MECONIUM ASPIRATION SYNDROME

Background

1. Definition: meconium aspiration refers to fetal aspiration of meconium stained amniotic fluid (MSAF) during the antepartum or intrapartum period. Meconium aspiration syndrome (MAS) refers to newborn respiratory distress secondary to the presence of meconium in the tracheobronchial airways.
2. General:
    - MAS is distinct from aspiration of other substances such as blood and amniotic fluid (which may produce similar respiratory symptoms)

Pathophysiology

1. Pathology of Disease
    - Meconium is made of amniotic fluid, lanugo, skin cells, and vernix swallowed by the fetus, combined with biliary acids, proteins, and cells of the gastrointestinal tract[1]
    - Passage of meconium is normally inhibited but may occur as a result of:
        - Increased motilin at term, leading to expulsion of the meconium plug
        - Vagal stimulation, possibly associated with fetal distress or states such as hypoxia or acidosis which relax the anal sphincter.
    - MAS causes significant respiratory distress immediately-to-shortly after delivery.
        - Mild or moderate MAS usually results from aspiration of MSAF at birth in a vigorous infant
        - Severe MAS is most likely caused by chronic in-utero insult or placental insufficiency[2]
    - Meconium aspiration takes place in utero in most cases,[3] caused by:
        - Decreased alveolar ventilation related to lung injury, ventilation-perfusion-mismatch and air-trapping.
        - Pneumothorax or pneumomediastinum in 15-30% of cases
        - Persistent pulmonary hypertension (PPHN) in severe MAS(increased pulmonary vascular resistance with right-to-left shunting)
        - Fetal acidemia[4]
        - Chemical pneumonitis
        - Surfactant inactivation caused by meconium's disruption of surface tension
2. Incidence, Prevalence
    - 10-15% of deliveries involve meconium-stained amniotic fluid[5]
    - 5-12% of infants delivered through meconium-stained fluid develop meconium aspiration syndrome[6]
    - 25,000 to 35,000 cases of MAS per year in US[7]
3. Risk Factors:
    - MSAF: thick meconium more likely than thin meconium to result in MAS but does not predict severity.
    - Risk factors for MSAF include:[8]
        - Abnormal fetal heart rate patterns
        - Intrauterine growth retardation
        - Maternal hypertension

        - Maternal diabetes mellitus
        - Maternal heavy cigarette smoking
        - Maternal chronic respiratory or cardiovascular disease
        - Oligohydramnios
        - Poor biophysical profile
        - Post-term pregnancy
        - Pre-eclampsia or eclampsia
    - MAS:
    - Opiate use: opiate-dependent patients have a subsequent 6-fold greater risk of obstetric complications including MAS.[9]
    - Post-term delivery:
        - MSAF and MAS occur more often after 40 or 41 weeks.[10]
        - Decline in MAS from 5.8% to 1.5% from 1990 to 1997 attributed to 33% reduction in births after 41 weeks gestation.[11]
    - Fetal macrosomia:
        - In a US retrospective cohort study including 5,983,409 births, birthweight > 4500g was associated with an increased risk of meconium aspiration syndrome [adjusted odds ratio of 1.5 (95% confidence interval 1.3 to 1.7][12]
    - APGAR score: Thick meconium and APGAR score less than 7 at 1 and 5 minutes associated with 80% probability of MAS.[13]
    - Cesarean vs. vaginal delivery: elective cesarean delivery reduces the occurrence of birth asphyxia, trauma, and MAS.[14]
    - Non-Hispanic black race: associated with 80% higher risk of MSAF, 67% higher risk of MAS when compared to non-hispanic whites, but no difference in mortality[15]
    - Choriamnionitis:
        - Chorioamnionitis caused by Listeria can cause a greenish tint to amniotic fluid, mimicking MSAF
        - Unclear whether causative.
4. Morbidity / Mortality
    - Approximately 1,000 deaths per year related to MAS occur in the US
    - 2.5% mortality rate associated with MAS requiring mechanical ventilation in Australia and New Zealand[16]
    - Small studies suggest MAS survivors are more likely to develop obstructive airway disease in childhood, alveolar hyperinflation and airway hyper-reactivity to exercise.[17-19]

Diagnostics

1. History
    - MSAF may be thin (translucent), moderate (opaque) or thick (opaque and particulate).
    - Risk factors as listed above
    - Respiratory distress not accounted for by another cause
    - Typically requiring oxygen therapy
    - Onset within first 2 hours of life
2. Physical Examination
    - General: Decreased vigor and tone, APGAR score less than 7 at 1 minute and/or at 5 minutes

- ENT: Meconium seen on cords if endotracheal intubation/suction performed
- Respiratory: Tachypnea, retractions, grunting, nasal flaring, coarse bilateral rhonchi
- CV: May have murmur, cyanosis
- Dermatologic: Skin, nails and umbilical cord may be meconium-stained .

