

RESPIRATORY DISTRESS SYNDROME IN INFANTS- AN OVERVIEW

Article: Review

Running title: Respiratory distress syndrome.

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Abstract: Respiratory distress syndrome (RDS) is a breathing disorder that affects newborns. RDS rarely occurs in full-term infants. The disorder is more common in premature infants born about 6 weeks or more before their due dates. In fact, nearly all infants born before 28 weeks of pregnancy develop RDS. RDS is more common in premature infants because their lungs aren't able to make enough surfactant (sur-FAK-tant). Surfactant is a liquid that coats the inside of the lungs. It helps keep them open so that infants can breathe in air once they're born. Without enough surfactant, the lungs collapse and the infant has to work hard to breathe. He or she might

not be able to breathe in enough oxygen to support the body's organs. The lack of oxygen can damage the baby's brain and other organs if proper treatment isn't given. Most babies who develop RDS show signs of breathing problems and a lack of oxygen at birth or within the first few hours that follow. Due to improved treatments and medical advances, most infants who have RDS survive. However, these babies may need extra medical care after going home. Some babies have complications from RDS or its treatments. Serious complications include chronic (ongoing) breathing problems, such as asthma and BPD; blindness; and brain damage. This paper will outline the clinical course, diagnosis, treatment for the same and also will draw a simple conclusion.

Keywords: Respiratory distress syndrome, surfactant, hyaline membrane disease, tachypnea, tachycardia, chest wall retractions (recession), expiratory grunting, nasal flaring, cyanosis, glycoproteins, pneumocytes, air-bronchograms, glucocorticoid.

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1. Introduction

There are many diseases that can be seen in infants such as anemia, breathing problems, congenital heart defects, hypoglycemia, jaundice, macrosomia, necrotizing enterocolitis, retinopathy of prematurity, intraventricular haemorrhage, bronchopulmonary dysplasia, intrauterine growth restriction, sepsis, feeding problems, inability to control body heat, gastroschisis and many more. Infants or premature babies are often anemic and this means that they don't have enough red blood cells.[1] Normally, the fetus stores iron during the latter months of pregnancy and uses it after birth to produce red blood cells. Hence, infants born too soon may not have had enough storage of iron. Loss of blood from frequent blood

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tests also can contribute to anemia. Anemic infants may be treated with dietary iron supplements, drugs that increase red blood cell production, and also in some cases, a blood transfusion can be done. An infant or a premature baby also may stop breathing for about 15 to 20 seconds or more. Thus, this interruption in breathing is called apnea and it may be accompanied by a slow heart rate called bradycardia. Infants in the NICU are constantly monitored for apnea and bradycardia.

Not only that but sensors on the baby's chest will help send information about the breathing regulation and heart rate to a machine located near the incubator.[2] If the infant stops breathing, an alarm will begin beeping. Bronchopulmonary dysplasia is a chronic lung disease which is most common in infants and premature babies who have been treated for respiratory distress syndrome. Infants with respiratory distress syndrome have immature lungs. They sometimes need a mechanical ventilator to help them breathe. Some infants who are treated for respiratory distress syndrome may develop symptoms of bronchopulmonary dysplasia, including fluid in the lungs, scarring, and also not to forget lung damage. Bronchopulmonary dysplasia also occasionally occurs in full-term newborn which after they have had pneumonia or any other acute or chronic infections.[2,3] Respiratory distress syndrome in infants can be divided into three types, and they are as following the first one is acute respiratory distress syndrome which follows a catastrophic pulmonary or non-pulmonary events, such as asphyxia, , shock, sepsis and disseminated intravascular coagulation. The second type is of idiopathic respiratory distress syndrome mainly seen in selective cesarean section babies and the third type is respiratory distress syndrome relating to inherited surfactant disorders, inherited disorders of surfactant metabolism which is a rare condition but also associated with morbidity and mortality. Furthermore, bronchiolitis is usually the result of a viral inflammation of the very small airways called bronchioles. It affects children of less than 2 years of age and it is characterised by rapid breathing, chest retraction and also by wheezing. Respiratory syncytial virus infection is the most common cause of bronchiolitis and other lower respiratory tract infections during the first year of life, and is also one of the major causes of hospital admissions in infants under 1 year of age. The infants were characteristically present with symptoms of a viral infection with mild rhinorrhoea, cough, and, also a low-grade fever. Moreover, within 1 or 2 days, these symptoms are followed by rapid respiration, wheezing and chest retraction. The infant may be irritable, lack appetite and may vomit. Other causative viruses for bronchiolitis are human meta-pneumovirus, adenovirus, adenovirus and also influenza virus.[3] The first hours and days of life are very crucial and have a lot of importance for the newborn infant. As the infant starts adapting to the extra-uterine environment, the new born infant is vulnerable and delicate to a range of respiratory diseases, at this period of early life fluid-filled fetal lungs adapt to the extrauterine environment. The clinical signs of respiratory distress are very important to recognise and thus further investigations are done to identify the underlying cause.[4]

