

Meconium is a Mess. Prudence and Equipoise in the Delivery Room when Caring for Non-Vigorous Neonates with Thick Meconium in the Amniotic Fluid

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Abstract

Background: Meconium is the normal bowel movement of newborn babies during the first few days; it sometimes “makes a real mess”. On the other hand, meconium passed in utero could be serious. Meconium-stained amniotic fluid (MSAF) could be of different consistency or texture and can occur from 5% of all births to as high as 22%. Meconium aspiration syndrome (MAS) is a heterogeneous condition with wide spectrum of severity. It could be estimated that around 1,600,000 newborns will have MAS worldwide and about 5 - 12% of them die. We can find more than 2,000 publications on this topic, but the appropriate management of the non-vigorous neonate with thick MSAF is still an unanswered question. Some of the publications and recommendations of the last decade have led to confusion of some practitioners and it has created a mess for them and for the sick babies and their families.

Objective: To raise nonjudgmental awareness and attention to current issues related to airway management in the delivery room of non-vigorous newborns with thick or “pea soup” meconium.

Methods: Analyze recommendations, recent studies and randomized controlled trials (RCT) focusing specifically on the findings reported for airway management in the delivery room (DR) of non-vigorous infants born with thick meconium in the amniotic fluid and briefly explore the responses of 1,265 neonatal health care professionals regarding their practices in the DR for such infants.

Results: Several changes have occurred in the recommendations made for the management of the airway in infants born through MSAF. Many publications include in the denominator all newborns with MSAF of any consistency and there are few publications that specify the MSAF texture and/or separate clearly the findings specifically for non-vigorous infants with thick meconium. There is significant variability in airway management for these infants in the DR.

Conclusion: The majority of babies born through MSAF do not need endotracheal tube suctioning (ETS). However, there is a need for a large, high-quality RCT of ETS with a sufficient sample size of non-vigorous infants born through thick meconium to better inform on future decision making in order to tidy up “the current mess”.

Keywords: Meconium-Stained Amniotic Fluid; Meconium Aspiration Syndrome; Randomized Controlled Trials; Delivery Room

Abbreviations

MSAF: Meconium-Stained Amniotic Fluid; MAS: Meconium Aspiration Syndrome; ETS: Endotracheal Tube Suctioning; RCT: Randomized Controlled Trial

Introduction

The purpose of this commentary is to raise nonjudgmental awareness and attention to current issues related to the airway management in the delivery room of non-vigorous newborns born with thick or “pea soup” meconium in whom airway obstruction at birth is evident or suspected.

We can count thousands of published articles regarding meconium aspiration syndrome (MAS). In this century alone there have been more than 44 manuscripts published per year on the topic, some years with as many as 60 - 65 such articles. Of course, they cannot be quoted in this commentary in which we will summarize concisely some issues, including background and some history, scope of the problem of the wide spectrum of meconium-stained amniotic fluid (MSAF) and MAS, and a brief analysis of a few recent studies and randomized controlled trials (RCT). We will end with “the current mess” of clinical practices and management in the delivery room of the airway of newborns born non-vigorous and through thick MSAF.

Background

The term meconium derives from ancient Greek “meconium-arion”, or “opium-like.” Aristotle developed the term because he believed that it induced fetal sleep. Interestingly, Voltern in 1687 described thick meconium as a marker of fetal death and Jesse in 1888 described the incidence of meconium-stained amniotic fluid (MSAF) in 314 of 3,304 deliveries (9.5%) with differences in MSAF of thin consistency, moderately thick consistency and thick consistency (also called “pea soup” MSAF).

Meconium-stained amniotic fluid (MSAF) is found in about 10% to 15% of all births (variability in reports range from 5 - 22%). MSAF is a wide spectrum condition and with different consistency or texture of the meconium in the amniotic fluid. Eight to 20% of infants born through MSAF are depressed and non-vigorous, with bradycardia, inadequate respiratory effort and poor tone. About 3 - 12% of the babies born through MSAF develop meconium aspiration syndrome (MAS).

Worldwide, the incidence of MAS has declined in developed countries thanks to improved obstetric practices and perinatal care while challenges persist in developing countries. Such a positive trend can be explained by the reduced incidence of post-maturity and the improvement in perinatal and neonatal management at birth and in the NICU. The transfer of knowledge and training, together with approaches and equipment from high to low resource settings will play a crucial role in the global improvement of the management and outcome of non-vigorous infants with MSAF. However, despite the decreased incidence and improved survival rate over the last decades, MAS is associated with considerable morbidity and mortality and the long-term morbidity among survivors remains a major concern.

