Meconium-stained amniotic fluid

Sian Mitchell

Edwin Chandraharan

Abstract

Passage of meconium usually occurs within 48 hours after birth. However, some fetuses may pass meconium in-utero leading to meconium staining of amniotic fluid (MSAF). The vast majority of fetuses pass meconium in-utero due to the physiological maturation of the fetal gut with advancing gestation leading to normal defaecation in utero. However, clinicians need to exclude 'non-physiological' causes of MSAF, especially an ongoing hypoxia or chorioamnionitis, to improve perinatal outcomes. Meconium aspiration syndrome (MAS) is a potentially serious fetal condition with increased risk of severe morbidity and mortality. The use of the cardiotocograph (CTG), timely recognition of ongoing hypoxia or infection, consideration of the overall clinical picture and avoidance of injudicious use of oxytocin may help avoid poor perinatal outcomes and resultant medico-legal consequences.

Keywords bile acids; bile pigments; cardiotocograph (CTG); chorioamnionitis; chronic hypoxia; meconium; meconium aspiration syndrome (MAS); primary pulmonary hypertension (PPH)

Introduction

Meconium refers to the first stool passed by the fetus and consists of gastrointestinal contents of the fetus. It is first formed in the gastro-intestinal tract of a fetus at 11–14 weeks' gestation and most babies pass meconium after birth, usually within the first 48 hours. The greenish colour is due to bile pigments and the constituents of meconium are given in Box 1.

The incidence of meconium passage in-utero has been shown to increase steadily with increasing gestational age. Meconium stained amniotic fluid (MSAF) has been shown to occur in 5% of pregnancies before 37 weeks' gestation, 25% of births at term pregnancy and in up to 52% in post term pregnancies.

Why do some fetuses pass meconium in utero?

Motilin, a polypeptide responsible for peristalsis, was initially attributed to the passage of meconium and it has been shown that higher levels of motilin were noted in the umbilical cord blood in term infants with MSAF. Meconium passage has also been shown to increase with increasing gestational age due to increasing maturation of the fetal intestinal myelination and ganglion cells and the parasympathetic system. Fetal bowel movements and sphincter relaxation are controlled by parasympathetic autonomic nervous system. Colonic filling may lead to the activation of the parasympathetic nervous systems causing meconium passage. Risk factors for in-utero passage of meconium is given in Box 2.

Constituents of meconium

70–80% water
Intestinal epithelial cells
Squamous cells
Lanugo
Amniotic fluid
Bile acids and salts
Inflammatory modulators (IL8, phospholipase A2)
Mucus glycoproteins
Lipids
Proteases

Box 1

What are the intrapartum risk factors for the passage of meconium?

Fetal hypoxia and acidosis have long been associated with meconium stained amniotic fluid and several theories have been put forward to explain the underlying mechanisms. Experimental studies demonstrating fetal swallowing and defaecation have been conducted in fetal rabbits. In the presence of fetal hypoxia, there is accumulation of radioactive technetium within the amniotic cavity suggesting that normal processes clearing meconium in a fetus are impaired in hypoxic situations. Erythropoietin production is caused by hypoxia in the fetus and this does not

Risk factors for passage of meconium prior to birth

Maternal factors:
Obstetric Cholestasis
Maternal hypertension
Diabetes
Smoking and cocaine abuse

Placental factors:
Pre-eclampsia
Placental insufficiency

Fetal abnormalities

Gastroenteritis (e.g. listeria)

IUGR (i.e. chronic hypoxia)

Chorioamnionitis and bowel abnormalities

Box 2

Sian Mitchell *MBBS Bsc Clinical Fellow in Obstetrics and Gynaecology, St. George's University Hospitals NHS Foundation Trust, London, UK. Conflicts of interest: none declared.*

Edwin Chandraharan *MBBS MS (Obs & Gyn) DFFP DCRM FSLCOG FRCOG Consultant Obstetrician and Gynaecologist/Lead Clinician Labour Ward, St. George's University Hospitals NHS Foundation Trust and Honorary Senior Lecturer, St George's University of London, UK. Conflicts of interest: none declared.*

Please cite this article in press as: Mitchell S, Chandraharan E, Meconium-stained amniotic fluid, Obstetrics, Gynaecology and Reproductive Medicine (2018), https://doi.org/10.1016/j.ogrm.2018.02.004

cross the placenta. Richey reported that erythropoietin levels were significantly increased in the fetus with MSAF secondary to hypoxia. In addition, the parasympathetic nervous system responsible for fetal bowel movements is sensitive to umbilical cord compression and hypoxic insult. Therefore it is possible that stimulation of the vagus nerve during hypoxia may cause peristalsis of the bowel and relaxation of the anal sphincter leading to the passage of meconium into the amniotic cavity. However, several experimental studies in animals have disputed this theory.

In contrast, scientific evidence suggests a stronger association between the passage of meconium and intra-amniotic infections with higher incidence of chorioamnionitis and endometritis. However, it is unclear whether infection causes fetal peristalsis (i.e. ingested infected amniotic fluid causing gastro-enteritis and bowel irritation), causing meconium passage, or if the presence of the meconium within the amniotic cavity promotes bacterial growth due to the inactivation of neutrophil phagocytosis.

