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Meconium Aspiration Syndrome-Current Perspective

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ABSTRACT

Meconium is a sterile, thick, greenish material observed in fetal intestine during the last trimester of pregnancy. Meconium aspiration refers to respiratory distress in an infant born through MSAF whose symptoms cannot be otherwise explained with X ray feature suggestive of the same. In utero passage of meconium is common after 42 weeks of gestation & passage before that indicates in utero fetal distress due to any cause. Severe MAS indicates chronic in utero insult & is usually associated with adverse pulmonary & neurologic outcome. Prevention of MAS remained a challenge in current era of medicine. Treatment is usually symptomatic with oxygen, ventilation, vasopressors, surfactant, iNO & ECMO. Prognosis remain grim,with severe disease with more favourable prognosis in infants with milder disease

Meconium is a sterile, thick, black-green, odorless material observed in the fetal intestine as early as third month of gestation. It contains accumulated debris, desquamated cells from the skin and intestine, mucin, lanugo , lipid material from the intestinal secretions, vernix caseosa and amniotic fluid. It consists upto 80% water , cholesterol , lipids, enzymes (pancreatic phospholipase A2), protein, and bile salts

MSAF complicates pregnancies in about 8 to 25% of cases, primarily in situations of advanced fetal maturity or stress. Most infants are delivered beyond 37 weeks and it rarely appears in amniotic fluid before 32 weeks of gestation due to lack of 'motilin,' which assists in moving meconium through intestine (Abramovich et al.,1982; Ramon et al.,2003). The meconium aspiration syndrome,occurs in about 5% of these infants. (Cleary et al.,1998; Dargaville., 2006)

Pathophysiology and Risk factors

MAS is defined as respiratory distress in an infant born through MSAF whose symptoms cannot be otherwise explained.(Cleary et al.,1998)

There are three steps in development of MAS:

• In utero passage of meconium: Uncommon due to relative lack of peristalsis, good anal sphincter tone , and a 'cap' of viscous meconium in rectum. Several factors promoting the passage of meconium in utero include:

Pregnancy continued beyond 42 weeks, placental insufficiency, rise in PCO2 or fall in PO2 due to umblical cord compression without metabolic acidosis, maternal hypertension, oligohydramnios, maternal drug intake ,e.g. tobacco & cocaine, fetal distress , amnionitis, Idiopathic

Theories proposing in utero passage of meconium:

a. Increased GI motility (rising motilin levels) (Miller et al.,1975)

Direct hypoxic bowel stimulation

b. hypoxic vagal stimulation Relaxation of anal sphincter Meconium passage (Mitchell et al., 1985)

c. Fetal colon predominantly express CRF-R2 receptors. However, stress induces CRF-R1 receptor expression in fetal colonic tissue mediated by increased glucocorticoid levels ultimately leading to in utero passage of meconium. (Wang et al.,2000)

• Meconium aspiration occurs, during 2nd stage of labour or after delivery with the first few breaths. Fetal distress may lead to inutero fetal gasping with subsequent aspiration of meconium. (Starks et al.,1980). Evidence suggest that a chronic in utero insult may be responsible for most cases of severe MAS as opposed to an acute pre or intrapartum event. (Ghidini et al.,2001)

• Classification of MAS (Wiswell & Cleary) (Cleary et al.,1998)

Mild MAS : Requiring <40% oxygen for <48hr.

Moderate MAS : Requiring >40% oxygen for >48hr without air leak

Severe MAS : Requiring assisted ventilation for > 48 hr , often associated with PPHN/air leaks

It was found that the severity of lung destruction is not related to the amount of meconium aspirated but rather to the degree of hypoxia and acidosis present at delivery (Jovanovic et al.,1989). Severe MAS may not be causally related to the aspiration but rather to processes occurring in utero e.g. chronic asphyxia, infection or PPHN.