There are an estimated 130 million babies born each year around the globe and, therefore, it could be estimated that about 16,000,000 are exposed to MSAF and that around 1,600,000 will have MAS. The literature reports that one third of infants with MAS requires intubation and mechanical ventilation and 5 - 12% die. This would mean that there are about 160,000 deaths attributed to MAS worldwide every year. Not an insignificant number at all! And we know very little about and the long-term morbidity among survivors.

MAS results from the aspiration of MSAF during gasping in intrauterine life or during the first breaths after birth. MAS is a typical disease of near-term, term or post-term newborns and is a heterogeneous condition with wide spectrum of disease severity. Some infants with MAS have very mild disease, but about 5-20% of infants with MAS develop pulmonary hypertension. In one NICU, 0.66% of newborns admitted were diagnosed with MAS. Of the newborns with severe MAS, 73% had pulmonary hypertension and they required significantly more days of oxygen therapy, mechanical ventilation, nitric oxide, inotropic, and surfactant therapy, as well as longer hospital stay [1].

Many risk factors have been described for MAS and they include thick meconium and airway obstruction. The problem (or “the mess”) truly exists with non-vigorous infants born through thick meconium MSAF. More so if there is suspected or clear evidence of airway obstruction in the individual infant.

In 1974 Dr Gregory and associates [2] reported that 56% of neonates born with thick MSAF had meconium in the trachea and that 10% of those who did not have meconium in the upper airway had meconium below the vocal cords. Due to the reported findings, they recommended endotracheal intubation and airway aspiration in newborns with thick MSAF. Other publications suggested that timely suction and unclogging interventions could prevent severe MAS and resulting death. Gluck in 2020 [3] reported morbidity in 24,445 neonates over 37 weeks' gestation with MSAF of different texture, classifying them as clear, light, intermediate and thick meconium. The associated morbidity and adverse neonatal outcome increase exponentially when there is intermediate meconium and, more so, with thick MSAF.

It has been clear, from the literature and from clinical practice, that a vigorous newborn with thin MSAF in the low extreme of severity, is not the same as a non-vigorous newborn with thick MSAF and airway obstruction, on the other extreme of severity.

Changes in recommendations regarding airway management in the delivery room

In the last 10 - 20 years many changes have occurred in the recommendations for the management of the airway in infants born through MSAF. In 2010, endotracheal tube suctioning (ETS) for non-vigorous infants was still recommended due to insufficient evidence to change practice [4]. The recommendation was overturned in 2015, when it was stated that ETS for non-vigorous infants should be implemented only if obstruction was suspected, due to insufficient evidence to continue with the previous practice [5]. In 2020, this indication was confirmed in the last consensus on science and supported by a systematic review [6]. However, such an indication was based on a low certainty of evidence and the most appropriate approach is still a matter of debate [6].

Are outcomes similar in non-vigorous infants with thick MSAF when no ETS is performed?

In an RCT, 2997 newborns were delivered during the study period at one center, and 383 had MSAF (12.8%); 152 of them (39.7%) were found to be non-vigorous after birth, and 132 were randomized after excluding 20 newborns for various reasons. Authors concluded that ETS at birth does not reduce the incidence of MAS, complication rates, and mortality risk in non-vigorous neonates born through MSAF. They clearly mention some of the limitations of their study but some other important limitations are not included. For example: a) The sample size was small: 132 non-vigorous neonates with MSAF randomized to receive ETS (n = 66) or no-ETS (n = 66). This small number can lead to a Type II error. Additionally, b) thick meconium was noted in only 42.4% or 28 infants in the ETS group and 45.4% or 30 infants in the non-ETS group. The rest of the non-vigorous infants are classified as having been born through thin MSAF. The data and results are reported combined for both groups and nothing is described separately about the clinical outcomes for the non-vigorous infants with thick meconium [7].

Oommen., *et al.* [8] investigated the impact of policy change in delivery room resuscitation from routine ETS of non-vigorous neonates born through MSAF to immediate non-invasive respiratory support in a single-center cohort study. Non-vigorous neonates born through MSAF managed according to the 2015 guidance of commencing respiratory support without prior suctioning were compared to non-vigorous neonates born through MSAF who underwent routine ETS the previous years. The policy change towards no routine ETS for non-vigorous neonates born through MSAF at birth was not associated with an increase in the local incidence of MAS and was associated with fewer NICU admissions. However, the authors did not mention the texture of the meconium in the MSAF nor how many of the non-vigorous neonates were born with thick meconium [8].

