Best Practice Guideline article

What (not) to do at and after delivery? Prevention and management of meconium aspiration syndrome

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A R T I C L E   I N F O

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Intubation
Endotracheal
Resuscitation
Pulmonary hypertension

A B S T R A C T

Meconium aspiration syndrome (MAS) is a life-threatening disorder in newborn infants. Universal intrapartum suction of infants with meconium stained amniotic fluid (MSAF) and postnatal suction of vigorous infants have been used in an attempt to decrease the incidence and severity of the disease by clearing the airway. Both procedures have been proven fruitless when challenged through randomised control trials (RCTs). Endotracheal intubation and suctioning are currently recommended only for non-vigorous infants. Respiratory failure in infants with MAS is frequently treated initially with conventional or synchronized mechanical ventilation. Surfactant administration and high-frequency ventilation (HFV) are commonly used as rescue therapy for severe cases. Nitric oxide (NO) is added when severe pulmonary hypertension is demonstrated. ECMO is an option when other treatments have failed. In the pathophysiology of severe MAS, asphyxia and pulmonary hypertension are considered to be more important than the obstruction of the airways and/or damage to the lung produced by meconium.

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1. Delivery room management

The approach to the management of infants with MSAF in the delivery room has been changing for over 30 years. The initial clinical studies were based on the belief that respiratory distress occurring in infants with MSAF was primarily caused by obstruction of the airways and filling of
alveoli with meconium. Chemical pneumonitis, inflammation, infection and surfactant inhibition by meconium were also considered important aspects in the pathophysiology of MAS.

Not surprisingly then, during the 70s, oro- and nasopharyngeal suctioning before the delivery of the shoulders and immediate postnatal intubation and tracheal suctioning were practices considered as valuable measures to prevent MAS in infants born through MSAF [1–3]. During the 80s and 90s, a more selective approach for intubation was taken. But it is only in 2000 that results from large RCTs became available [4–6].

As is the case in many other areas of medicine, evidence-based studies demonstrated that some of the therapeutic approaches traditionally advocated by obstetricians and neonatologists for patients with MSAF were in fact useless. The results of those trials have led to changes of current recommendations.

1.1. Delivery room intrapartum management: Suction of the oro- and nasopharynx before the delivery of the shoulders

In 1976, Carson et al. published a study aimed at evaluating the impact of suctioning of the hypopharynx before delivery of the shoulders in infants born through MSAF [3]. They evaluated a group of 273 infants managed with a combined approach consisting of intrapartum suctioning before delivery of the infant’s shoulders, laryngoscopy, and intubation when meconium was visualized at the level of the vocal cords. The authors compared this cohort with a historical control group in which no intrapartum suctioning had been performed. The patients managed with this combined approach had a lower incidence of MAS (1 out of 273 [0.4%] vs. 18 out of 947 [1.9%]). Although these differences did not reach statistical significance (p = 0.071), the authors suggested that a combined approach of intrapartum and postnatal suction of the oropharynx and large airways decreased the risks and mortality in this group of infants. Widespread adoption of this approach followed publication. A few years later, Falciglia compared 742 infants born with MSAF in whom intrapartum suctioning had not been performed with a group of 755 infants born at the same centre after the adoption of prenatal suction. The incidence of MAS was similar in both groups (~2%) in this study [7]. In a subsequent prospective observational study, Falciglia et al. compared the incidence of MAS in infants who were or were not suctioned before delivery of the shoulders. He found an incidence of 10 and 7% respectively [8]. The 8 cases of pulmonary air leak in the study (pneumothorax or pneumomediastinum) occurred all in the intrapartum suctioned group.