It is unclear whether obstruction to airways plays any role in the development of MAS as it can occur well before delivery

in the absence of labour, being reported in infants delivered by elective caesarean section. Although, the presence of meconium during labour increases the risk of perinatal morbidity and mortality, most babies have favourable outcomes necessitating early recognition of such pregnancies so as to optimize the preventive strategies. Risk factors for MAS includes heavy MSAF, nullipar-

ity, post term pregnancy, fetal heart rate abnormalities, meconium below the vocal cords, caesarean delivery, low Apgar scores and maternal ethnicity (Urbaniak et al.,1996; Falciglia et al.,1992)

Prevention of MAS

• Prevention of in utero passage of meconium: Identification of mothers at risk for uteroplacental insufficiency and, thus, MSAF includes preeclampsia, chronic respiratory or cardiovascular disease, poor intrauterine fetal growth, postterm pregnancy, and heavy smokers.

a. Continuous intrapartum fetal heart monitoring:To detect fetal hypoxemia so as to reduce the risk of adverse neonatal outcomes. Several authors have noted an increase in the frequency of FHR abnormalities in association with MSAF. (Jovanovic et al.,1989; Hageman et al., 1993)

b. Amnioinfusion: Involves transcervical infusion of saline into the amniotic cavity. It has been proposed to reduce MAS by mechanical cushioning of the umbilical cord, and dilution of meconium reducing its mechanical and inflammatory effects in pathogenesis of MAS.

It remains a reasonable approach to the treat repetitive variable decelerations, regardless of amniotic fluid meconium status. (ACOG.,2006)

c. Caesarean Section: There are no data to support caesarean section delivery of all infants born through MSAF. However, in pregnancies that continue past the due date, induction as early as 41 weeks may help prevent MAS by avoiding passage of meconium.

Delivery room management of babies delivered through MSAF

The AAP no longer recommends routine intrapartum oronasopharyngeal suctioning before delivery of the shoulder based on a large RCT. (Vain et al., 2004)

a. Initial assessment : At a delivery complicated by MSAF, the clinician should determine whether the infant is vigorous, demonstrated by HR >100/min., spontaneous respirations, and good muscle tone. The infant will be depressed in 20-30% of cases.

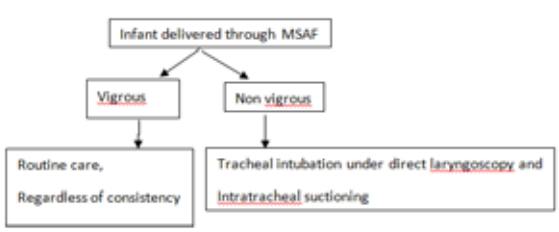

Fig.2: delivery room management of baby born through MSAF

Management of Meconium Aspiration Syndrome

a. Observation: Infants having had meconium suctioned from the trachea are at risk of MAS and should be provided post resuscitation care in NICU, closely observing for respiratory distress, oxygen saturations, activity/sensorium, hemodynamic status, renal status

b. Supportive care for neonates with MAS consists of maintaining euthermia, normoglycemia, adequate hydration & appropriate management of shock.

c. Stepwise Approach to Respiratory Support

1. Oxygen therapy: Mainstay of treatment and in many cases is the only therapy required. Given the high incidence of pulmonary hypertension, a pre-ductalSpO2 is preferable, targeting between 91- 95% with pO2 between 60–100 mm Hg (preductal). With considerable PPHN, titration of FiO2using postductal pO2values is not advisable.

2. Continuous Positive Airway Pressure: Of all infants requiring mechanical respiratory support because of MAS, approximately 10–20% are treated with CPAP alone. (Singh et al., 2009;Wiswell et al.,2000) Additionally, up to one-quarter of infants requiring intubation, receive CPAP before and/or after their period of ventilation .CPAP, is typically initiated at a pressure of 5–8 cm H2O. Intolerance of the device is a concern!

3. Intubation: Approximately one-third of infants with MAS require intubation and mechanical ventilation(Cleary et al.,1998). Indications for intubation includes (a) FiO2> 0.8 (b) respiratory acidosis, with arterial pH <7.25, (c) pulmonary hypertension, and (d) shock (Goldsmith.,2008). Most of these babies requires sedation with opiate (e.g., morphine or fentanyl) (Aranda et al.,2005)to improve tolerance , supplemented with a benzodiazepine. Additionally, muscle relaxants are helpful , particularly in infants with pulmonary hypertension.

