Neonatal Pneumonia

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Pneumonia is an important cause of morbidity and mortality among newborn infants. It remains a difficult disease to prospectively identify and treat. Clinical manifestations are often nonspecific and include respiratory and hemodynamic signs. Radiographic and laboratory findings also have limited diagnostic value. Attempts to identify the specific microbes responsible for pneumonia are often unsuccessful. This could be because the organisms may be difficult to recover from intrapulmonary sites without being contaminated by airway commensals, may be uncultivatable primarily or because of ongoing antibiotic treatment, and inflammation may result from noninfectious causes, such as aspiration of meconium, food or blood.

Frequency and extent of problem

Pneumonia occurs frequently in newborn infants, although reported rates vary considerably depending on the diagnostic criteria used and the characteristics of the population under study. Frequencies in hospital born babies range from 5-50 per 1000 live births(1-3). Higher rates are observed in the settings of maternal chorioamnionitis, prematurity, and meconium in the amniotic fluid. Determination of mortality rates among infants with congenital pneumonia is complicated by variations in diagnostic criteria. Mortality rate in pneumonia was 25 times higher in neonates than in post neonatal infants (4). Of all deaths that occur in neonates, pneumonia is a contributing factor in 20% (5).

Host defenses in the lung

To prevent injury by microorganisms and foreign substances, a variety of defense mechanisms have evolved, both systemic and within the respiratory tract. Some mechanisms are nonspecific and are directed against any invasive agent, while others are targeted against specific antigens.

Nonspecific defenses include the glottis and vocal cords, ciliary escalator, airway secretions, migratory and fixed phagocytes, nonspecific antimicrobial proteins and opsonins, and the normal airway flora (alpha-hemolytic streptococci and coagulase-negative staphylococci). Anatomic structures of the upper airway and associated reflexes discourage particulate material from entering, while coordinated movement of the microscopic cilia on the tracheal and bronchial epithelia tends to sweep particles and mucous up the airway and away from the alveoli and distal respiratory structures. Mucoid airway secretions provide a physical barrier that minimizes epithelial adhesion and subsequent invasion by microorganisms. These secretions typically contain complement components, fibronectin, iron-binding proteins, lysozymes, and defensins. Many of the defenses are compromised in the fetus and newborn infant. Newborn infants typically have sterile respiratory mucosa at birth. Access to distal respiratory structures and bypass of the ciliary escalator occurs in infants who require endotracheal intubation. In these infants, increased physical disruption of epithelial and mucous barriers also occurs. Exposure to high oxygen concentrations and airway pressures interferes with ciliary function and mucosal integrity. Secretory antibodies and mucosal lymphoid tissue are absent or minimally functional for the first month of life. Circulating complement components are present at approximately 50% of the concentration found in older children, although components of the alternative pathway are present in sufficient quantities to serve as effective opsonins. The neonatal granulocytes frequently decrease in response to early infection, while the phagocytes that are present often move

much more sluggishly to the inflammatory focus.

Pathogenesis

In neonatal pneumonia, injuries are caused directly and indirectly by the invading microorganisms or foreign material and by inappropriate responses by the host defense system . This tends to increase airway smooth muscle tone and resistance, mucous secretion, and the presence of inflammatory cells and debris in these secretions. These materials may further increase airway resistance and obstruct the airways, causing airtrapping and atelectasis. Disruption of endothelial and alveolar epithelial integrity, meconium or pathogenic microorganisms. may allow surfactant to be inactivated by proteinaceous exudate (6).The myocardium has to work harder to overcome the alterations in pulmonary vascular resistance that accompany the changes of pneumonia.

Pneumonia that becomes clinically evident within 24 hours of birth or later may originate at 3 different times. Overlap often exists among the 3 types, and assigning a particular pneumonic episode to one of these categories may be difficult. The 3 categories of congenital pneumonia are (i) true congenital pneumonia, (ii) intrapartum pneumonia, and (iii) postnatal pneumonia. Not all pneumonia diagnosed in the first 24 hours of life is infectious. True congenital pneumonia is acquired transplacentally and is one of the features of a greneralised congenital infection.It is established long before birth or relatively shortly before birth. The infant has clinical signs of pneumonia almost immediately after birth. Intrauterine pneumonia is a pathological diagnosis. Features of inflammation of lungs are seen on autopsy of still births or of babies who die soon after birth.

Transmission of congenital pneumonia usually occurs via 1 of 3 routes:

Hematogenous transmission: If the mother has a bloodstream infection, the microorganism can readily cross the few cell layers that separate the maternal from the fetal circulation at the villous pools of the placenta.

Ascending transmission: Ascending infection from the birth canal and aspiration of infected or inflamed amniotic fluid have significant common features. Infected amniotic fluid often involves ascending pathogens from the birth canal but may result from hematogenous seeding or direct introduction during pelvic examination, amniocentesis, placement of intrauterine catheters, or other invasive procedures.

