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Best practice guidelines

The aetiology of meconium-stained amniotic fluid: Pathologic hypoxia or physiologic foetal ripening? (Review)

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ABSTRACT

Introduction: Despite the many efforts to study the (patho)physiology of meconium release before delivery, it still remains an indistinct subject. Some studies have reported a relationship between hypoxia and MSAF, whilst others have not. The most common association found however, is between MSAF and the term of gestation.
Methods: MEDLINE, EMBASE and the Cochrane library were electronically searched. Papers about the (patho) physiology of meconium-stained amniotic fluid in English were included. Papers about management strategies were excluded (see elsewhere this issue).
Results: Different theories have been proposed including acute or chronic hypoxia, physiologic foetal ripening and peripartum infection.
Conclusion: We suggest that meconium-stained amniotic fluid should be regarded as a symptom rather than a syndrome becoming more prevalent with increasing term and which might be associated with higher levels of infection or asphyxia.

Contents

1. Introduction

As a result of passing of foetal colonic contents, meconium-stained amniotic fluid (MSAF) can be observed in 7–22% of all deliveries at term [1]. Historically MSAF has been regarded as an indicator of foetal asphyxia. In 1962 Leonard has already suggested a possible relation between foetal anoxia, foetal distress, perinatal death and MSAF [2]. Since then, many studies have been performed to evaluate the clinical relevance of MSAF in terms of prediction of foetal asphyxia. Despite the many efforts to study the (patho)physiology of meconium release before delivery, it still remains an indistinct subject. Some studies have reported a relationship between hypoxia and MSAF, whilst others have not. The most common association found however, is between MSAF and the term of gestation. In post-date pregnancies incidences of MSAF of up to 40% have been described [3]. In this systematic review we want to give an overview of the aetiology and pathophysiology of MSAF. Until now, the presence of MSAF results in an increase of

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interventions during delivery, as described in most studies; perhaps due to more foetal distress, but definitely enhanced by the 'historic meaning' of MSAF [4–7].

2. Methods

2.1. Search strategy

MEDLINE, EMBASE and the Cochrane library were electronically searched through May 2013. The search comprised the terms 'meconium-stained amniotic fluid', 'aetiology', 'pathophysiology', 'foetal distress' and related entry terms. In addition, reference lists of identified articles and related reviews were hand searched. Titles, abstracts and entire texts were searched for potentially relevant articles. Papers were included when the aetiology or (patho)physiology of meconium-stained amniotic fluid were analysed. Both human and animal studies have been included. Retrospective studies as well as prospective studies, reviews and experimental researches have been included (Table 1). Publications about the management strategies were excluded (see elsewhere this issue). There was a language restriction to English. There were no restrictions concerning the year of publication. The most important reports on the aetiology of meconium-stained amniotic fluid are presented in table 1. Based on the included papers, the aetiology of MSAF could be divided into three categories: foetal hypoxia, foetal ripening and peripartum infection.