3. Diagnostic Testing
   - Laboratory evaluation generally non-specific for MAS
     - Evaluate as for neonatal sepsis until infectious cause ruled out
     - CBC with manual differential for I/T ratio and neutropenia/neutrophilia
     - Aerobic blood culture
     - Blood sugar
     - Consider urinalysis, urine culture and Chem-7 if greater than 24 hours of age
     - Consider,CRP, LP
     - Consider ABG if respiratory distress
       - Since severe cases of MAS may have normal acid-base status at delivery, evaluation of acid-based status via scalp PH or cord gas does not predict MAS (SOR A).[1]
   - Diagnostic imaging
     - Chest X-ray
       - Typically shows coarse, irregular infiltrates, hyperinflation, or atelectasis (though a normal chest X-ray does not exclude MAS)
       - Assess for pneumothorax
       - MAS may present with or without the radiological features of aspiration pneumonia
     - Consider echocardiogram if murmur present to evaluate for congenital heart disease.

Differential Diagnosis

Key Differential Diagnoses

- Congenital heart disease
- Delayed transition
- Hypovolemia
- Infection (e.g., pneumonia, sepsis)
- Persistent pulmonary hypertension of the newborn
- Pneumothorax
- Respiratory Distress Syndrome (hyaline membrane disease)
- Transient tachypnea of the newborn

Extensive Differential Diagnoses

- Anemia
- Birth Trauma
- Congenital malformations of respiratory system[2]
- Electrolyte abnormality (Na, K, Ca, Mg)
- GERD
- Hypoglycemia

- Medications: maternally administered, which may contribute to neonatal respiratory depression (e.g. Methadone, Meperidine, Morphine)
- Metabolic abnormalities
- Neurologic abnormalities (e.g. intracranial hemorrhage)
- Polycythemia
- Prematurity
- Upper airway obstruction

Therapeutics

1. Acute Treatment:
   - ABCs
   - Suctioning and Resuscitation:
     - Oro-, naso- and hypopharyngeal suctioning before or after shoulder delivery does not affect the rate of MAS, mortality, need for or duration of mechanical ventilation, oxygen delivery or hospital care.[2]
     - Transfer newborn to resuscitation area for assessment of vigor
     - If neonate is not vigorous, assessment should include laryngoscopy and suction by a healthcare professional trained in neonatal advanced life support.[20]
     - Follow Neonatal Resuscitation Protocol for newborns in respiratory distress, including evaluation for ventilatory support.[1,21]
     - May require mechanical ventilation. Ventilatory support may include high frequency ventilation
   - Oxygenation:
     - Ensure adequate oxygenation to correct hypoxemia and acidosis, to prevent pulmonary vasoconstriction.
     - The suggested target range for SaO_2 is 94-98%; target PaO_2 60-90 mm Hg
     - In the vigorous neonate exposed to MSAF, tracheal intubation can be deferred without increasing risk of MAS (SOR A).[2,22]
       - In a Cochrane review of 4 randomized controlled trials, endotracheal intubation was not superior to routine resuscitation.[23]
       - In many infants, oxygenation is the only respiratory therapy needed.[20]
       - Intubation and positive pressure ventilation may be required in cases of persistent hypoxemia ($SaO_2 < 90\%$, $PaO_2 < 50$) or respiratory acidosis with $pH < 7.20$.
     - Nasal CPAP may be considered in infants with MAS with moderate respiratory distress and hypoxemia
   - IV Fluids: management as for neonatal sepsis with IV resuscitation if unable to feed PO; including monitoring blood glucose
   - Antibiotics:
     - IV antibiotics should be initiated if pneumonia or sepsis is suspected, and continued until primary bacterial infection is excluded.[20]
     - Typically Ampicillin and Gentamicin