In a recent meta-analysis [9] with four randomized controlled trials (RCT), a total of 581 non-vigorous meconium-stained infants fulfilled the inclusion criteria, comprising 292 infants in the non-ETS group and 289 in the ETS group. There was no statistically significant difference found for MAS (RR 0.98; 95% CI 0.71 to 1.35), but the certainty of evidence was low for survival at discharge and very low for all other outcomes. However, the authors concluded that initiating ETS soon after birth in non-vigorous meconium-stained infants may

not alter their neonatal outcomes [9]. No discrimination as to the texture of the meconium was made in this manuscript. We would like to stress that a non-vigorous infant with thin or moderately thick MSAF is not the same as a non-vigorous infant with thick or “pea soup” MSAF.

Edwards, *et al.* [10] in their study on the impact analysis post the new guideline implementation had shown that a significant proportion (28.9%) of the non-vigorous neonates born through MSAF underwent ETS in the delivery room even after the adoption of the new guidelines. The authors do not report nor discriminate between different consistencies of meconium and they comment that the limitations in their study preclude inferring that the new guideline is safe or effective [10].

In a very recent Cochrane Review the authors report uncertainty about the effect of tracheal suction on the incidence of MAS and its complications among non-vigorous neonates born through MSAF [11].

Worse outcomes in non-vigorous infants with thick MSAF when no ETS is performed?

Two studies, on the other hand, report worse outcomes when no ETS is performed. Chiruvolu, *et al.* [12] in a multicenter cohort study, compared 130 non-vigorous newborns with thick MSAF treated during the year prior to the implementation of the new resuscitation guidelines with 101 newborns born during one year after changing clinical practice to not aspirate the airway. In these non-vigorous newborns with thick MSAF, the practice change was associated with a higher incidence of admissions to the NICU for respiratory problems and with an increased need for mechanical ventilation, oxygen, and surfactant therapy [12]. The second study is an RCT performed over one year period at a tertiary care teaching hospital [13]. There were 155 non-vigorous infants randomized to receive either ETS (n = 76) or no ETS (n = 79). With similar limitations as mentioned previously for other studies, ETS at birth in non-vigorous infants born through MSAF decreased the incidence of MAS and duration of hospital stay, but overall incidence of respiratory distress and mortality remained unchanged [13].

Potential complications of ETS

ETS could be performed with an endotracheal tube or a wide-gauge suction catheter but conducting ETS may not only be ineffective in many babies, but it may also delay effective resuscitation, thus prolonging and worsening the hypoxic-ischemic insult. Tracheal suctioning has a potential to cause complications in newborn. Failure of endotracheal suctioning to prevent MAS could be attributed to occurrence of aspiration of meconium in utero and to the inability to retrieve meconium from trachea due to migration of meconium to distal airways. Even if meconium is retrieved on tracheal suctioning, distal airways, beyond the reach of tracheal suctioning, may still be plugged with meconium. This could explain failure of endotracheal suctioning to prevent MAS in some newborns, in addition to mechanical obstruction of airways. The main reasons leading to no ETS were potential procedure-related complications (such as apnea, bradycardia, airways and esophageal injuries, dislocation of the vocal cords, stridor) and the risk due to a delay in starting positive pressure ventilation. Nonetheless, some studies have reported a very low incidence of such complications. Additionally, a recent manikin study showed a clinically irrelevant magnitude of the delay in starting positive pressure ventilation [14].

An elegant narrative review [15] describes important details on this issue. Despite progress in the knowledge of the pathogenesis, prevention and treatment, MAS remains a severe neonatal disease. Understanding the causes (inflammation, infection, hypoxia) triggering fetal bowel activity and disclosing the mechanisms contributing to the meconium passage in utero is warranted to improve MAS prevention. The current treatment of MAS infants is supportive and current strategies do not act directly on the pathogenetic mechanism of lung damage. Further, the specific role of the timing of the injury (antenatal, perinatal or postnatal) affecting the long-term neurodevelopmental and pulmonary outcome is still not well understood. An adoption of less invasive ventilation approaches to prevent pulmonary damage and the treatment of PPHN with newer agents (i.e. L-Citrulline, endothelin receptor antagonists) may have a role in preventing lung damage [15].

In the middle of all this, clinicians are confused and some of them feel “flooded or overwhelmed” by so many publications with conflicting results and changes in recommendations by various groups. However, they still need to make a decision when face with a sick infant born through thick MSAF.