3. Results and discussion

3.1. Hypoxia

In many studies MSAF is related to poorer neonatal outcome [4, 7–12]. This includes lower APGAR-scores and lower cord blood pH-levels. Furthermore, in some studies more neonatal admittance to intensive care units is described [7,11] and more perinatal death incidents [7,9]. This association is seen as a proof that hypoxia leads to more intrauterine meconium release. One of the known risks of MSAF is the meconium aspiration syndrome (MAS). About 5% of the infants with MSAF develop MAS, which still has a mortality rate of 2.5% in the developed world and up to 35% in the developing world [13,14]. The lower APGAR-scores, the more admittance to a neonatal ICU and the higher perinatal death figures could therefore be an effect of MAS rather than that it supports the theory that foetal hypoxia leads to more MSAF. Lower pH-levels and thus more acidosis on the other hand cannot be related to MAS only and supports the theory of foetal hypoxia leading to MSAF. However, in some studies no differences in pH levels are found in the case of MSAF [15,16]. In a study of Ciftici et al. in rats, the aortas were clamped to effectuate hypoxic stress; none of the animals released meconium [17]. Therefore the authors suggested that the association between MSAF and poor neonatal outcome might be due to a reduced clearance of meconium, rather than due to increased meconium release [17]. Furthermore they performed sympathectomy in animal models and then put those animals in a hypoxic environment. Compared to controls, there was no meconium release in the sympathectomised animals, but all animals in the control group did defecate after the hypoxic event. Furthermore, meconium by itself can have a vasoconstrictive effect on the umbilical cord and lead to necrosis and ulceration of the cord [18] which can result in more foetal hypoxia. This does not necessarily mean that more hypoxia leads to foetal meconium release. Therefore, we cannot determine the exact pathophysiologic mechanism underlying the association between MSAF and foetal hypoxia. In a small study, placentas from neonates with MSAF have been pathologically examined and placenta's thickening of the basal membrane was observed and more apoptosis was found [12]. These findings have also been described in growth-restricted infants and placentas of infants with foetal distress and are therefore suggested to be ultra-structural changes to hypoxia. Small for gestational age is also an independent risk factor for meconium-stained amniotic fluid [19]. In an experimental animal study it has been indicated that hypoxemic stress leads to reduced swallowing of meconium-stained amniotic fluid, instead of more meconium release [17]. This might explain the association between more meconium-stained amniotic fluid and poor perinatal outcome, but not in the pathophysiologic way as previously proposed.

4. Chronic or acute hypoxia

If MSAF is indeed associated with foetal distress the question is whether MSAF is related to an acute hypoxic event or if MSAF is a symptom of chronic distress. In some studies a distinction has been made between thin and thick meconium [5,6]; thick but not thin meconium-stained amniotic fluid was associated with poor neonatal outcomes in

Table 1
Reports of aetiology of meconium stained amniotic fluid.

Author	Year of publication	Hypoxia	Infection	Maturation	Number of subjects (N) and type of article
Meis	1982	+/−	−	−	N = 128 cases, N = 134 controls. Case–control study.
Wen	1993	−	+	−	N = 200. Retrospective case–control study.
Chapman	1995	−	+	−	N = 200. Retrospective case–control study.
Richey	1995	+/−	−	−	N = 56. Case–control study. No difference in cord pH were found, however elevated EPO levels
Maymon	1998	+	+	−	N = 37085. Cross-sectional cohort study.
Piper	1998	−	+	−	N = 936. Cohort study.
Sienko	1999	+	−	−	N = 4. Histologic study.*
Ciftici	1999	+/−	−	−	N = 16. Rat study.*
Jazayeri	2000	+/−	−	+	N = 203 (N = 70 with MSAF). Higher EPO levels but no differences in cord pH or APGAR.
Sheiner	2002	+/−	−	−	Prospective study. N = 586. (N = 106 with MSAF).
Ahanya	2005	+	+	+	Review.
Locatelli	2005	+	−	−	N = 19,090. Cohort study.
Ohja	2006	+/−	−	−	N = 52 cases, N = 42 controls. Case–control study.
Modarressnejad	2006	+	−	−	N = 400. Prospective study.
Oyelese	2006	−	−	+	N = 6403. Retrospective study.
Lakshmanan	2007	+	−	−	N = 12 cases, N = 12 controls. Rat study.*
Shaikh	2010	+	−	−	N = 250 cases, N = 250 controls. Cross sectional study.
Balchin	2011	+	−	++	N = 499,096. Retrospective study.
Lee	2011	+	−	+	N = 4376. Retrospective cohort study.
Brailovschi	2012	+/−	−	−	N = 204,102. Case–control study to intrapartum death.
Kumari	2012	+	−	−	N = 75. Observational study.
Yurdakul	2012	+	−	−	N = 13 cases, N = 24 controls. Histologic study.*
Gun Eriyilmaz	2013	+	−	−	N = 40 cases, N = 40 controls. Cross sectional cohort study.

* Low number of subjects due to study type; histologic or animal studies.