Journal of Perinatology (2008) 28, S43–S48

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REVIEW

Meconium aspiration syndrome: experiences in Taiwan

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Meconium aspiration syndrome (MAS) is still one of the most challenged diseases for the neonatologists. We reviewed our earlier studies of MAS in an attempt to provide some idea for more understanding of MAS. This study is a retrospective review and summarization of our earlier studies in MAS at two tertiary neonatal centers in Taiwan. Incidence of MAS was decreased sharply in Taiwan. MAS infants who required resuscitation in the birth room being out-born, birth asphyxia and infants who developed persistent pulmonary hypertension (PPHN) and pneumothrax were associated with increasing mortality. In MAS infants who neither required mechanical ventilation nor had a history suggestive of perinatal infection, antibiotic treatments would not affect the outcome of MAS. Dexamethasone did reduce inflammation response and improve cardiopulmonary perfusion. However, steroids did not prevent the development of PPHN. Our review provided the risk factors of mortality for MAS. Antibiotic treatments should not be a routine for every infant with MAS. Although steroids reduce pulmonary inflammation, their role in the prevention of PPHN remains to be further studied.
Journal of Perinatology (2008) **28**, S43–S48; doi:10.1038/jp.2008.157

The incidence of meconium aspiration syndrome (MAS) varies from population to population and from countries to countries.[1–4] With the recent improvement in socioeconomic status and the advances in prenatal care in Taiwan, the incidence of MAS in Taiwan sharply decreased in the past decade.[1] The adoption of National Healthcare Insurance System is probably the most important factor leading to better health access and care. Table 1 shows some of the factors that characterized health care in Taiwan. At present, nearly 100% of the pregnant women have prenatal care and majority of the deliveries are carried out in large hospitals. However, the mean age of the mother at the time of first childbirth is about 26 years, older than that in most of the developing and developed countries.

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Incidence of MAS

Table 2 compares the incidence and mortality of infants suffering from MAS between the United States and one of the tertiary centers in Taiwan (China medical university hospital, Taichung, Taiwan).[1–3] It is interesting to note that data of the incidences of meconium staining of amniotic fluid, MAS and mortality are almost comparable with those from the United States. However, these data are obtained from one tertiary center with many high-risk maternal transfers; the actual overall incidence in Taiwan could be much lower. The outborn infants have higher mortality rates (7.3%) than inborn infants (0.81%) (Table 3).

Perinatal and postnatal factors and mortality in MAS

A review of 314 cases of MAS between 1995 and 2001[1,5] indicated that infants who required resuscitation in the birth room, who were first out-born or with birth asphyxia, and infants who developed persistent pulmonary hypertension (PPHN) and pneumothorax are important factors associated with increased mortality in MAS (Table 4).

Management of meconium-stained amniotic fluid in delivery room

Since 1995, the management of meconium-stained amniotic fluid has followed a guideline as shown in Figure 1.[6] This guideline is not much different from the recent recommendations of American Academy of Pediatrics.[7,8] We do endotracheal suction in infants who have thick meconium staining, who have low Apgar score or who have respiratory distress shortly after birth.[9] We perform intrapartum oro- and nasopharyngeal suction in all infants if there is meconium staining of amniotic fluid.[6,10] We feel that this procedure is simple and does not carry significant adverse effects. Using this guideline, about 50% of meconium-stained infants required endotracheal suction. We do amnioinfusion only if there is oligohydramnio and thick meconium staining.[11–15]

The role of antibiotics in MAS

Meconium has been shown to enhance bacterial growth *in vitro*, particularly Gram-negative organisms. It is a common practice to place these infants on antibiotics. We have conducted a study on 259 MAS infants who did not require mechanical ventilation and who did not have a history suggesting perinatal infection.[5] The infants were divided into two groups; one received antibiotics and the other did not. Both groups were comparable in their baseline data. There was no significant difference between the groups in clinical course and mortality (Table 5).

Thus, antibiotic treatments would not affect the clinical course and outcome in MAS without perinatal risk factors for infection and without ventilator use.

Table 1

Health care in Taiwan

NHIS coverage
Prenatal care 98–100%
Average age of mother for first child—26 years
Uniform population and easy access for medical care
Establishment of regionalization of perinatal care
Minimal years of maternal education 9–12 years
Average number of children per family—1.2

Abbreviation: NHIS, National Healthcare Insurance System.

