal endogenous corticosteroids. The benefits of AS on lung development may be less significant in the IUGR fetus compared to the normally grown fetus , with a poor response to the immediate physiologic demands imposed by corticosteroids (7). IUGR fetuses across all gestational ages were found to be at significant risk of having respiratory complications, particularly bronchopulmonary dysplasia (BPD) . Although this risk reduces as gestation increases, it remains amplified in growth-restricted fetuses when compared to normally grown fetuses (8, 9).

Choriamnionitis

The term chorioamnionitis is used to describe the inflammation of the amniochorionic (fetal) membranes of the placenta in response to microbial invasion or due to other pathological process (10). Histologic chorioamnionitis is diagnosed in more than 50% of preterm deliveries; the more preterm the delivery, the more often histological chorioamnionitis is detected. Clinical chorioamnionitis occurs in 5-10% of preterm deliveries (11). In the animal models of chorioamnionitis, the fetal lung has a more mature lung structure with more surfactant and better compliance improving gas exchange, but lung development can be impaired with alveolar semplification , inhibition of vascular development and modulation of the fetal immune system (1, 12). The immature preterm lung is prone to injury and maternal chorioamnionitis primes the lung for further injury in response to postnatal ventilation, oxygen and nosocomial infection. Continuous exposure of the developing lung before and after delivery to inflammation may be central to the development of BPD. A single course of antenatal steroids can be considered safe for mother and child in clinical as well as histological chorioamnionitis (13). Initial reports suggest that in preterm infants histological chorioamnionitis is associated with a decreased incidence of RDS, while the incidence of BPD is increased. Considerable variation exists in the findings of subsequent human studies but recent studies generally seem to confirm the effect of chorioamnionitis on RDS incidence, while no effect on BPD is seen. The increased use of antenatal steroids and the diminished effects of secondary pro-inflammatory hits seem to explain part of this change (14).

Conclusion

Current evidence underlines the role of "inflammatory" and "placental dysfunction" disorders in pregnancy on prematurity-associated morbidity, particularly respiratory outcome. A short-term beneficial effect of histological, but not clinical chorioamnionitis on incidence and severity of RDS in preterm infants is evident. This maturational effect is accompanied by a susceptibility of the lung for further postnatal injury which predisposes for BPD. Placental restriction of fetal growth is not associated with reduced risk of RDS but it may increases the risk of BPD; otherwise in this category antenatal steroid treatment may be not beneficial or even potentially harmfull. Impact of chorioamnionitis and fetal growth restriction on adverse respiratory outcome remain substantial through their causal relationship with preterm birth.

References

1. Gantert M, Been JV, Gavilanes AWD, Garnier Y, Zimmermann LJI, Kramer BW. Chorioamnionitis: a multiorgan disease of the fetus? *Journal of Perinatology* 2010; 30: S21-S30.

2. Faye-Petersen OM. The placenta in preterm birth. *J Clin Pathol* 2008; 61: 1261-75.
3. Sankaran S. Aetiology and pathogenesis of IUGR. *Best Pract Res Clin Obstet Gynaecol* 2009; 23: 765-77.
4. Lipsett J, Tamblyn M, Madigan K, et al. Restricted Fetal Growth and Lung Development: A Morphometric Analysis of Pulmonary Structure. *Pediatr Pulmonol* 2006; 41: 1138-45.
5. Rozance PJ, Seedorf GJ, Brown A, et al. Intrauterine growth restriction decreases pulmonary alveolar and vessel growth and causes pulmonary artery endothelial cell dysfunction *in vitro* in fetal sheep. *Am J Physiol Lung Cell Mol Physiol* 2011; 301 (6): L860-71.
6. Orgeig S, Crittenden TA, Marchant C, McMillen IC, Morrison JL. Intrauterine growth restriction delays surfactant protein maturation in the sheep fetus. *Am J Physiol Lung Cell Mol Physiol* 2010; 298: L575-L583.
7. Vidaeff AC, Blackwell SC. Potential risks and benefits of antenatal corticosteroid therapy prior to preterm birth in pregnancies complicated by severe fetal growth restriction. *Obstet Gynecol Clin N Am* 2011; 38: 205-14.
8. Damodaram M, Story L, Kulinskaya E, Rutherford M and Kumar S. Early adverse perinatal complications in preterm growth-restricted fetuses. *Aust N Z J Obstet Gynaecol* 2011; 51 (3): 204-9.
9. Engineer N, Kumar S. Perinatal variables and neonatal outcomes in severely growth restricted preterm fetuses. *Acta Obstet Gynecol Scand* 2010; 89 (9): 1174-81.
10. Menon R, Taylorb RN, Fortunato SJ. Chorioamnionitis – A complex pathophysiologic syndrome. *Placenta* 2010; 31: 113-20.
11. Edwards RK. Chorioamnionitis and labor. *Obstet Gynecol Clin N Am* 2005; 32: 287-29.
12. Kramer BW, Kallapur S, Newnham J, Jobe AH. Prenatal inflammation and lung development. *Semin Fetal Neonatal Med* 2009; 14 (1): 2-7.
13. Thomas W, Speer CP. Chorioamnionitis: important risk factor or innocent bystander for neonatal outcome? *Neonatology* 2011; 99: 177-87.
14. Been JV, Zimmermann LJI. Histological chorioamnionitis and respiratory outcome in preterm infants. *Arch Dis Child Fetal Neonatal Ed* 2009; 94: F218–F225.

Correspondence:
Prof. Fabio Mosca
Department of Maternal and Pediatric Sciences,
University of Milan
Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico
Via Della Commenda 12 – 20122 Milano
Tel. +3902/5503.2907
Fax +3902/5503.2429