2. Respiratory Distress Syndrome in Infants

Respiratory Distress Syndrome in Infants (RDS) is also called respiratory distress syndrome of newborn, neonatal respiratory distress syndrome, infant respiratory distress syndrome (IRDS) or increasingly surfactant deficiency disorder (SDD) and also previously called hyaline membrane disease (HMD). It is a syndrome seen in premature infants caused by developmental insufficiency of surfactant production and structural immaturity in the lungs.[2,5] Furthermore, it can also result from a genetic problem with the production of surfactant associated proteins. RDS affects about 1% of newborn infants and it is the leading cause of death in preterm infants. The incidence decreases with gestational age, from about 50% in babies born at 26–28 weeks, to about 25% at 30–31 weeks.[6] The syndrome is frequent in infants of diabetic

mothers and in the second born of premature twins.[7] Embryonic period – At approximately 26 days of gestation, the embryonic stage begins with the first appearance of the fetal lung, which appears as a protrusion of the foregut. The initial branching of the lung occurs at 33 days gestation forming the prospective main bronchi, which begin to extend into the mesenchyme. Further branching forms the segmental bronchi as the lung enters the next stage of development. RDS is more distinctive when compared to pulmonary hypoplasia which is another leading cause of neonatal death.[8] Certain useful questions are asked for better assessment of the RDS. The initial assessment of an infant with respiratory distress syndrome should include blood tests which includes full blood count, C- reactive protein, blood culture and blood gases. Not only that but, pulse oximetry and chest radiography are done too. The initial treatment will aim to reverse the hypoxia, hypercapnia and acidosis that may have been developed. Fatality rates were significantly higher in infants with severe RDS if self-sustaining, spontaneous breathing was delayed more than one minute after birth.[8,9]

Clinical course

RDS begins shortly after birth and the symptoms are as such tachycardia, tachypnea, chest wall retractions, expiratory grunting, cyanosis and nasal flaring during breathing efforts.[10] As the disease progresses, the baby may develop breathing difficulties which is rise in the carbon dioxide concentrations in the blood, and prolonged cessations of breathing which is termed as apnea. Whether the infant is treated or not, the clinical course for the acute disease lasts for about 2 to 3 days. During the first day the patient worsens and requires more support and during the second day the baby may be absolutely stable on adequate support and resolution is noted during the third day.[11] Despite various advances in care, RDS remains the most common single cause of death in the first month of life in the developed world. Complications include metabolic disorders (acidosis, low blood sugar), patent ductus arteriosus, low blood pressure, intracranial hemorrhage, and chronic lung changes. The disease is frequently complicated by prematurity and its additional defects in other organ functions.[11][12]