The role of pulmonary inflammation in the development of PPHN in MAS

Pulmonary hypertension or PPHN of the newborn occurs in 10 to 15% of infants with MAS. This condition usually presents as persistent hypoxemia occurred at 6 to 24 h after birth. A spontaneous recovery usually occurs within 3 to 4 days if the patient survives, suggesting that a functional vascular constriction is probably involved in the pathogenesis.

Pulmonary hypertension or PPHN in infants with MAS could be due to (1) hypertrophy or neo-muscularization of

Table 2 Incidences of MAS and mortality in the United States and Taiwan

	USA (Wiswell et al.[2]*)* *1997*	*Taiwan (Lin* et al.[1]*)* *1995–2001*
Incidence of meconium staining	10–15%	13%
MAS/meconium staining	5%	5.9%
IMV/MAS	33%	(inborn 0.81%)
Incidence of MAS/liveborn	0.5%	0.7%
Mortality/MAS	5%	4.8%

Abbreviations: IMV, intermittent mandatory ventilation; MAS, meconium aspiration syndrome.

Table 4 Risk factors of mortality in MAS by logistic regression model

Variable	P-*value*	*Odds ratio*	*CI lower*	*CI upper*
Asphyxia	0.0032	0.026	0.002	0.293
Outborn	0.0869	0.124	0.011	1.353
PPHN	0.0145	0.065	0.007	0.581
Shock	0.4246	2.50	0.263	23.771
Pneumothorax	0.0143	0.158	0.036	0.692

Abbreviations: MAS, meconium aspiration syndrome; PPHN, persistent pulmonary hypertension of the newborn.
Adapted from Lin *et al.*[1]

Table 3 Incidence and mortality rate of MAS from 1995 to 2001

	1995	*1996*	*1997*	*1998*	*1999*	*2000*	*2001*	*Total*
Inborn babies (n)	14	22	14	12	16	21	24	123
Outborn babies (n)	26	18	19	19	31	43	35	191
Survival (n)	36	39	32	29	43	63	57	299
Expired (n)	4	1	1	2	4	1	2	15
Mortality rate (%)	4/40	1/40	1/33	2/31	4/47	1/64	2/59	15/314
	(10.0)	(2.5)	(3.0)	(6.5)	(8.5)	(1.6)	(3.4)	(4.8)
Incidence of MAS in inborn (%)	14/154	22/24	14/23	12/216	16/24	21/26	24/23	123/15
	9	59	72	3	06	58	60	967
	(0.90)	(0.89)	(0.59)	(0.55)	(0.66)	(0.79)	(1.01)	(0.77)
Incidence of mortality in inborn (%)	1/14	0/22	0/14	0/12	0/16	0/21	0/24	1/123
	(7.14)	(0)	(0)	(0)	(0)	(0)	(0)	(0.81)

Abbreviation: MAS, meconium aspiration syndrome.
Adapted from Lin *et al.*[1]

postacinar pulmonary capillaries as a result of chronic intrauterine hypoxia, (2) functional pulmonary vasoconstriction as a result of hypoxemia, hypercarbia or acidosis or (3) functional pulmonary vasoconstriction as a result of lung inflammation. We hypothesized that lung inflammation may play an important role in pulmonary vascular constriction and hypertension. We therefore conducted a MAS study on newborn piglet models.[16] The purposes of the study were to investigate the following: (1) Does MAS in newborn piglets produce pulmonary hypertension? (2) Does pulmonary inflammation play a role in the development of pulmonary hypertension. (3) Can anti-inflammatory agents, such as dexamethasone, prevent pulmonary hypertension. Figure 2 shows the method of the study on 35 newborn piglets (aged 1 to 7 days).[16] We also administered dexamethasone early in several infants.[17] The results of piglet and newborn studies are shown in Tables 6 and 7. On the basis of the results of this study, we made the following conclusions:

(1) Following meconium aspiration, elevation of pulmonary arterial pressure appears to be biphasic, the early phase starting

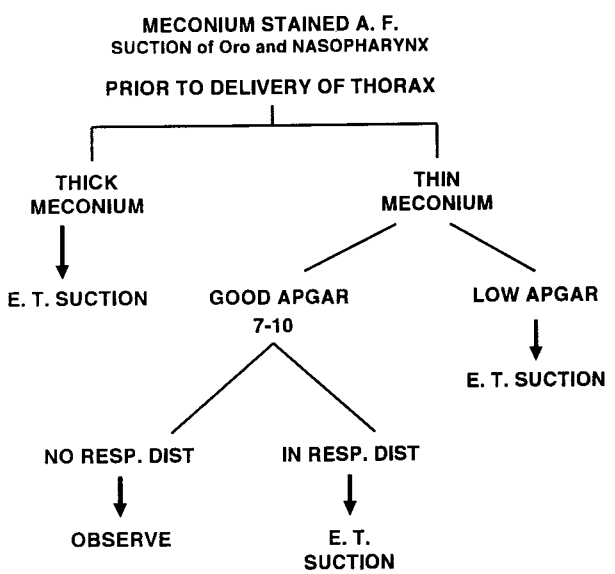

Figure 1 A guideline for the management of meconium staining of amniotic fluid in the delivery room.