Results from a large survey in Latin America

In order to try to identify what was the current approach for clinical management of the airway in non-vigorous newborns with thick MSAF in multiple and varied centers of different Latin American countries, we performed a large survey from the Ibero American Society of Neonatology (SIBEN). We sent 1,600 electronic, confidential and voluntary surveys, to health care professionals in Latin America, members of SIBEN, dedicated to neonatal care. We received 1,265 complete responses (79%). Professionals from 19 Latin American countries responded. The countries with the highest response rate were México (31%), Argentina (15%), Colombia (10%) and Perú (9%). The results show wide differences, lending support to the fact that thick meconium in non-vigorous neonates is a “real mess”. Briefly, the findings of the survey on the use of ETS for non-vigorous neonates with thick meconium are shown in table 1. Table 2 shows mortality in non-vigorous neonates with thick MSAF according to ETS vs no ETS.

	% responses
Provided always ETS	58%
Provided some times ETS	36%
Never provided ETS	4%
Did not answer this question	2%

Table 1: Frequency of ETS in non-vigorous newborns with thick meconium in the institutions of the 1,265 neonatal health care professionals from Latin America that responded.

	Newborns with ETS 1,124 (57%)	Newborns with no ETS 846 (43%)	p value (Test Chi²)
Died in delivery room n (%)	23 (2%)	34 (4%)	> 0,05
Died in NICU n (%)	90 (8%)	152 (18%)	< 0,001
Total n (%)	113 (10%)	186 (22%)	< 0,001

Table 2: Mortality in non-vigorous neonates with thick MSAF according to ETS vs no ETS in the 1,970 newborns reported by 693 neonatal health care professionals of Latin America.

In summary, this survey shows that in Latin America there is variability in the management of non-vigorous neonates with thick MSAF, similar to what seems to be the case in developed nations [10]. Also, the responses unfortunately showed that, in some institutions, trained personnel for adequate care at birth are not available 24 hours/day every day of the week. Finally, the data suggests that lack of tracheal aspiration to clear the airway in non-vigorous neonates exposed to thick meconium could be detrimental. Some of these infants may benefit from releasing the thick meconium from an obstructed airway before ventilating.

Final Comments

It is clear that the majority of babies born through MSAF do not need ETS. However, this is not the same as saying that no baby could benefit by ETS. Education and clinical training, together with approaches and equipment from high to low resource settings can still play a crucial role in the global improvement in individualized management of non-vigorous infants with thick MSAF and obstructed airway.

Part of the confusion that exists in clinical care has been generated by publications that include in the denominator all newborns with MSAF of any consistency, whether or not they are vigorous at birth. There are few publications that specify the texture of the MSAF and/

or separate the results for those non-vigorous infants with thick MSAF. This smaller group of infants represent a different population, even more so if they are with airway obstruction at birth or if they are postmature or with intrauterine growth restriction.

Despite recent decreasing rates of ETS due to changes in official recommendations on neonatal resuscitation, a proportion of MAS patients still may benefit by ETS at birth.

Students, clinicians and the population at large are all still taught that a basic step for successful resuscitation is to ensure that the baby's nose, mouth and throat are patent or clear and to remove any blockage if present, to maintain a patent airway as a prerequisite. Whatever the cause of airway obstruction, prompt recognition and effective treatment is indispensable as an open and clear airway is essential to help ensure adequate ventilation. With this in mind, ETS at the time of birth with an intent to clear the trachea of meconium before regular breathing efforts began may be beneficial in some non-vigorous neonates with thick meconium and obstructed airway. For such a reason, a person skilled in neonatal intubation should always be available in case the need arises.

There is some analogy of all this with the Heimlich Maneuver, for which there is insufficient evidence as provided by RCT's to be a useful procedure to save choking humans with acute airway obstruction. Despite this, since the Heimlich Maneuver was introduced in 1974, it has saved the lives of more than 120,000 people. In 1985, then U.S. Surgeon General Dr. C. Everett Koop endorsed the Heimlich Maneuver as the only safe method for saving a choking victim.

Many authors write about the need for additional research to provide a definitive answer for clinicians regarding the "meconium mess". Dr. Wiswell wrote that the appropriate management of the non-vigorous meconium-stained neonate is an unanswered question [16]. He has called for large, high-quality randomized controlled trials of ETS of non-vigorous infants born through MSAF to inform on future decision making. We agree with this, but would add that in order to really clarify "this mess", such an RCT should include a sufficient sample size of non-vigorous infants born through thick meconium with suspected or clear evidence of airway obstruction in such a trial.

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Conflict of Interest

No conflict of interest of any of the authors.

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