

Title page**Resuscitation of non-vigorous neonates born through meconium stained amniotic fluid - A post policy change impact analysis**

Oommen VI¹, Ramaswamy VV¹, Szyld E², Roehr CC^{1,3}

Affiliations: 1) Newborn Services, John Radcliffe Hospital, Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom; 2) Division of Newborn Medicine, Department of Pediatrics, University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma; 3) National Perinatal Epidemiology Unit, Nuffield Department of Population Health, Medical Sciences, Division, University of Oxford, Oxford, United Kingdom.

Primary Author - Vinod Idicula Oommen

Registrar,
Newborn Services, John Radcliffe Hospital
Oxford University Hospitals NHS Foundation Trust
Oxford, United Kingdom

Author - Viraraghavan Vadakkencherry Ramaswamy
Registrar,
Newborn Services, John Radcliffe Hospital
Oxford University Hospitals NHS Foundation Trust
Oxford, United Kingdom

Author - Edgardo Szyld
Professor of Research,
Division of Newborn Medicine, Department of Pediatrics,
University of Oklahoma Health Sciences Center,
Oklahoma City, Oklahoma

Author - Charles Christoph Roehr*
Academic Consultant,
Newborn Services, John Radcliffe Hospital,
Oxford University Hospitals NHS Foundation Trust,
Medical Sciences Division, National Perinatal Epidemiology Unit,
Nuffield Department of Population Health,
University of Oxford, Oxford, United Kingdom

***Corresponding Author -**

A./Prof. Charles Christoph Roehr
Newborn Services, John Radcliffe Hospital, Headley Way, Headington, Oxford OX3 9DU, UK
Tel. 0044-1865-227791
Email: charles.roehr@ouh.nhs.uk

Word count - 1169

Tables - 2

Funding - None

Conflict of interest - None

Keywords

meconium stained amniotic fluid, meconium, non-vigorous meconium stained amniotic fluid neonates, endotracheal suctioning, tracheal suctioning, meconium aspiration syndrome

ABSTRACT

Background: We investigated the impact of policy change in delivery room resuscitation from routine endotracheal (ET) suctioning of non-vigorous neonates born through meconium stained amniotic fluid (MSAF) to immediate non-invasive respiratory support.

Design: Single center cohort study. Prospective group (October 2016 - September 2017) – Non-vigorous MSAF neonates managed according to the current (2015) guidance of commencing respiratory support without prior suctioning. Retrospective group (August 2015 - July 2016) – Non-vigorous MSAF neonates who underwent routine ET suctioning.

Results: 1138 MSAF neonates were analysed. No differences in the incidence of MAS, requirement of mechanical ventilation, inhaled nitric oxide or surfactant therapy were found between groups. Less NICU admissions were necessary in prospective cohort compared to retrospective group (19.1% vs 55.6% respectively, $p < 0.05$).

Conclusion: The policy change towards not routinely suctioning non-vigorous MSAF neonates at birth was not associated with an increase in the local incidence of MAS, and was associated with fewer NICU admissions.

INTRODUCTION

In 2015, the European Resuscitation Council (ERC) and the American Heart Association (AHA) amended the guidelines for management of non-vigorous neonates born through meconium-stained amniotic fluid (MSAF), recommending to initiate positive pressure ventilation (PPV) immediately after birth as opposed to the previous practice of routine endotracheal suctioning of non-vigorous MSAF neonates before providing respiratory support. [1] Three recent observational studies from North-America investigated the outcomes of non-vigorous MSAF after adoption of the new guidelines, using historical cohorts as comparators.[2-4] These studies provide mixed results with one study showing an increase in admissions to the Neonatal Intensive Care Unit (NICU) and increased requirements of oxygen support in non-vigorous MSAF after the implementation the new guidelines. Until today, no study has reported such outcomes from Europe. Thus, we present the single-center outcomes of non-vigorous MSAF neonates who were resuscitated as per the 2015 ERC newborn resuscitation guideline and compare these outcomes with a historical cohort which was managed according to the 2010 ERC newborn resuscitation guideline [ERC 2010]. [5]

OBJECTIVES

The primary objective was to assess the incidence of meconium aspiration syndrome (MAS) in the non-vigorous MSAF neonates in the prospective group and to compare this with the incidence of MAS in the historical cohort.

The secondary objectives were to compare the incidence of NICU admissions, requirement of invasive mechanical ventilation (IMV), inhaled nitric oxide, surfactant, extra-corporeal membrane oxygenation (ECMO) and mortality between the two groups.