Transmission via aspiration: Most bacterial infections produce clinical signs of infection in the mother, but infections may not be evident if the membranes rupture shortly after inoculation, similar to drainage of an abscess. Some nonbacterial organisms, such as Ureaplasma urealyticum, may be present in the amniotic cavity for long periods and cause minimal symptoms in the mother. If the fetus aspirates infected fluid prior to delivery, organisms that reach the distal airways or alveoli may need to cross only 2 cell layers (alveolar epithelium, capillary endothelium) to enter the bloodstream.

Intrapartum pneumonia is acquired during passage through the birth canal. Intrapartum pneumonia may be acquired via hematogenous or ascending transmission, or it may result from aspiration of infected or contaminated maternal fluids or from mechanical .

Postnatal pneumonia originates after the infant has left the birth canal. It may result from some of the same processes as the other forms.

Aetiology

Organisms responsible for pneumonia mirror those responsible for early-onset neonatal sepsis. Group B Streptococcus has been the most common bacterial isolate in the west. However, Group B Streptococcus is not commonly seen in India. Commonly implicated bacterial organisms in India include Klebsiella pneumoniae, Escherichia coli and Staphylococcus aureus (1, 7). Transplacental pneumonia usually occurs in association with congenital syphilis, cytomegalovirus, herpes virus, rubella, toxoplasma, listeria monocytogenes and mycoplasma infections. These infants show involvement of many organ systems and

manifestations of pneumonitis may be obscured (8). Chlamydia is presumably transmitted at birth during passage through an infected birth canal, although most infants are asymptomatic during the first 24 hours and develop pneumonia only after the first 2 weeks of life.

Respiratory pathogens, such as respiratory syncytial virus, influenza, adenovirus, and others, may be transmitted by contact with infected family members or caregivers shortly after birth, but infection by these organisms rarely is manifested during the first 24 hours. Frequency of neonatal pneumonia due to chlamydia and viruses has not been evaluated in India

Clinical Features

Prenatal features that suggest an increased risk for congenital pneumonia include rupture of membranes before the onset of labor or more than 18 hours before delivery, maternal fever (>38°C), uterine tenderness, foul-smelling amniotic fluid, meconium in the amniotic fluid, recurrent maternal urinary tract infection and unexplained preterm labor. Intrapartum antibiotic therapy reduces the risk of postpartum maternal infection and infection of the infant in the presence of some of these risk factors, but the experience is confined to Group B Streptococcus. Absence of these risk factors does not exclude pneumonia.

Physical findings are mostly nonspecific and may be seen in many other common neonatal conditions. Some findings are insensitive and seen in relatively few infants with pneumonia.

Pulmonary findings include tachypnea (respiratory rate >60/min), expiratory grunting, accessory respiratory muscle recruitment, such as nasal flaring and retractions at subcostal, intercostal, or suprasternal sites. Occasionally, signs of distress cannot be manifested if the infant is affected by other processes like birth asphyxia that result in apnea. Airway secretions may vary substantially but are most often profuse and progress from serosanguinous to a more purulent appearance. Rales, rhonchi, and cough are all observed much less frequently in infants with pneumonia than in older individuals. However, they may also be caused by noninflammatory processes, such as congestive heart failure, condensation from humidified gas administered during mechanical ventilation, or endotracheal tube displacement. Cyanosis of central tissues, such as the trunk, implies a deoxyhemoglobin concentration of more than 5 g/dL However, congenital heart disease, hemoglobinopathy, polycythemia, and pulmonary hypertension (with or without other associated parenchymal lung disease) may also cause cyanosis.

Infants may have external staining or discoloration of skin, hair, and nails when meconium or blood are aspirated. Infants with pneumonia may manifest asymmetry of breath sounds and chest excursions, which suggest air leak or emphysematous changes secondary to partial airway obstruction. Systemic findings often mirror manifestations seen with sepsis or other severe infections.

Diagnosis

Diagnostic criteria for neonatal pneumonia are unsatisfactory (9). World Health Organisation defines pneumonia as respiratory rate greater than 60 per minute (10). In a study, 12% neonates had respiratory rates lower than this and fatality in these neonates was significantly higher (7). Any of the conditions causing respiratory distress may have superimposed pneumonia as well. Presence of respiratory distress, sepsis screen, blood culture and X ray chest in combination are useful in making the diagnosis as X-ray chest alone may be non contributory in 15% and blood culture positivity is only 48% (7). However, blood culture results can be used for therapeutic decisions and prognostic and infection control considerations. Although the foul smell of amniotic fluid in the setting of maternal chorioamnionitis is often attributable to anaerobes, these organisms are seldom shown to be causative. Culturing of fungi, viruses, U urealyticum, and other nonbacterial organisms often requires different microbiologic processing but may be warranted because of suggestive clinical settings.