        - A Cochrane review is currently underway to determine whether the use of antibiotics affects morbidity or mortality for infants with signs consistent with MAS
2. Further Management (24 hrs)
    - All newborns born through MSAF should be observed closely for 12-24 hours
    - Extracorporeal Membrane Oxygenation is a life support procedure for newborns with MAS at or near term with severe respiratory failure and ineffective conventional and/or oscillatory ventilatory support
        - In a retrospective review of 3235 MAS patients from 1989 to 1998 delayed use of ECMO resulted in prolonged ECMO needs and post-ECMO ventilation[24]
    - Inhaled Nitric Oxide (iNO):
        - A Cochrane review reported reduced need for ECMO by using iNO, 10-80ppm, for hypoxic, mechanically ventilated term or near-term newborns with oxygenation index (OI)> 25, PaO_2 < 100 and FiO_2 = 1.
            - OI = mean airway pressure x FiO_2 x 100/PaO_2
            - NNT = 5.3. (Number of newborns requiring treatment with iNO to prevent 1 infant from requiring ECMO was 5.3)[25]
            - Methemogloblin levels must be carefully monitored, but treatment with NO for up to 23 days was not problematic
        - Minimum effective dose yet to be established.
    - Corticosteroids: The use of both systemic and inhaled corticosteroids may significantly decrease duration of hospital stay, shorten duration of assisted ventilation and oxygen therapy, and promote earlier progression to full enteral feeding (SOR C).[26]
    - Surfactant: While previous evidence suggested that surfactant might reduce severity of disease and decrease the need for ECMO, a recent Cochrane review concluded there is insufficient evidence to recommend surfactant or surfactant lavage for newborns with MAS.[27]
    - Sildenafil: Insufficient evidence to support the use of Sildenafil for the treatment of PPHN, a condition frequently associated with MAS[28]
3. Long-Term Care and Follow-Up
    - Small case-control studies demonstrate higher incidence of chronic lung problems in MAS survivors at 6 months to 11 years of age. No accepted standard for surveillance, screening or referral[16,17, 32-34]

Prognosis

1. Survivors of MAS generally recover without clinical sequelae[29,30]
2. MAS survivors:
    - In small but consistent studies, may develop childhood asthma, obstructive airway disease, alveolar hyperinflation and airway hyper-reactivity to exercise at a rate of 30-40% vs. 10-12% in the general population, but develop normal aerobic capacity.[17-19,31,32,33]
    - Develop pulmonary sequelae less frequently than newborns with bronchopulmonary dysplasia or prematurity.
    - Have significantly higher rates of acute otitis media and tympanostomy in the first 4 years of life.[34]

- Are at higher risk for both cerebral palsy and neonatal seizures compared to gestational age-matched babies without MAS.[35]

Prevention

1. Amnioinfusion: Routine prophylactic amnioinfusion for dilution of MSAF is not recommended (SOR C).
   - For moderate or thick MSAF, amnioinfusion has been associated with decreased overall incidence of MAS (RR 0.24) in a Cochrane review of small studies, but there was no significant difference in mortality (SOR C)[21]
   - In a multicenter, randomized controlled trial with 1998 pregnant women comparing amnioinfusion to standard care, there were no significant differences in composite primary outcome, perinatal death, cesarean delivery, or MAS.[36]
   - In a systematic review of randomized controlled trials evaluating whether amnioinfusion reduces MAS, amnioinfusion did not decrease the risk of MAS, or the 5-minute APGAR score <7, or the rate of cesarean delivery in settings with standard perinatal surveillance.[37]
   - The American College of Obstetricians and Gynecologists (ACOG) Committee Opinion 346 concluded that amnioinfusion does not prevent MAS[38]
2. Antibiotics: neither intrapartum intravenous antibiotics nor antibiotic amniotic infusion have been shown to reduce the occurrence of MAS[39]
3. Suctioning: since aspiration likely occurs in utero, delivery should not be impeded for naso- or oro-pharyngeal suction at the perineum.
   - Oro-, naso-, or hypopharyngeal suctioning before shoulder delivery do not prevent MAS (SOR B)[2,25]
4. Tracheal intubation:
   - If MSAF and newborn is depressed, tracheal intubation with suctioning below the glottis for meconium or other aspirated materials is recommended.[40,41]
   - If the newborn is vigorous, tracheal suctioning is unnecessary and there is no benefit to routine intubation (SOR A)[2,15]
5. Fetal pulse oximetry: FDA approved in 2000; may be used for intrapartum monitoring but does not decrease the rate of cesarean section or improve infant outcomes. (SOR C)[42]

Patient Education

1. Meconium Aspiration Handout English

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