In spite of the methodological limitations of Carson’s study and the opposite results reported by Falciglia in papers of comparable design and quality, the combined approach of intrapartum and immediate postnatal suctioning of meconium stained infants was widely accepted and led to its inclusion in the guidelines of the American College of Obstetricians and Gynaecologists (ACOG) and the American Academy of Pediatrics (AAP) [9,10]. Interestingly, the extremely low incidence and mortality rates of MAS reported by Carson were never demonstrated by any other study. As is the case in many other areas of medicine, evidence-based studies demonstrated that some of the therapeutic approaches traditionally advocated by obstetricians and neonatologists for patients with MSAF were in fact useless. The results of those trials have led to changes of current recommendations.

### Table 1

**Effect of intrapartum suction on clinical aspects (Ref. [5]).**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Suction (n = 1263)</th>
<th>No suction (n = 1251)</th>
<th>RR (95% CI)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meconium aspiration syndrome</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>52</td>
<td>47</td>
<td>0.9 (0.6–1.3)</td>
<td></td>
</tr>
<tr>
<td>%</td>
<td>4%</td>
<td>4%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>99% CI (2.8–5.8)</td>
<td>2.5–5.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Need for mechanical ventilation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>24</td>
<td>18</td>
<td>0.8 (0.4–1.4)</td>
<td></td>
</tr>
<tr>
<td>%</td>
<td>2%</td>
<td>1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>99% CI (1.1–3.1)</td>
<td>0.7–2.6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortality</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>9</td>
<td>4</td>
<td>0.4 (0.1–1.5)</td>
<td></td>
</tr>
<tr>
<td>%</td>
<td>1%</td>
<td>0.3%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>99% CI (0.2–1.6)</td>
<td>0.1–1.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Need for endotracheal intubation, suction and PPV in the delivery room</td>
<td>106</td>
<td>113</td>
<td>1.1 (0.8–1.4)</td>
<td></td>
</tr>
<tr>
<td>Other respiratory disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>61</td>
<td>79</td>
<td>1.3 (0.9–1.8)</td>
<td></td>
</tr>
<tr>
<td>%</td>
<td>5%</td>
<td>6%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>99% CI (3.4–6.6)</td>
<td>4.7–8.3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>1</td>
<td>3</td>
<td>1.0 (0.12–8.25)</td>
<td></td>
</tr>
<tr>
<td>(0.2%)</td>
<td>(0.2%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Outcomes (SD = standard deviation)**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Suction (n = 1263)</th>
<th>No suction (n = 1251)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Range of one-minute Apgar scores</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–3</td>
<td>22 (2%)</td>
<td>15 (1%)</td>
<td>0.29</td>
</tr>
<tr>
<td>4–6</td>
<td>65 (5%)</td>
<td>73 (6%)</td>
<td></td>
</tr>
<tr>
<td>7–10</td>
<td>1174 (93–0%)</td>
<td>1163 (93–0%)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>2 (0–1%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Range of five-minute Apgar scores</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–3</td>
<td>0</td>
<td>0</td>
<td>0.29</td>
</tr>
<tr>
<td>4–6</td>
<td>13 (1–0%)</td>
<td>5 (0–4%)</td>
<td></td>
</tr>
<tr>
<td>7–10</td>
<td>1230 (97%)</td>
<td>1231 (98%)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>2 (0–2%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Duration of oxygen therapy (days) in infants with MAS (mean ± SD)</td>
<td>5.7 ± 8.8 (n = 52)</td>
<td>5.1 ± 7.1 (n = 47)</td>
<td>0.91</td>
</tr>
<tr>
<td>Duration of mechanical ventilation (days) in infants with MAS (mean ± SD)</td>
<td>5.1 ± 4.9 (n = 21)</td>
<td>4.2 ± 4.6 (n = 14)</td>
<td>0.49</td>
</tr>
<tr>
<td>Duration of hospitalisation (days) in infants with MAS (mean ± SD)</td>
<td>8.2 ± 10.7 (n = 50)</td>
<td>9.0 ± 8.6 (n = 43)</td>
<td>0.14</td>
</tr>
</tbody>
</table>

MAS—Meconium aspiration syndrome. ppV—positive-pressure ventilation. * p values calculated for continuous variables.
Effects of endotracheal intubation and suction of vigorous meconium stained infants (Ref. [4]).