METHODS

This was a single-center cohort study, conducted in a perinatal tertiary referral center in Oxford, United Kingdom. We included neonates of ≥ 34 weeks gestational age who were born through MSAF from 1st October 2016 to 30th September 2017 (prospective group). A retrospective group of MSAF neonates from one year prior to the implementation of the 2015 ERC resuscitation guidelines,

born between August 1st 2015 and July 31st 2016, was taken as comparator. There was a wash-out period of two months (August - September 2016) for implementation of the policy change.

Definition of MAS

MAS was defined as respiratory distress in a neonate born through MSAF with hypoxemia, a characteristic chest radiograph picture of patchy infiltrates with or without focal hyperinflation and no other plausible explanation for the respiratory distress.

Resuscitation policies

As per the current newborn resuscitation guidelines at the time, all non-vigorous (limp / HR < 100min⁻¹ / not breathing) MSAF neonates were taken to the resuscitaire after early cord clamping. The initial steps of drying, oral suctioning (if indicated) and stimulation were performed. In the retrospective group, routine endotracheal suctioning was performed prior to the initiation of PPV and resuscitation proceeded according to ERC 2010. [5] In the prospective group, compromised MSAF neonates with no / poor respiratory efforts were given PPV via a T-piece resuscitator using a starting peak inspiratory pressure of 25 cm H₂O and positive end expiratory pressure of 5 cm H₂O without prior suctioning of the airways. [1]

STATISTICAL ANALYSIS

The outcomes between the two groups were compared using two tailed students *t* test for continuous variables and Fisher's exact test / Pearson's χ^2 test for categorical variables. The data is presented as Odds Ratios with 95% confidence intervals, where appropriate. A p-value of < 0.05 was considered as statistically significant.

ETHICS

The study was classed as a service evaluation, which, according to the local ethics committees' regulations does not require ethics' approval.

RESULTS

The characteristics and initial management of infants from both the groups are summarised in Table 1. We found no statistically significant difference in the incidence of MAS between the two study periods. However, there was a significant reduction in the proportion of the non-vigorous MSAF neonates who were admitted to NICU in the prospective group. There were no statistically significant differences in the other secondary outcomes between the two groups (Table 2).

DISCUSSION

Our comparative study of two different approaches to MSAF neonates at birth found no statistically significant difference in the incidence of MAS between the two epochs. This is consistent with the findings of a recent comprehensive meta-analysis comparing routine endotracheal suctioning versus no suctioning in non-vigorous MSAF neonates. [6] A study of post policy change by Chirovulu et al. reported similar findings on the incidence of MAS, whilst Edwards et al. and Kalra et al., quite like our study, showed a significant decrease in the incidence of MAS in their recent cohorts. [2-4]

NICU admissions were significantly reduced in the prospective arm of our study. Similarly, decreased admission rates of MAS were documented by Kalra et al. and Edwards et al. [2,3] However, Chirovulu et al. described that NICU admissions for respiratory morbidities had increased after the adoption of the new guidelines, which is a cause of concern and emphasises the need for a large multicenter trial. [4]

The other indicators of severe respiratory disease, such as requirement of IMV, inhaled nitric oxide use and surfactant therapy were comparable in the two epochs. These findings are in agreement with the results of the meta-analysis by Trevisanuto et al. [6] However, they are contrary to those reported by Chirovulu et al. [4] In their study, the proportion of neonates requiring oxygen support, IMV and surfactant therapy was significantly higher in the prospective group not undergoing endotracheal suctioning. A possible explanation for this discrepancy could be that the prospective group in Chirovulu et al.'s study had a higher proportion of sicker neonates who had significant fetal distress compared to the retrospective group, which might have resulted in more NICU admissions in the prospective group.

The incidence of routine endotracheal intubation for non-vigorous MSAF neonates dropped significantly after the institution of the new guidelines in our prospective group (7%). Similar trends were reported by Chirovulu et al. [4] However, Edwards et al. in their study on the impact analysis post the new guideline implementation had shown that a significant proportion (28.9%) of the non-vigorous MSAF neonates underwent endotracheal suctioning in the delivery room even after the adoption of the new guidelines.[3]

Our study has its limitations. Firstly, this was a prospective observational study which used a retrospective group as its comparator. By this, we cannot control for selection bias or missing data. Secondly, many of the other non-respiratory co-morbidities of MAS, such as hypoxic ischemic encephalopathy, sepsis and duration of hospital stay, have not yet been analysed. Finally, there is a possibility of baseline demographic differences between the two groups as determinants of outcomes in non-vigorous MSAF neonates, such as severity of fetal distress and consistency of the meconium, were not assessed.

