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Factors Leading to Respiratory Distress Syndromes in Premature Infants

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Abstract: Key risk factors, including prematurity and maternal diabetes, are reviewed, as well as the role of antenatal corticosteroids and exogenous surfactant in improving outcomes. Particular attention is paid to new methods of respiratory support, such as non-invasive ventilation and high-frequency oscillatory ventilation, and their impact on reducing complications, including bronchopulmonary dysplasia. Prospects for research aimed at optimizing therapy and prognosis are discussed. The article is intended for neonatologists, pediatricians and researchers in the field of perinatal medicine.

Keywords: Respiratory distress syndrome, maternal diabetes, preterm infants, surfactant, hypoxia, adverse outcome, risk factors, epidemiology.

Introduction: Respiratory distress is difficulty breathing. In order for newborns to breathe freely, the air sacs in the lungs must remain open and filled with air. Under normal conditions, the lungs produce a substance called surfactant. Surfactant coats the surface of the air sacs, reducing surface tension. Low surface tension allows the air sacs to remain open throughout the respiratory cycle.

Normally, the fetus begins producing surfactant around 24 weeks of gestation. By 34 to 36 weeks of gestation, the fetus has enough surfactant in its lungs to keep the alveoli open. Thus, the more premature the infant, the less surfactant it has, and the more likely it is to develop respiratory distress syndrome after birth. Respiratory distress syndrome occurs almost exclusively in premature infants, but it can also occur in full-term or near-term infants whose mothers had diabetes during pregnancy. Other risk factors include multiple pregnancies (eg, twins, triplets, quadruplets) and being male and Caucasian. In rare cases, this syndrome is caused by a mutation in certain genes that causes surfactant deficiency. This genetically determined type of respiratory distress syndrome can also occur in full-term babies .

Main part: Premature infants or infants whose mothers had diabetes during pregnancy are at increased risk of developing respiratory distress syndrome. These newborns have severe difficulty breathing and may appear blue or gray due to a lack of oxygen in the blood. The diagnosis is based on breathing problems, blood oxygen levels, and chest X-rays. Oxygen is given; a continuous positive airway pressure machine may be used to keep the alveoli open, and if the newborn's breathing becomes too difficult, mechanical ventilation may be needed. Sometimes surfactant is given until newborns begin to produce enough of their own surfactant. If treatment fails to improve low blood oxygen levels, the syndrome can lead to brain damage or death. If the fetus is expected to be born prematurely, the mother may be given corticosteroid injections to speed up the fetus's production of surfactant.

Research and result: YF Zhang et al. (2021) analyzed the neonatal course of 7150 newborns from 17 hospitals in southwestern Hubei and found that acute respiratory distress syndrome, which met the 2017 diagnostic criteria, occurred in only 66 (0.92%) children. Moderate and severe ARDS were diagnosed in 42% and 23% of cases, respectively. The main primary diseases in ARDS were: perinatal asphyxia (35%), pneumonia (27%), sepsis (18%), and meconium aspiration syndrome (15%). Fatal outcomes were recorded in 10 (15%) children. The authors conclude that ARDS in neonates, corresponding to the Montreux definitions, in most cases occurs in a mild or moderate form, perinatal asphyxia and infection are its main causes, and intraventricular hemorrhage is the most common concomitant pathology.

S. Ding et al. (2022), having assessed the outcomes of hypoxemic respiratory failure in newborns, found that it most often develops in children who required resuscitation in the delivery room (93%). The most common causes of hypoxemia were respiratory distress syndrome (36.4%) and pneumonia/sepsis (35.3%). The use of surfactant in children with a birth weight of less than 1500 g contributed to a significant improvement in treatment outcomes. The overall mortality rate in hypoxemic respiratory failure was 18.4%, but in children with ELBW at birth and a gestation period of less than 28 weeks, it was significantly higher: 70% and 54%, respectively. Using multiple regression, it was found that the highest probability of a fatal outcome in hypoxemic respiratory failure in newborns is observed with meconium aspiration syndrome, congenital developmental anomalies, birth weight less than 1500 g, and necrotizing enterocolitis.

The undoubted importance of neonatal infections as a cause of ARDS and death in newborns is evidenced by the results of the study by SM Dhaded et al. (2022), which demonstrated that the main maternal risk factors for neonatal mortality are maternal hypertension, preterm birth, funiculitis, and chorioamnionitis. The main neonatal causes of death were: intrauterine hypoxia (34%), intra-amniotic infection (20%), neonatal infections (20%), and respiratory distress syndrome (20%). Before birth, doctors can check the maturity of the fetal lungs by measuring the level of surfactant in the amniotic fluid. During a procedure called amniocentesis, amniotic fluid is taken from the gestational sac or from the mother's vagina if the membranes rupture. Surfactant levels help doctors determine the best time to deliver the baby. The risk of developing respiratory distress syndrome is significantly reduced if delivery can be safely delayed until the fetal lungs produce sufficient surfactant.

If preterm labor cannot be avoided, the midwife may give the mother injections of a corticosteroid (betamethasone). The corticosteroid passes through the placenta to the fetus and speeds up the production of surfactant. Within 48 hours of the injections, the fetal lungs may mature enough to significantly reduce the risk of developing respiratory distress syndrome after birth or, if the syndrome does develop, to have a milder course.

After birth, doctors may prescribe a surfactant preparation for newborns at high risk for developing respiratory distress syndrome. Those at risk include newborns born before 30 weeks of gestational age , especially those whose mothers did not receive corticosteroids. Using a surfactant preparation can save the baby's life and reduce the risk of certain complications, such as a collapsed lung (pneumothorax). A surfactant preparation works in the same way as natural surfactant.

Surfactant therapy is given to newborns using a tube inserted into the mouth and then into the trachea (called endotracheal intubation). It can be given immediately after birth in the delivery room to prevent respiratory distress syndrome before symptoms develop.

Conclusion: In recent years, there has been a persistent trend towards an increase in the number of cases of respiratory distress syndrome and transient tachypnea of the newborn, which is due to improved results in the care of premature infants and an increase in indications for cesarean section.

Low birth weight and short gestational age at birth are the main risk factors for adverse neonatal outcomes, especially in hospitals in developing countries with insufficient staff training and material and technical equipment. Premature infants with ELBW are a special risk group, especially if they have severe infections and sepsis. The incidence of respiratory distress in full-term infants is quite low, and is most often associated with the development of transient tachypnea of the newborn, especially after operative delivery, but in most cases there is a favorable course with full recovery.

The most effective method for preventing respiratory distress in preterm infants is antenatal prophylaxis with corticosteroids, while their use in full-term infants does not significantly affect the incidence of respiratory complications and the course of the neonatal period.

One of the risk factors for the development of respiratory distress in premature infants is hypothermia, which is an extremely pressing problem for maternity hospitals in resource-poor countries, indicating the need for careful monitoring of body temperature and maintaining an optimal temperature regime in the first minutes and hours of a child's life.

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