There has been an independent association reported between maternal serum bile acid levels and MSAF and thus a higher incidence of MSAF in obstetric cholestasis. Animal studies have demonstrated high maternal serum bile acids stimulate colonic motility causing passage of meconium. Vaginal misoprostol has been shown to have a direct effect on bowel motility causing MSAF.

Why is MSAF harmful?

MSAF is associated with poor perinatal outcomes. In autopsy examinations conducted by Alshutler et al., meconium exposure was associated with tissue inflammation in the neonatal lung and placental tissues and damage to the umbilical cord, such as severe ulceration. The corrosive nature of the bile salts and pigments and epithelial cells in MSAF has been associated with skin damage, namely physiological desquamation of the skin and erythema toxicum neonatorum. Moreover, umbilical cord vasospasm has been demonstrated in the presence of meconium. Montgomery showed that meconium can inhibit the contractile effect of U46619, a thromboxane A2 analogue.

Meconium also changes the antibacterial properties of the amniotic fluid. Meconium is known to inhibit phagocytosis and reduce neutrophilic oxidative burst, thus permitting bacterial growth. There is no evidence, however, to support the effectiveness of administration of prophylactic antibiotics in these cases to prevent growth of bacterial isolates such as *E. coli* and reduce maternal and fetal morbidity. When compared to deliveries with clear amniotic fluid, labours complicated by MSAF have higher rates of chorioamnionitis and endometritis, even when confounding factors are taken into consideration.

Meconium Aspiration Syndrome (MAS)

Meconium aspiration syndrome (MAS) is a severe complication of MSAF and is associated with a neonatal mortality rate of 20% and may occur in up to one in ten births with MSAF. It more commonly occurs in fetuses with thick meconium and has a multifactorial pathophysiology. Meconium induces the activation of macrophages and neutrophils, and releases cytokines, including tumour necrosis factor α and interleukins. The subsequent direct damage to lung tissues caused by these inflammatory mediators, and the increase in vascular leakage and further mediator release, impair type 2 pneumocytes and decrease surfactant production, resulting in decreased lung compliance, hypoxia and acidosis. Meconium can also result in airways obstruction, pulmonary air trapping and ventilation/perfusion mismatch. In addition, primary pulmonary hypertension (PPH) has been documented in up to 40% of cases of severe MAS, which is characterized by right to left shunting through a patent PDA or foramen ovale secondary to pulmonary vasoconstriction. This contributes to newborn hypoxia, resulting in severe metabolic acidosis and further pulmonary vasoconstriction. MSAF is also associated with increased risk of neonatal sepsis and, for all these reasons, admission to neonatal intensive care units.

How to avoid MAS?

Amnioinfusion (i.e. instillation of saline into the amniotic cavity via the cervix to dilute the thickness of meconium) has been a proposed to reduce the incidence of MAS. However, a Cochrane Systematic review has not found amnioinfusion to improve MAS and perinatal outcomes in centres where facilities for continuous electronic fetal heart rate monitoring are available. In low resource settings where facilities for CTG monitoring is not available, the use of amnioinfusion may help dilute the meconium and decrease the incidence of variable decelerations due to umbilical cord compression. However, the clinicians need to consider the underlying pathology behind the passage of thick meconium stained amniotic fluid (i.e. chronic hypoxia or chorioamnionitis), prior to making an attempt to dilute the meconium.

Continuous electronic fetal heart rate monitoring using a cardiotocograph (CTG) is used to screen for the underlying pathological causes of meconium passage, such as fetal infection and hypoxia. Persistent fetal tachycardia has been described as the most important predictor of severe MAS. In addition to this, fetuses with an unstable baseline and thick meconium present at labour are at increased risk of developing MAS. Mitchell demonstrated that fetal heart traces are a poor predictor of fetal acidosis in the presence of meconium. These conflicting views could be solely down to differing study designs and variables being measured. It is very important to appreciate that repetitive and sustained compression of the umbilical cord characterized by repetitive, 'atypical' variable decelerations (Figure 1) and

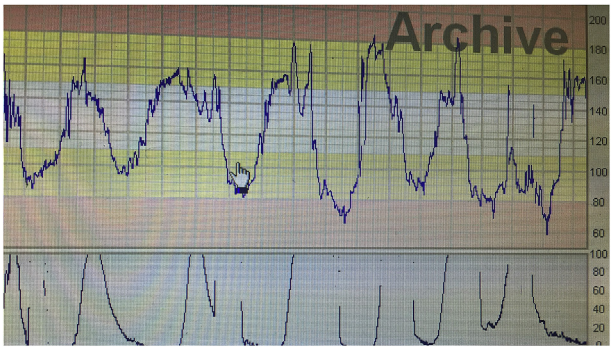

Figure 1 Repetitive atypical variable decelerations on the CTG trace.

Please cite this article in press as: Mitchell S, Chandraharan E, Meconium-stained amniotic fluid, Obstetrics, Gynaecology and Reproductive Medicine (2018), https://doi.org/10.1016/j.ogrm.2018.02.004