CONCLUSIONS

In our single center study, we found that the policy change in accordance to the 2015 ERC newborn resuscitation guidelines towards not routinely suctioning non-vigorous MSAF neonates prior to providing PPV was not associated with an increase in the local incidence of MAS, requirement of IMV, inhaled nitric oxide, surfactant, ECMO or mortality. We observed fewer NICU admissions of non-vigorous MSAF neonates since policy change.

REFERENCES

1. Wyllie J, Bruinenberg J, Roehr CC, Rüdiger M, Trevisanuto D, Urlesberger B. European Resuscitation Council Guidelines for Resuscitation 2015: Section 7. Resuscitation and support of transition of babies at birth. *Resuscitation*. 2015;95:249-63.

2. Kalra VK, Lee HC, Sie L, Ratnasiri AW, Underwood MA, Lakshminrusimha S. Change in neonatal resuscitation guidelines and trends in incidence of meconium aspiration syndrome in California. *J Perinatol*. 2020;40(1):46-55.
3. Edwards EM, Lakshminrusimha S, Ehret DEY, Horbar JD. NICU admissions for meconium aspiration syndrome before and after a national resuscitation program suctioning guideline change. *Children* 2019;6(5):68.
4. Chiruvolu A, Miklis KK, Chen E, Petrey B, Desai S. Delivery room management of meconium-stained newborns and respiratory support. *Pediatrics* 2018;142(6):e20181485.
5. Richmond S, Wyllie J. European Resuscitation Council Guidelines for Resuscitation 2010 Section 7. Resuscitation of babies at birth. *Resuscitation* 2010;81:1389–1399.
6. Trevisanuto D, Strand ML, Kawakami MD, et al. Tracheal suctioning of meconium at birth for non-vigorous infants: a systematic review and meta-analysis. *Resuscitation* 2020;149:117-126.

Table 1 - Comparison of delivery room characteristics of both the groups

	Retrospective Group	Prospective Group	p - value*
Total Number of Deliveries	8341	8075	
Total Number of MSAF neonates n (% of total deliveries)	446 (5.3)	692 (8.6)	<0.0001
Gestational age in weeks (+/- SD)	39.6 (+/-1.3)	40.2(+/- 1.2)	<0.0001
Mean Birth weight (+/-SD)	3571.9 (+/-452.3)	3657.1(+/-468.6)	0.002
Total Non-vigorous MSAF neonates n (% of total babies born out of MSAF)	72 (16.1)	157 (22.7)	0.007
Endotracheal suctioning done n (% of non-vigorous MSAF neonates)	68 (94.4)	11 (7.0)	<0.0001
Total NICU admissions n (% of total deliveries)	485 (5.8)	481(5.9)	0.82
NICU admissions of vigorous MSAF neonates n (% of vigorous MSAF neonates)	10 (2.7)	13(2.4)	0.81
NICU admissions of non-vigorous MSAF neonates n (% of non-vigorous MSAF neonates)	40 (55.6)	30 (19.1)	< 0.0001

* p - Values in bold are statistical significant

Table 2 - Comparison of respiratory morbidities of neonates born through MSAF during the two epochs

	Retrospective group	Prospective Group	p - value	Odds ratio
Incidence of MAS n (% of total babies born out of MSAF)	25 (5.6)	30 (4.3)	0.33	1.30 (0.70, 2.20)
Requirement of mechanical ventilation n (% of MAS)	6 (24)	5 (16.7)	0.50	1.58 (0.42, 5.96)
Requirement of high frequency oscillation ventilation n (% of MAS)	2 (8)	0 (0)	0.11	-
Requirement of surfactant n (% of MAS)	1 (4)	2 (6.7)	0.67	0.58 (0.05, 6.84)
Requirement of inhaled nitric oxide n (% of MAS)	5 (20)	5 (16.7)	0.75	1.25 (0.32, 4.93)
Severe respiratory morbidity n (% of MAS)^	14 (56)	12 (40)	0.24	1.91 (0.65, 5.60)

* MAS - Meconium Aspiration Syndrome

+MSAF - Meconium stained amniotic fluid

^ Requirement of mechanical ventilation (conventional and high frequency oscillation ventilation), inhaled nitric oxide or surfactant administration