Histopathology

The characteristic histopathology features seen in babies who die from RDS was the source of the name "hyaline membrane disease". Waxy-appearing layers of hyaline membrane lined the collapsed alveoli of the lung. In addition, the lungs show bleeding, overdistention of airways and also damage to the lining cells. Alveoli are poorly developed and are frequently collapsed. Pink hyaline membranes which lines the respiratory bronchioles, alveolar ducts and random alveoli can be seen. On histologic examination the lungs have a peculiar appearance.[13] The alveoli are collapsed and the alveolar ducts and respiratory bronchioles are expanded and dilated. Within these spaces cellular debris can be seen, proteinaceous edema fluid and some red blood cells accumulation. The lining of the alveolar ducts is covered with excessive thin fibrin-rich hyaline membranes. Furthermore the walls of the collapsed alveoli are thick, thus the capillaries are congested, and the lymphatics are filled with proteinaceous material.[13,14]

Pathophysiology

The lungs of infants with respiratory distress syndrome are developmentally deficient in a material called surfactant, which helps prevent collapse of the terminal air-spaces throughout the normal cycle of inhalation and exhalation. Surfactant is made up of a complex system of lipids, glycoproteins and proteins which are produced in specialized lung cells called Type II cells or Type II pneumocytes. The surfactant is packaged by cells in structures called lamellar bodies, which extends into the air-spaces. The lamellar bodies then unfold into a complex lining of the air-space. This layer reduces the surface tension of the fluid that lines the alveolar air-space. Surface tension is responsible for approximately

2/3 of the inward elastic recoil forces. For example, a bubble will contract to give the smallest surface area for a given volume, so that the air or water interfaces the liquid surface will appear as small as possible, thus causing the air-space to contract.[15]By reducing surface tension, surfactant prevents the air-spaces from completely collapsing on exhalation. In addition, the decreased surface tension allows re-opening of air-space with a lower amount of force. Therefore, without any adequate amounts of surfactant, the air-spaces collapse and are difficult to expand. Microscopically, a surfactant deficient lung is characterized by collapsed air-spaces alternating with, vascular congestion, hyper-expanded areas and, hyaline membranes. Hyaline membranes are composed of fibrin, cellular debris, red blood cells, rare neutrophils and macrophages.

They appear as an eosinophilic, amorphous material, which lines or fill the air spaces and blocks gas exchange. As a result, blood passing through the lungs is unable to pick up oxygen and unload carbon dioxide. Blood oxygen level falls and carbon dioxide rises, resulting in rise in blood acid levels and hypoxia. Structural immaturity, as manifested by decreased number of gas- exchange units and thicker walls, also contributes to the disease process. Therapeutic oxygen and positive-pressure ventilation, while it is potentially life-saving, can also damage the lungs. [16]

Risk Factors

The risk of RDS increases inversely with the decreasing gestational age hence the commonest at-risk group to be affected are the preterm infants. Moreover, gestational age, low birthweight, maternal age, elective and emergency caesarean section and male sex are all risk factors for RDS too. Usage of antenatal corticosteroids to boost foetal lung surfactant and antioxidant enzyme production is now a threat in preterm labour between the 24th and 34th week of gestation and sometimes considered at 35–36 weeks gestation. Reducing elective caesarean sections can help, whereas RDS is secondary to Caesarean sections which accounts for only a small number of the total incidence everywhere. [16,17]

Diagnosis

The diagnosis is made by the clinical picture and by observing the chest x-ray, which shows decreased lung volumes (bell-shaped chest), absence of the thymus (after about 6 hours), discrete, uniform infiltrate (sometimes described as a "ground glass" appearance that involves all lobes of the lung, and air-bronchograms for example the infiltrate will outline the larger airways passages which remains air-filled. In severe cases, this becomes exaggerated until the cardiac borders become in apparent which is a 'white-out' appearance.[18]

Prognosis

A literature has been reviewed on the outcome of infants given surfactant for RDS and concluded that the risk of respiratory abnormalities later in infancy such as recurrent wheezing, asthma, respiratory infection, pulmonary function test abnormalities and early childhood remains high for preterm infants with respiratory distress syndrome'. The long term effects of respiratory disease in the newborn however require further study and research to be carried out.[18,19]