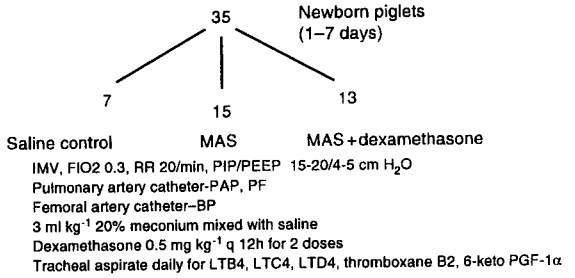

Figure 2 Method for Newborn Piglet MAS study. Adapted Wu *et al.*[16]

Table 6 Cardiac SV

	Before	*0–12 h*	*12–24 h*	*d-2*	*d-3*	*d-4*
S.V. (mg kg^{-1})						
C	1.5 ± 0.4	1.4 ± 0.5	1.5 ± 0.4	1.6 ± 0.5	1.6 ± 0.4	1.9 ± 0.8
MAS	1.4 ± 0.4	1.2 ± 0.3	1.1 ± 0.2**	1.3 ± 0.4*	1.6 ± 0.3	1.8 ± 0.4
MAS+D	1.4 ± 0.5	1.3 ± 0.4	1.3 ± 0.3	1.4 ± 0.3	1.5 ± 0.5	1.9 ± 0.3
mBP (mm Hg)						
C	118 ± 16	107 ± 11	99 ± 7	96 ± 8	87 ± 9	92 ± 10
MAS	120 ± 11	118 ± 11	110 ± 16	106 ± 14**	103 ± 8*	102 ± 7
MAS+D	119 ± 17	120 ± 12	124 ± 15*	120 ± 10**	118 ± 8*	101 ± 6
mPAP (cm H_2O)						
C	19 ± 6	19 ± 5	20 ± 5	20 ± 8	21 ± 6	22 ± 9
MAS	20 ± 3	24 ± 5*	23 ± 5*	25 ± 4*	24 ± 7	22 ± 6
MAS+D	20 ± 6	27 ± 10*	24 ± 6*	24 ± 8*	26 ± 10	23 ± 4

Abbreviations: MAS, meconium aspiration syndrome; MAS+D, meconium aspiration syndrome+dexamethasone; mBP, mean blood pressure; mPAP, mean pulmonary arterial pressure; SV, stroke volume.
*$P<0.05$, **$P<0.01$ (as compared with saline control).
C: saline control, $n = 7$; MAS, $n = 15$; MAS+D, $n = 13$.
Adapted from Wu *et al.*[16]

Table 5 MAS treated with or without antibiotics

	No antibiotics (n = 127)	*Antibiotics group (n = 132)*	P-*value*
Tachypnea (days)	5.9 ± 2.7	6.2 ± 3.5	0.91
Duration of O_2 (days)	4.6 ± 1.7	3.6 ± 1.3	0.46
Duration of CPAP (days)	2.2 ± 1.8	3.0 ± 2.2	0.65
Nasal CPAP (case)	29/127	33/132	0.68
Pulmonary air leaks (case)	4/127	7/132	0.39

Abbreviations: CPAP, continuous positive airway pressure; MAS, meconium aspiration syndrome.
Mean values ± s.d.
Adapted from Lin *et al.*[5]