4. Ventilation strategies:

a. Conventional Mechanical Ventilation :

Mode of ventilation : Mode and patient-triggering have been incompletely studied in MAS. Amongst 2 RCTs with patient-triggered ventilation, one found no advantage of SIMV over IMV in 15 infants with MAS (Chen et al., 1997). While other , found SIMV to be associated with a shorter duration of ventilation compared with IMV in 93 infants (includes an unspecified number with MAS) (Bernstein et al., 1996). It seems logical to use synchronized mode of ventilation in any spontaneously breathing ventilated infant with MAS. Trigger sensitivity should be set somewhat higher due to the risk of autocycling if there is a tube leak (Bernstein et al., 1995). However, none of the clinical trials have compared SIMV and SIPPV modes. Given the risk of air trapping , there is some concern that using later may lead to inadvertent PEEP and hyperinflation. Hence, SIMV may be the most appropriate mode of ventilation .

Positive End-Expiratory Pressure: Application of PEEP must balance the risk of overcoming atelectasis vs overdistension and air leak. The greatest benefit have been observed between 4 -7 cm H2O,with higher settings (8–14 cm H2O) giving minimal benefit (Walsh et al., 2000). There is no clinical data to select PEEP in MAS. Physiological principles dictate that if atelectasis predominates, increasing PEEP should improve oxygenation with switch over to high frequency ventilation if requirement rise , whereas for regional or global hyperinflation a lower PEEP (3-4 cm H2O) may beeffective(Goldsmith.,2008).

Inspiratory Time: Must take into account the balance between atelectasis and overdistension. Term infants normally have longer time constants than their preterm counterparts and thus require a longer inspiratory time (around 0.5 sec). Even longer inspiratory times may be useful if atelectasis is prominent.

Peak Inspiratory Pressure: Due to reduced compliance, PIP required is often high (30 cm H2O) .However, this may lead to ventilator-induced lung injury in infants with MAS. If using a "volume guarantee" mode target tidal volume is 5-6 mL/kg, with peak pressure limit set at or near 30 cm H2O . If requirement is persistently greater than 30 cm H2O, high frequency ventilation should be considered.

Ventilator Rate: If X ray reveals air trapping and expiratory airflow limitation, optimal ventilation requires lower rate

(<50bpm) avoiding inadvertent PEEP. Hyperventilation induced alkalosis, which anecdotally appeared to reduce the need for ECMO in infants with PPHN(Walsh et al., 2000),is no longer recommended, due to the risk of sensorineural hearing loss & adverse neurological outcome.(Hendricks-Munoz et al.,1988)

High-Frequency Oscillatory Ventilation: HFOV has become an important means of providing respiratory support for infants with severe MAS failing conventional ventilation .Published series from large databases showed that 20–30% of all infants require high-frequency ventilation(Tingay et al., 2007), with most receiving HFOV rather than HFJV. Once oxygenation has improved, most infants can be stabilise using a PAW around 16–20 cm H2O, with gradual weaning thereafter (Dargaville et al., 2007). Infants with prominent air trapping may not tolerate the recruitment process, with reductions in oxygenation , systemic blood pressure and exacerbation of pulmonary hypertension.

Choice of oscillatory frequency is critically important in MAS, with evidence suggesting that frequency should not be greater than 10 Hz and preferably be set at 8 or even 6 Hz. HFOV can also lend an advantage in infants with significant coexisting PPHN, as the response to iNO is better when delivered on HFOV compared to conventional ventilation. (Kinsella et al., 1997). More recent experience suggests that only 5%of infants treated with HFOV and iNO fail to respond and require ECMO (Dargaville., 2006).

High-Frequency Jet Ventilation: The combination of atelectasis and air trapping may be better managed with HFJV than HFOV ,due to the former offering ventilation at a lower PAW. A number of experimental studies have shown HFJV, either alone or in combination with surfactant therapy, to be beneficial in animal models.(Wiswell et al.,1992) Some infants with severe MAS have shown improvement when transitioned from HFOV to HFJV using a low frequency (240–360 bpm)and a low conventional ventilator rate.(Kamlin et al.,2002)

Adjunctive Respiratory Therapies

a. Corticosteroid: Steroid therapy has been investigated in MAS for more than 3 decades, but none of these have given a definitive result. One recent trial suggested that dexamethasone could dampen the inflammatory response in MAS. (Tripathi et al., 2007). In the absence of further trials, it cannot be recommended at present.