Prevention

Most cases of respiratory distress syndrome in infants can be prevented if mothers who are about to give birth in a premature state, are administered with glucocorticoids. This speed the production of surfactant. For very premature delivery, a glucocorticoid is given without testing the fetal lung maturity. The American College of Obstetricians and Gynecologists (ACOG), Royal College of Medicine, and other major organizations have recommended antenatal glucocorticoid treatment for women at risk for preterm delivery prior to 34 weeks of

gestation.[19,20] Multiple courses of glucocorticoid administration, compared with a single course, doesn't seem to increase or decrease the risk of death and also the neuro developmental disorders of the child. In pregnancies of greater than 30 weeks, the fetal lung maturity can be tested by sampling the amount of surfactant in the amniotic fluid by amniocentesis, where a needle is inserted through the mother's abdomen and uterus. Several tests are available that correlate with the production of surfactant. These include the lecithin-sphingomyelin ratio ("L/S ratio"), the presence of phosphatidylglycerol (PG), and more recently, the surfactant/albumin (S/A) ratio. For the L/S ratio, if the result is less than 2:1, the fetal lungs may be deficient in surfactant. The presence of PG indicates fetal lung maturity and for the S/A ratio, the result given as mg of surfactant per gm of protein. An S/A ratio <35 indicates immature lungs, between 35-55 is indeterminate, and >55 indicates mature surfactant is produced. [20]

Prevalence

The overall incidence of respiratory distress syndrome was 6.7% and in preterm babies, they had the highest incidence (30.0%) followed by post-term (20.9%) and term babies (4.2%). Transient tachypnea of newborn was found to be the commonest (42.7%) cause of respiratory distress syndrome in infants followed by infections (17.0%), hyaline membrane disease (9.3%) and also birth asphyxia (3.3%). Transient tachypnea of newborn was found to be common among both term and preterm babies. While Hyaline membrane disease was seen mostly among preterm babies. Overall case fatality rate for respiratory distress syndrome in infants was found to be about 19%, being highest for the hyaline membrane disease (57.1%), followed by infection (15.6%). The results indicate that respiratory distress syndrome in infants is a common neonatal problem worldwide. [20] The risk of developing respiratory distress syndrome increases with Caucasian race, most common in male sex, an older sibling with a history of respiratory distress syndrome, cesarean delivery, perinatal asphyxia, and maternal diabetes too. In 2003, the total number of live births in the United States for all races was 4,089,950 and about 0.6 percent of newborns had respiratory distress syndrome which is about 24,000 and in 2005, there were about 4,138,000 live births in the United States, and a slightly a larger number of babies were affected with respiratory distress syndrome because the rate of premature births had increased from 11.6 percent to 12.7 percent. This is mainly due to a rise in late preterm births which is about 34 to 36 weeks of gestation and even though the number of respiratory distress syndrome in infants cases in the United States is increasing, the infant mortality rate for RDS has dramatically decreased from about 25,000 deaths per year in the 1960s to 860 deaths in the year 2005 because of surfactant replacement therapy. Infant deaths from RDS were seen 2.6 times greater in African American babies than in Caucasian babies, although Caucasian babies are at a higher risk to develop this particular condition.[21]

Treatment

Oxygen is given with a small amount of continuous positive airway pressure ("CPAP"), and intravenous fluids are administered to stabilize the blood sugar, blood salts, and blood pressure. If the baby's condition worsens, an endotracheal tube is inserted into the trachea and intermittent breaths are given by a mechanical device. An exogenous preparation of surfactant, either synthetic or which has been extracted from animal lungs, is given through the breathing tube into the lungs. One of the most commonly used surfactants is Survanta, derived from cow lungs, which can decrease the risk of death in hospitalized very-low-birth-weight infants by 30%. Such small premature infants may remain ventilated for months. A line of research shows that an aerosol of perfluorocarbon can reduce inflammation in piglets. Chronic lung diseases including bronchopulmonary dysplasia are common in severe RDS. The mortality rate for babies greater than 27 weeks gestation is less than 10%. Extracorporeal membrane oxygenation (ECMO) is a potential treatment, which provides oxygen through an apparatus that imitates the gas exchange process of the lungs. However, newborns cannot be placed on