Spinal fluid may yield a pathogen when blood

does not (especially following maternal antibiotic pretreatment), or the presence of the pathogen in spinal fluid may indicate the need for alteration in the selection, dosage, and duration of antibiotic therapy even if cultures from other sites yield the same organism. Urine culture may yield the organism. During the first 3 days of life, most urinary tract infections) are hematogenous.

Culturing and Gram staining of an endotracheal aspirate obtained by aseptic technique as soon as possible after intubation may be useful (11). Under typical circumstances, airway commensals take as long as 8 hours to migrate down the trachea. The longer the tube has been in place, the greater the likelihood that recovered organisms represent colonizers rather than invasive pathogens.

A number of factors may interfere with the ability to cultivate a likely pathogen from the sites noted, including the following: (i) pretreatment with antibiotics that limit in vitro but not in vivo growth, (ii) contaminants that overgrow the pathogen, (iii) pathogens that do not replicate in currently available culture systems, (iv) sampling of an inappropriate site, and (v) patients in whom the process is inflammatory but not infectious, such as with meconium aspiration.

Imaging studies : Numerous radiographic patterns are consistent with neonatal pneumonia and a multitude of other pathologic processes. A synthesis of all available information and careful consideration of the differential diagnosis is essential to establishing the diagnosis. Sonography may be helpful in selected circumstances. Sonograms are particularly useful for identifying and localizing fluid in the pleural and pericardial spaces. CT or MRI may be helpful in selected circumstances. CT or MRI may be helpful for excluding tumors, aberrant vessels, sequestered lobes, or other primary pulmonary anomalies and for establishing the presence of an infiltrate.

Bronchoscopy specimens have an increased risk of contamination with oral or airway commensals. Sites distant from the larger bronchi often cannot be sampled.

Aspiration of lung may be performed for culturing or biopsy analysis if a prominent infiltrate can be adequately localized in multiple planes (12). Aspiration is associated with a greater risk of post procedural air leaking and usually requires a larger-bore needle than is used to obtain pleural fluid.

Since the risk is increased, this technique usually is reserved for circumstances in which empiric therapy fails after several days, less invasive cultures and detection tests are unrewarding, or the infant continues to deteriorate.

Treatment

Therapy in infants with neonatal pneumonia is multifaceted. The goals of therapy are to eradicate infection and provide adequate support of gas exchange to ensure the survival and eventual well being of the infant.

Initial empiric antibiotics are selected according to the susceptibility pattern of the likely pathogens, based on experience at the institution and tempered by knowledge of delivery of that agent to the suspected infected sites within the lung. At most institutions, initial empiric therapy consists of combinations of ampicillin, gentamicin and cefotaxime. Dosage regimens vary according to gestational and postnatal age, as well as renal function. Recovery of a specific pathogen from a normally sterile site narrows the spectrum of antimicrobial therapies and thus reduces the selection of resistant organisms and costs of therapy. Decreasing respiratory support requirements, clinical improvement, and resolution revealed on radiographs support the efficacy of therapy.

Although meconium usually is sterile, most clinicians opt for adjunctive antimicrobial therapy, since concurrent aspiration of pathogens or antecedent bacteremia as a cause of intrauterine meconium passage and subsequent aspiration usually cannot be excluded.

The duration of antimicrobial therapy for neonatal pneumonia is 7-10 days if clinical signs resolve rapidly. Longer periods of therapy may be warranted if a sequestered focus is seen, such as

empyema or abscess, or if metastatic infection develops.

Delivery of adequate amounts of glucose and maintenance of thermoregulation, electrolyte balance, and other aspects of neonatal supportive care also are warranted. Attempts at enteral feeding usually are withheld in favor of parenteral nutritional support until respiratory and hemodynamic status is sufficiently stable.

Adequate gas exchange depends not only on alveolar ventilation, but also on perfusion and gas transport capacity of the alveolar perfusate. Ventilatory support may be rendered unusually challenging by alveoli with variable degrees of inflation from the unpredictable distribution of surfactant inactivation, partial airway obstruction, and fluid exudation. Exogenous surfactant may be beneficial when mechanical ventilation is required with a greater than 60% oxygen concentration, although randomized controlled trials for this indication are lacking (13).

The use of high-frequency or patient-triggered ventilatory techniques may offer better recruitment of alveolar lung volume, but data are sparse. Pulmonary hypertension with significant intrapulmonary and extrapulmonary shunting is not uncommon with pneumonia, especially in postterm, term, and near-term infants with sufficient pulmonary vascular smooth muscle to develop systemic or suprasystemic pulmonary vascular resistance.

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