<table>
<thead>
<tr>
<th>Intubate \ Expectant</th>
<th>Intubate (n=1051)</th>
<th>Expectant (n=1043)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occurrence of MAS (n=62)</td>
<td>Overall</td>
<td>34/1051 (3.2%)</td>
<td>28/1043 (2.7%)</td>
</tr>
<tr>
<td></td>
<td>Thin MSAF</td>
<td>5/447 (1.1%)</td>
<td>2/453 (0.4%)</td>
</tr>
<tr>
<td></td>
<td>Moderately-thick</td>
<td>7/301 (2.3%)</td>
<td>6/307 (2.0%)</td>
</tr>
<tr>
<td></td>
<td>Thick MSAF</td>
<td>22/303 (7.3%)</td>
<td>20/283 (7.1%)</td>
</tr>
<tr>
<td>Occurrence of other respiratory disorders (n=87)</td>
<td>Overall</td>
<td>40/1051 (3.8%)</td>
<td>47/1043 (4.5%)</td>
</tr>
<tr>
<td></td>
<td>Thin MSAF</td>
<td>6/447 (1.3%)</td>
<td>8/453 (1.8%)</td>
</tr>
<tr>
<td></td>
<td>Moderately-thick</td>
<td>10/301 (3.3%)</td>
<td>15/307 (4.9%)</td>
</tr>
<tr>
<td></td>
<td>Thick MSAF</td>
<td>24/303 (7.9%)</td>
<td>24/283 (8.5%)</td>
</tr>
<tr>
<td>Occurrence of any type of respiratory distress (n=149)</td>
<td>Overall</td>
<td>74/1051 (7.0%)</td>
<td>75/1043 (7.2%)</td>
</tr>
<tr>
<td></td>
<td>Thin MSAF</td>
<td>11/447 (2.5%)</td>
<td>10/453 (2.2%)</td>
</tr>
<tr>
<td></td>
<td>Moderately-thick</td>
<td>17/301 (5.6%)</td>
<td>21/307 (6.8%)</td>
</tr>
<tr>
<td></td>
<td>Thick MSAF</td>
<td>46/303 (15.2%)</td>
<td>44/283 (15.5%)</td>
</tr>
</tbody>
</table>
Some guidelines published in France continue to advise compression of the chest to hold the first breath and direct laryngoscopy as part of the recommended flowchart for thick meconium stained babies even when they are vigorous at birth [36].

Thus, non-recommended manoeuvres continue to be performed in delivery room settings [19,20].

1.4. Decrease in the frequency of MAS in the last decade

Yoder et al. reported a progressive decrease in the incidence of MAS within a period of 9 years and attributed this to changes in obstetrical practice, among them: [37]

- Use of amnioinfusion [6]
- A better diagnosis of abnormalities by electronic foetal monitoring,
- Higher frequency of caesarean sections,
- Increased use of prenatal ultrasound,
- Significant decrease of post-term deliveries.

2. NICU management of infants with meconium aspiration

From 3 to 14% of infants born with MSAF develop MAS [21,38]. This wide range in the frequency of MAS is related to characteristics of each study population and, more importantly, to the various criteria used by different authors to diagnose MAS.

We will discuss first the clinical management, which is essentially that of respiratory distress in term infants. Some aspects, however, have been subject of specific research and will also be discussed later in this chapter.

2.1. Radiographic findings

Typical radiographic findings described in infants with MAS are over-expansion of the lungs with widespread coarse infiltrates. However, the severity of the X-ray pattern does not always correlate with the clinical picture. Some patients with severe disease may have minimal X-ray findings, while others have marked X-ray findings without clinical disease. The lack of correlation between clinical severity and radiographic pattern suggests that the disease is less dependent on the amount of meconium obstruction and parenchymal damage than on other aspects of MAS, such as the presence and severity of pulmonary hypertension.