ECMO if they are under 4.5 pounds (2 kg), because they have extremely small vessels for cannulation, thus a blockage is created and adequate flow will not take place because of limitations from cannula size and subsequent higher resistance to blood flow. Furthermore, in infants aged less than 34 weeks of gestation several physiologic systems are not well-developed, especially the cerebral vasculature and germinal matrix, resulting in high sensitivity to slight changes in pH, PaO₂, and intracranial pressure. Subsequently, preterm infants are at unacceptably high risk for intraventricular hemorrhage (IVH) if administered ECMO at a gestational age less than 32 weeks. Not only that, given the risk of IVH, it has become standardized practice to get an ultrasound of the brain prior to administering ECMO. Therefore, the device cannot be used for most premature new-borns the combination of surfactant replacement and mechanical ventilation was introduced in the 1980's. Not only that but currently, this combination is used as both prophylactic and also as a rescue therapy for respiratory distress syndrome, with a reduction in mortality.

When surfactant is given prophylactically at birth, some infants who do not need the medication are also treated. On the other hand, waiting until respiratory distress syndrome has developed may be that the treatment is given too late to benefit some babies. Furthermore, mechanical ventilation may have complications such as suction of the trachea may cause hypoxia and suboptimal ventilatory settings may cause leakage of air and depletion of surfactant and more.[21] Nutrition is important and essential for normal lung development and maturation. Several studies have shown that poor nutrition, especially lack of protein after birth may increase the risk of lung injury that can lead to bronchopulmonary dysplasia. Vitamin A, a nutrient which is important for cell growth, has been shown to decrease the risk of bronchopulmonary dysplasia in some studies. Other nutrients may also provide premature infants with added protection against this condition.[21]

3. Recommendations

Based on the primary and secondary information gathered on respiratory distress syndrome in infants, the causes, risk factors, histopathology, pathophysiology, prevalence and more was gathered in this review article. Thus, for further knowledge and more information, a study or research should be carried out based on the information given in this review which might be useful for other study or research purposes.

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5. Conclusion

Sex did not appear to affect survival of the newborn infants who had respiratory distress syndrome in severe forms. Male premature infants with birth weights of about 1,500 gm were three times more likely to have severe respiratory distress syndrome than female infants. Not only that but, race did not appear to alter the fatality rate among infants with severe respiratory distress syndrome. The effect of birth weight on survival in respiratory distress syndromes depends on how the scope of was defined. When infants with the mild form of the syndrome were excluded, no significant decrease in fatality rates was observed. Moreover, as the birth weight increased from about 1,251 to 2,250 gm the infants with both severe and mild forms of the syndrome were included, there was a very significant decrease in fatality rates as birth weight increased. This inverse relationship data was related to the fact that the ratio of mild to severe cases increased with the birth weight. Fatality rates were significantly higher among infants with severe respiratory distress syndrome if spontaneous breathing was delayed more than one minute after birth or even by self- sustaining ability. Surfactant treatment in preterm infants and term newborns with respiratory distress syndrome like severe respiratory failure has become a part of an individualized treatment strategy in many neonatal intensive care units around the world. These infants are heterogeneous groups of gestational ages, lung maturity, as well as of underlying disease which includes postnatal interventions. Despite the fact that the majority of suggested indications, there is no data that exist from randomized controlled trials.

Surfactant replacement seems to improve oxygenation and lung function in many infants with RDS without any apparent negative side effects .RDS has some similarities to Acute respiratory distress syndrome (ARDS). Transient hyperammonemia of the new born presents with respiratory distress syndrome in the preterm newborn. Famous victims of RDS are Patrick Bouvier Kennedy (in 1963), son of President John F. Kennedy and First Lady Jacqueline Kennedy, who died of RDS two days after his premature birth at 34 weeks gestation.

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