Table 7 Respiratory status in MAS infants with and without dexamethasone therapy

	Before	*d-1*	*d-2*	*d-3*	*d-4*	*d-5*	*d-7*
IMV							
C	9	6	5	5	4	3	2
D	12	6	4	1	0	0	0
FIO2							
C	0.54 ± 0.31	0.35 ± 0.16	0.26 ± 0.16	0.29 ± 0.16	0.29 ± 0.08	0.29 ± 0.09	0.28 ± 0.18
D	0.52 ± 0.24	0.40 ± 0.20	0.30 ± 0.18	0.32 ± 0.29	0.30 ± 0.22	0.31 ± 0.24	0.30 ± 0.21
P_{O2} *(mm Hg)*							
C	86 ± 58	84 ± 33	74 ± 22	75 ± 30	70 ± 26	80 ± 18	75 ± 25
D	91 ± 80	86 ± 42	70 ± 42	78 ± 28	67 ± 23	76 ± 14	74 ± 14
P_{CO2} *(mm Hg)*							
C	43 ± 12	36 ± 9	36 ± 8	39 ± 5	43 ± 8	37 ± 8	41 ± 2
D	42 ± 12	34 ± 7	32 ± 5*	33 ± 9*	30 ± 7**	35 ± 7	39 ± 5
pH							
C	7.28 ± 0.12	7.41 ± 0.07	7.40 ± 0.05	7.40 ± 0.07	7.39 ± 0.09	7.39 ± 0.06	7.45 ± 0.17
D	7.30 ± 0.70	7.39 ± 0.05	7.40 ± 0.05	7.45 ± 0.03*	7.43 ± 0.04*	7.40 ± 0.06	7.44 ± 0.05

Abbreviations: IMV, intermittent mandatory ventilation; MAS, meconium aspiration syndrome.
*$P<0.05$, **$P<0.01$.
C: control infants, $n = 23$; D: dexamethasone-treated infants, $n = 27$. Adapted from Yeh *et al.*[17]

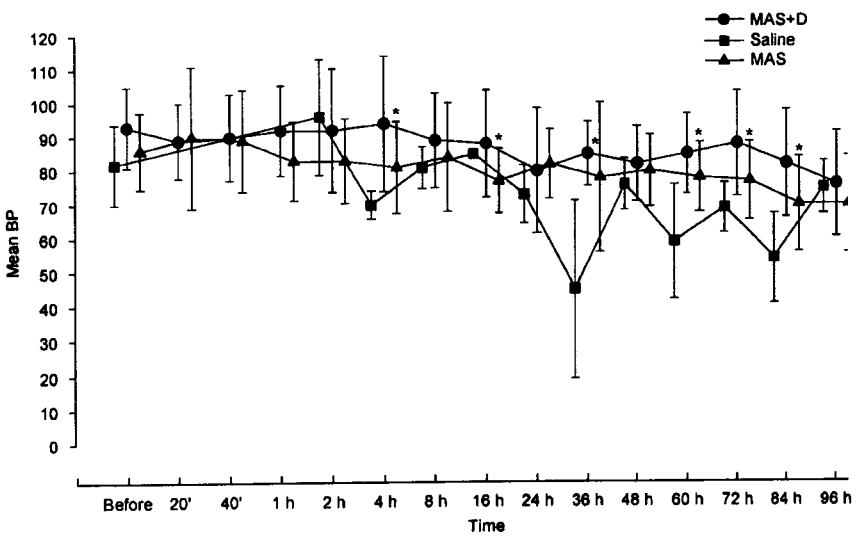

Figure 3 Mean blood pressure during the study. MAS piglets that received dexamethasone had significantly higher mean blood pressure at 4, 16, 36, 72 and 82 h than saline control piglets. *$P<0.05$. Adapted from Wu *et al.*[16]

from 2 to 6 h and the later phase starting from 48 h. (2) A good correlation was seen between tracheal aspirate TXB_2, leukotriene D_4 and mean pulmonary anterial pressure. (3) The use of dexamethasone reduced tracheal aspirate TXB_2 and 6-keto $PGF_{1\alpha}$. (4) Dexamethasone increased cardiac stroke volume, increased pulmonary blood flow and improved ventilation/perfusion match.

The role of pulmonary inflammation in the development of pulmonary hypertension or PPHN in MAS and the possible role of steroids in the prevention of PPHN remain to be further studied (Figures 3 to 7).