2.2. Respiratory support

In mild cases, oxygen can be supplied as part of treatment of pulmonary hypertension. High concentrations of oxygen need to be avoided to prevent pulmonary damage and the duration of oxygen therapy should be limited to avoid free oxygen radical damage. We avoid hyperventilation to prevent pulmonary damage and the duration of oxygen pulmonary hypertension. High concentrations of oxygen need to be avoided to prevent pulmonary damage.

1.2. Respiratory support

In mild cases, oxygen can be supplied as part of treatment of hypoxic respiratory failure without structural heart disease.

2.4. Surfactant

In vitro studies have shown that meconium interferes with surfactant in several ways: [32]

- Inactivation of its function depending on the concentration.
- Direct toxicity on type II pneumonocytes.
- Displacement of surfactant from the alveolar surface.
- Decrease of surfactant protein A and B levels.

Many studies assessed the benefits of surfactant use in animal models with controversial results [21]. Some clinical trials evaluated bolus administration of high doses of surfactant in infants. In 1998, Lotze et al. published a multicenter RCT of surfactant use in term newborn infants with severe respiratory diseases of various aetiologies (50% had MAS) [40]. There were fewer infants with MAS requiring ECMO within the group randomised to receive surfactant. A smaller study suggested also some clinical benefits and a reduction on hospital stay [41]. More recently, Maturana et al. reported the results of a multicenter RCT using surfactant for less severe MAS [42]. The study demonstrated no differences between the treated and non-treated group. Another RCT from China showed some physiologic improvement following surfactant administration but no effect in major clinical outcomes [43]. A recent meta-analysis of these 4 studies in full term and near term infants by the Cochrane Library concludes that surfactant administration may reduce the severity of MAS and decrease the number of infants with progressive respiratory failure requiring ECMO support [44].

Therefore, although bolus administration of surfactant cannot be recommended for routine use in infants with MAS, its use in selected...
patients with predominantly parenchymal disease and severe respiratory failure appears indicated.

Some case reports and small studies performing bronchial lavage with surfactant in infants with MAS have been published. The theory behind this technique is based on the potential removal of meconium, neutrophiles, remains of proteins, etc., leaving a therapeutic amount of surfactant in the lungs at the end of the procedure. Results of these studies are optimistic, but the technique is risky and should be tested by large clinical trials before it can be recommended for routine use [35,45–47].

2.5. Steroids

Based on studies suggesting that meconium generates an inflammatory response on lung tissue, steroids have been tried in infants with MAS [48]. Results are inconclusive and complications resulting from the use of these drugs are well known. However two recent studies suggested that systemic and inhaled steroids alter the course of MAS and favourably affect the outcome without serious adverse effects [49,50].

At present, there is insufficient evidence to propose routine steroid therapy in the management of meconium aspiration syndrome.

2.6. Antibiotics

The presence of meconium increases the chances of positive cultures from amniotic fluid in preterm and term infants. However, studies evaluating the development of sepsis in infants with MAS failed to demonstrate a relationship [24]. Although prophylactic antibiotics in infants with MAS are not justified, most of these patients receive antibiotics during the first days of life, before the diagnosis of pneumonia can be completely ruled out [51,52].

3. Conclusions

Although the incidence decreases, MAS continues to be a neonatal disorder with high morbidity and mortality, in spite of changes in obstetrical and neonatal care. Attempts to prevent the disease by relieving obstruction of the airways have failed when challenged by RCTs. Asphyxia and pulmonary hypertension are likely to be more important as a cause of severe MAS than the obstruction or damage caused by meconium in the airways and lungs. Respiratory management of patients with MAS depends on the infants’ pulmonary function. Surfactant administration may be of help. Maybe this is the time to change the name of the disorder to MSAF associated Respiratory Distress, which seems more appropriate than MAS.

Acknowledgements

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References


