Transient Tachypnea of the Newborn

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Background:

Transient tachypnea of the newborn (TTN) is a disease common in infants throughout the world and has been encountered by all physicians who care for newborn infants. Infants with TNN present within the first few hours of birth with tachypnea, increased oxygen requirement, and occasional hypoxia noted on arterial blood gases without concomitant carbon dioxide retention. When managing an infant with TTN, it is important to observe for signs of clinical deterioration that may suggest other diagnoses and to observe closely for the development of fatigue.

Pathophysiology:

Noninfectious acute respiratory disease develops in approximately 1% of all newborn infants and results in admission to a critical care unit. TTN is the result of a delay in clearance of fetal lung liquid. Respiratory distress typically was thought to be a problem of relative surfactant deficiency, but it is now characterized by an airspace-fluid burden secondary to the inability to absorb fetal lung liquid.

In vivo experiments have demonstrated that lung epithelium secretes Cl - and fluid throughout gestation but only develops the ability to actively reabsorb Na + during late gestation. At birth, the mature lung switches from active Cl - (fluid) secretion to active Na + (fluid) absorption in response to circulating catecholamines. Changes in oxygen tension augment the Na + -transporting capacity of the epithelium and increase gene expression for the epithelial Na + channel (ENaC). The inability of the immature fetal lung to switch from fluid secretion to fluid absorption results, at least in large part, from an immaturity in the expression of ENaC, which can be upregulated by glucocorticoids.

Both pharmacologic blockade of the lung's EnaC channel and genetic knockout experiments using mice deficient in the ENaC pore-forming subunit have demonstrated the critical physiologic importance of lung Na + transport at birth. When Na + transport is ineffective, newborn animals develop respiratory distress; hypoxemia; fetal lung liquid retention; and, in the case of the ENaC knockout mice, death. Bioelectrical studies of human infants' nasal epithelia demonstrate that both TTN and respiratory distress syndrome (RDS) have defective amiloride-sensitive Na + transport.

These results suggest that infants with neonatal RDS have, in addition to a relative deficiency of surfactant, defective Na + transport, which plays a mechanistic role in the development of the disease. An infant born by cesarean delivery is at risk of having excessive pulmonary fluid as a result of having not experienced all of the stages of labor and subsequent low release of counter-regulatory hormones at the time of delivery.

Frequency:

In the US: Frequency is equivalent universally. Approximately 1% of infants have some form of respiratory distress that is not associated with infection. Respiratory distress includes both RDS (ie, hyaline membrane disease) and TTN. Of this 1%, approximately 33-50% is TTN.

Mortality/Morbidity:

TTN is generally a self-limited disorder without significant morbidity. TNN resolves over a 24- to 72-hour period.

Race:

No racial predilection exists.

Sex:

Risk is equal in both males and females.

Age:

Clinically, TTN presents as respiratory distress in full-term or near-term infants.

History:

Signs of respiratory distress (eg, tachypnea, nasal flaring, grunting, retractions, cyanosis in extreme cases) become evident shortly after birth. The disorder is indeed transient, with resolution occurring usually by age 72 hours.

Physical: Physical findings include tachypnea, with variable grunting, flaring, and retracting. Extreme cases also may exhibit cyanosis.

Causes: The disorder results from delayed absorption of fetal lung fluid following delivery. TNN commonly is observed following birth by cesarean delivery because infants do not receive the thoracic compression that accompanies vaginal delivery.

- Cesarean delivery
    - Studies utilizing lung mechanic measurements were performed on infants born by either cesarean or vaginal delivery. Milner et al noted that the mean thoracic gas volume was 32.7 mL/kg for infants born vaginally and 19.7 mL/kg for infants born via cesarean delivery. Importantly, chest circumferences were the same. Milner et al noted that the infants born via cesarean delivery had higher volumes of interstitial and alveolar fluid compared to those born vaginally, even though the overall thoracic volumes were within the normal range.
    - Epinephrine release during labor has an effect on fetal lung fluid. In the face of elevated epinephrine levels, the chloride pump responsible for lung liquid secretion is inhibited, and

the sodium channels that absorb liquid are stimulated. As a result, net movement of fluid from the lung into the interstitium occurs. Therefore, in the lack of this normal surge in counter-regulatory hormones in the infant, excursion of pulmonary fluid is limited.

- Maternal asthma and smoking
    - In a recent study, Demissie et al performed a historical cohort analysis on singleton live deliveries in New Jersey hospitals during 1989-1992. After controlling for confounding effects of important variables, infants of mothers with asthma were more likely to exhibit TTN than infants of mothers in the control group.
    - Schatz et al studied a group of 294 pregnant women with asthma and a group of 294 pregnant women without asthma with normal pulmonary function test results. The groups of women were matched for age and smoking status. TTN was found in 11 infants (3.7%) of the women with asthma and in 1 infant (0.3%) of the women from the control group. No significant differences between asthmatic and matched control subjects in other TTN risk factors were observed.
- Prolonged labor
    - Other recent studies have found that obstetric histories of mothers of newborns with TTN were characterized by longer labor intervals and a higher incidence of failure to progress in labor leading to cesarean delivery.
    - Excessive maternal sedation, perinatal asphyxia, and elective cesarean delivery without preceding labor are not frequently associated with TTN.