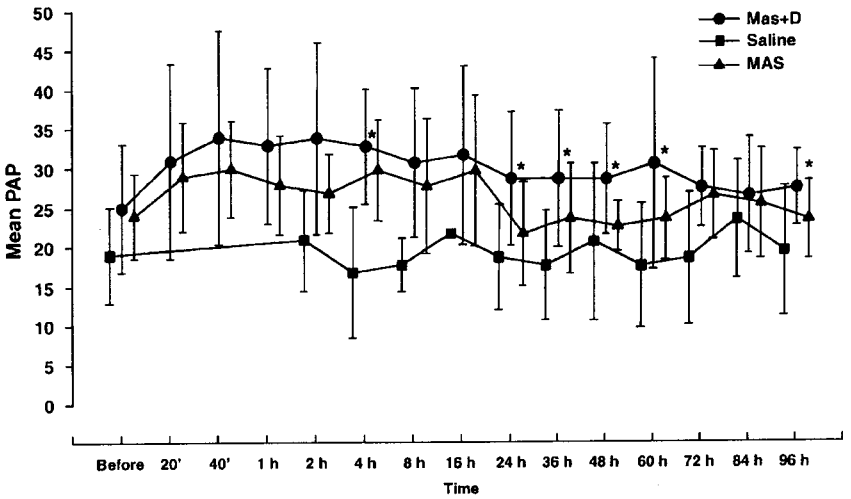

Figure 4 Mean pulmonary arterial pressure (PAP) changes during the study. Piglets with MAS and dexamethasone had significantly higher mean PAP than saline control piglets at 4, 24, 36, 48 and 60 h after study. There were simultaneous increases in cardiac stroke volume, suggesting that the increases of mean PAP is a result of increased pulmonary flow. *$P<0.05$. Adapted from Wu *et al.*[16]

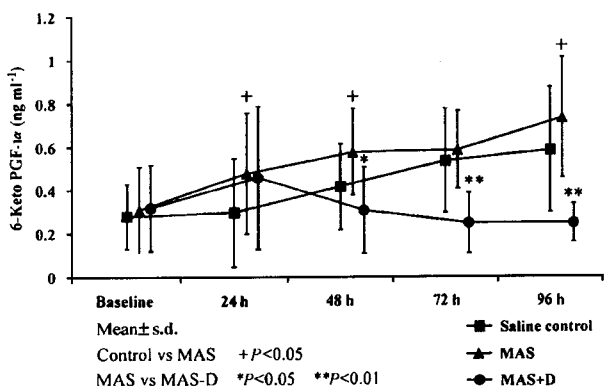

Figure 5 Changes of 6-keto prostaglandin $(PGF)_{1\alpha}$ in tracheal aspirate. MAS piglets had significantly higher 6-keto $PGF_{1\alpha}$ than saline controls. The use of dexamethasone significantly decreased 6-keto $PGF_{1\alpha}$. Adapted from Wu *et al.*[16]

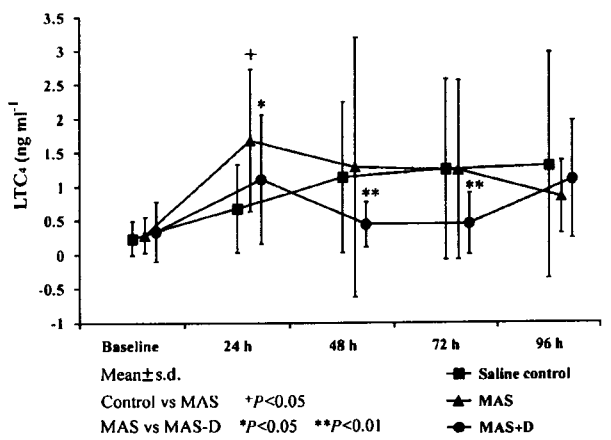

Figure 6 Changes of leukotriene (LTC_4) in tracheal aspirate during the study. Piglets with MAS had significantly higher LTC_4 than saline controls at 24 h. The use of dexamethasone significantly decreased LTC_4 at 48 and 72 h. Adapted from Wu *et al.*[16]

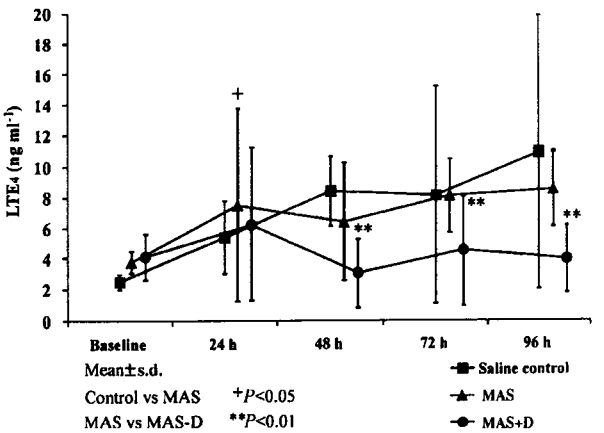

Figure 7 Changes of leukotriene (LTE_4) in tracheal aspirate during the study. Piglets with MAS had significantly higher LTE_4 than saline controls at 24 h. The use of dexamethasone significantly decreased LTE_4 at 48, 72 and 92 h. Adapted from Wu *et al.*[16]

Disclosure

The authors have declared no financial interests.

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