b. Inhaled Nitric Oxide : There is evidence that iNO in term infants with pulmonary hypertension, leads to a reduction in need for ECMO and in the composite outcome of death or need for ECMO (Finer et al.,2006). Management of infant with MAS and coexistent PPHN should initially focus on optimising the ventilator management , overcoming atelectasis ,avoiding hyperinflation, both of which are associated with pulmonary hypertension. If moderate-severe PPHN persists after appropriate ventilator manoeuvres withpO2 below 80–100 mm Hg and FiO2100% (Kinsella et al., 1997), iNO should commence at a dose of 20 ppm.

c. Bolus Surfactant Therapy: Pathophysiology of MAS includes inhibition of surfactant , both by meconium and exuded plasma proteins (Herting et al., 2001).The metaanalysis of four trials showed reduction in need for ECMO but not duration of ventilation or other pulmonary outcomes (Shahed et al., 2007). In developed nations, bolus surfactant therapy is used in 30–50% of ventilated infants with MAS (Singh et al., 2009).

d. Lavage Therapy: Animal studies and preliminary clinical evaluations have indicated that lavage therapy shorten duration of ventilation in MAS (Cochrane et al., 1998). A RCT of large-volume lung lavage using dilute surfactant have found higher rate of ECMO-free survival in the treated group with no effect on duration of respiratory support or other pulmonary outcomes (Dargaville et al., 2011).

e. Extracorporeal Membrane Oxygenation:. The indication for commencing ECMO is intractable hypoxaemia (OI persistently above 40). Follow up of these infants suggests a low rate of severe disability at one year (1.7% in the UK ECMO trial)

Morbidities associated with MAS

a. Duration of Ventilation and Oxygen Therapy: Median duration of invasive ventilation is 3 days (mean 4.8 days) . Infants with more severe disease, requiring at least one of HFOV, iNO or bolus surfactant, are ventilated for a median of 5 days . Median duration of oxygen therapy and length of hospital stay currently stand at 7 and 17 days, respectively (Dargaville et al., 2006) .

b. Mortality: Advances in intensive care and respiratory support have significantly reduced the in mortality related to MAS, with most population-based studies suggesting a mortality of 1-2 per 100,000 live births (Dargaville et al., 2006). Case-fatality rate in ventilated infants with MAS varies widely in published series (0–37%) (Cleary et al., 1998) and is influenced by availability of ventilation, adjunctive therapies (iNO), and ECMO. Approximately one-quarter to one-third of all deaths in ventilated infants with MAS are related to the pulmonary disease, with the remainder caused by HIE (Dargaville et al., 2006).

c. Short-Term Morbidities: Pneumothorax occurs in 10% of all ventilated infants with MAS (Dargaville et al., 2006), and it increases the risk of lung atelectasis, PPHN and mortality .Pulmonary haemorrhage occurs in a small subset of infants with MAS and can cause severe destabilisation and hypoxaemia.

Long-Term Morbidities: Up to 50% of infants may exhibit wheezing and coughing in the first year of life Older children may exhibit evidence of airway obstruction, hyperinflation, and airway hyperreactivity, but have normal aerobic capacity (Swaminathan et al., 1989). A diagnosis of MAS places a neonate at considerable risk of cerebral palsy and global developmental delay (Beligere et al., 2008).

Conclusion

Although the incidence of MAS has decreased in developed countries , it poses a significant problem in developing nations. The management of such babies is further complicated by lack of ventilation, adjunctive therapies (iNO) and ECMO increasing the toll of death. The role of newer therapies e.g. surfactant lavage vs bolus remains to be further elucidated.

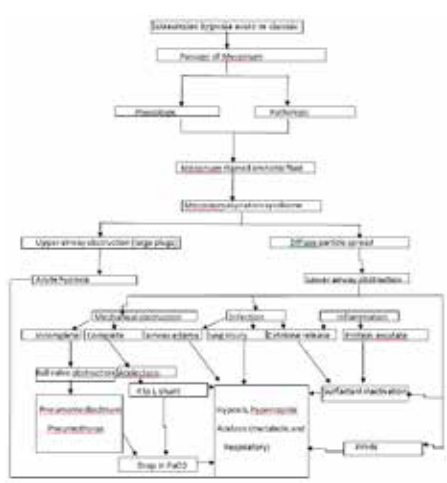

Fig.2: Pathophysiology of Meconium Aspiration Syndrome

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