Other Problems to be Considered:

Cerebral hyperventilation
Metabolic acidosis

Lab Studies:

- Arterial blood gas
    - An ABG is important to ascertain the degree of gas exchange and acid-base balance.
    - Consider an intraarterial catheter if the infant's inspired fraction of oxygen exceeds 40%.
    - Hypoventilation is very uncommon, and partial carbon dioxide tensions are usually low because of the tachypnea. However, a rising carbon dioxide tension in an infant with tachypnea may be a sign of fatigue and impending respiratory failure.
- Pulse oximetry
    - Continuously monitor infants by pulse oximetry for assessment of oxygenation.
    - Pulse oximetry allows the clinician to adjust the level of oxygen support needed to maintain appropriate saturation.

Imaging Studies:

- Chest x-ray
    - The chest x-ray (CXR) is the diagnostic standard for TTN.
    - The characteristic findings are prominent perihilar streaking, which correlates with the engorgement of the lymphatic system with retained lung fluid, and fluid in the fissures. Patchy infiltrates also have been described.
    - A follow-up CXR may be necessary if the clinical history suggests meconium aspiration syndrome or neonatal pneumonia. In these cases, the CXR shows persistent infiltrates. Abnormalities resolve by 72 hours of life in cases of TTN.

Medical Care:

- Medical care is supportive. As the retained lung fluid is absorbed by the infant's lymphatic system, the pulmonary status improves.
- Supportive care includes intravenous fluids and gavage feedings (until the respiratory rate has decreased enough to allow oral feedings). Supplemental oxygen to maintain adequate arterial oxygen saturation, maintenance of thermoneutrality, and an environment of minimal stimulation are the therapies necessary for these infants.
- As TTN resolves, the infant's tachypnea improves, oxygen requirement decreases, and the CXR shows resolution of the perihilar streaking.
- Infants with TTN may have signs that last from a few hours to several days. Rarely, an infant may develop a worsening picture of respiratory distress after several days. This may require more aggressive support including the use of continuous positive airway pressure (CPAP) by nasal prongs or endotracheal tube, or mechanical ventilation.

Consultations:

Infants with TTN occasionally may require consultation by a neonatologist. Consider this consultation if the fraction of inspired oxygen exceeds 40%, if metabolic or respiratory acidosis is present, if CPAP or mechanical ventilation is required, if the infant begins to display fatigue (periodic breathing or apnea), or if the infant fails to improve by age 48-72 hours.

Diet:

Infants with TTN generally are supported by intravenous fluids or gavage feedings. Oral feedings are withheld until the respiratory rate is consistently normal (<60 bpm).

Medication:

The use of medications for TTN is minimal. Aside from the use of antibiotics for a period of 36-48 hours after birth until sepsis has been ruled out, no further pharmacotherapy generally is prescribed. Diuretics have not been shown to be beneficial.

Drug Category: Antibiotics -- Used when sepsis is clinically suggested. Antibiotics generally consist of a penicillin (usually ampicillin) and an aminoglycoside (usually gentamicin) or a cephalosporin (usually cefotaxime). Choices are based on local flora and antibiotic sensitivities.

Further Inpatient Care:

- After resolution of TNN, focus further inpatient care on routine newborn management.
- No further medical therapy concerning the infant's pulmonary function is required.

Transfer:

- When managing an infant with TTN, it is important to have appropriately trained support staff. Infants with TTN and pneumonia or meconium aspiration may have similar clinical presentations. Therefore, staff members must be competent in recognizing worsening respiratory distress or impending failure and must be able to appropriately resuscitate the infant.
- Transfer generally is indicated by the need for a higher level of observation and/or care.

Complications:

- Few potential complications exist.
- Gross et al noted a population of 55 pregnancies after which newborns developed TTN compared to 355 pregnancies after which respiratory distress did not occur. Neonatal complications and procedures often associated with prematurity were found to be significantly increased in the infants who developed TTN. Therefore, potential complications can occur in these patients. Carefully monitor infants for signs of worsening respiratory distress.

Prognosis:

- Prognosis is excellent.
- Asthma: Schaubel et al looked at neonatal characteristics as risk factors for preschool asthma. The study demonstrated that infants with TTN are at an increased risk for hospitalization from asthma during the preschool years.

Patient Education:

Inform parents that TTN is usually a self-limited disorder and is not life threatening.

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