MEDWIN PUBLISHERS
Committed to Create Value for Researchers

Pediatrics & Neonatal Biology Open Access
ISSN: 2640-2726

The Role of Prophylactic Antibiotics in Newborn Born through Meconium Stained Amniotic Fluid (MSAF)

Chaurasiya OS*, Sethi AS and Verma SK

Department of Pediatrics, MLB Medical College Jhansi, India

***Corresponding author:** Om Shankar Chaurasiya, Department of Pediatrics, MLB Medical College Jhansi, UP, India, Email: chaurasiyaom@gmail.com

Research Article

Volume 7 Issue 2

Received Date: November 16, 2022

Published Date: November 28, 2022

DOI: 10.23880/pnboa-16000170

Abstract

Objective: The objective of the study was to evaluate the effect of administering prophylactic antibiotics on the development of neonatal sepsis in newborn born through meconium stained amniotic fluid (MSAF).

Method: Total 200 babies born through meconium stained amniotic fluid were included in this study. 100 babies randomized to group a (antibiotic group) received first line antibiotics for 3 days and 100 babies to group B (no antibiotic group) in which no antibiotics were given. Both group A and B evaluated clinically and by lab parameters (sepsis screen and blood cultures) for development of sepsis. Both groups received similar supportive management. The primary outcome measure was the development of infection. Details of clinical progress during were recorded. All neonates were monitored for development of complications

Result: The patient profiles were similar in both groups. The overall incidence of suspect sepsis was 9 % in the study population with no significant difference between group A and group B (7 %vs. 11 %, p=0.322). Incidence of culture-proven sepsis was also not significantly different between the two groups (5% vs. 7 %, p=0.3546). The incidence of mortality, meconium aspiration syndrome, and other complications was comparable amongst the two groups. Final outcome and duration of stay was also not significantly different in both group A and group B.

Conclusion: This study shows that there was no statistically significant difference in the incidence of development of infection, complication and final outcome in neonates born through meconium stained amniotic fluid when treated with or without antibiotics.

Keywords: Meconium-stained Amniotic Fluid; Prophylactic Antibiotics; Neonatal Sepsis

Abbreviations: HIE: Hypoxic Ischemic Encephalopathy; MSAF: Meconium-stained Amniotic Fluid; MAS: Meconium Aspiration Syndrome; PPHN: Persistent Pulmonary Hypertension of Newborn; UTI: Urinary Tract Infection.

Introduction

Meconium stained amniotic fluid (MSAF) as a result of passage of fetal colonic content in to the amniotic cavity, is noted in approximately 13 % of all deliveries [1,2]. Meconium aspiration syndrome (MAS), a life threatening neonatal respiratory disorder that result from aspiration of meconium in to lungs during intrauterine gasping or time of first breath develops in 5% of infants delivered through MSAF. More than 4%of MAS infants die, accounting for 2% of all perinatal deaths [1,3]. Meconium aspiration syndrome (MAS) is defined as respiratory distress in an infant born through meconium stained amniotic fluid (MSAF) with

characteristic radiological changes and whose symptoms cannot be otherwise explained. Although no studies have shown that infection plays a role in pathogenesis of MAS [4] and their efficacy in MAS is unproved [5], antibiotics have been a regular part of therapy in MAS. Several studies have shown that empirical use of antibiotics in the routine management of MAS is of no benefit [6-8]. Clinical instances, confirm by autopsy, in which infection is superimposed on even the most severe form are rare. The incidence of bacterial infection in neonates born through MSAF as well as those developing MAS has not been systematically evaluated till date [9]. Wide spread use of antibiotics in neonates is a matter of some concern [9]. Excessive use of antibiotics in neonatal units can lead to emergence of resistant bacteria strains. Researchers have not systematically evaluated the roll of antibiotics in infants born through MSAF. Thus the purpose of this study is to compare the clinical course, complications and infection related outcomes in cases of MSAF and MAS and role of antibiotic therapy in neonates born with MSAF.

Methods

This study was an open label randomized controlled trial study which included 200 neonates admitted in SNCU of Department of Pediatrics, MLB Medical College, Jhansi (U.P.) during Dec. 2020 to Dec. 2021.

Inclusion Criteria

All newborn babies born through meconium stained amniotic fluid admitted within 48 hrs of birth.

Exclusion Criteria

1. Presence of major congenital malformation,
2. Newborn received antibiotics prior to admission to our center
3. Parents refusing to give consent were excluded.
4. Newborn who went LAMA during study period.

Enrolled neonates were randomized into Group-A and Group-B based on randomization done using random no. table method.

- **Group-A:** 100 neonates received prophylactic intravenous antibiotics.
- **Group-B:** 100 neonates not received any antibiotic.

A detailed antenatal history was elicited to find out the etiology of passage of meconium into amniotic fluid. Detailed natal history and presenting complaints was taken. In all meconium stained infants APGAR score at 1 min was assessed and birth weight, gestational age (by Ballard scoring) and respiratory distress (by Downes' score) was noted. Detailed examination of the newborn was done with regard to gestational age estimation, anthropometric measurement, general examination and systemic examination. Estimation of gestational age was done by recording date of LMP and confirm by New Ballard scoring which includes neuromuscular maturity and physical maturity. Anthropometric measurement was included weight, length, head and chest circumference which was recorded in each case.

All babies irrespective of their group allocation were admitted to the nursery and worked up for sepsis using a sepsis screen and blood culture. Sepsis screen consisting of total leukocyte count, absolute neutrophil count and immature to total neutrophil ratio (by Coulter and peripheral smear examination), micro-ESR and C- reactive protein was performed at admission or thereafter if required. If two (or more) parameters are abnormal, it should be considered as a positive sepsis screen. Blood culture was performed at admission and thereafter if required. Symptomatic babies (presence of respiratory distress, lethargy, abdominal distension, temperature or hemodynamic instability, hypoglycemia, apnea, or any other systemic abnormalities), either from birth or any time during the course of stay, in both groups, was subjected to further investigations such as chest X-ray, arterial blood gas, and lumbar puncture as deemed necessary by the treating physician. Appropriate treatment was started or modified as per the decision of consultant-in- charge taken as one serving the best interest of the baby. All such cases requiring prolongation of antibiotics beyond 3 days in Antibiotic group, or starting of antibiotics in the No Antibiotic group (symptomatic or sepsis screen positive), was noted. All babies received supportive care in the form of maintenance of temperature, fluid balance, and blood glucose. Further respiratory, cardiac, or other system support as needed was provided as per standard unit protocol. All these neonates were monitored daily by the study coordinators for vital signs, i.e., heart rate, respiratory rate, blood pressure, oxygen saturation, and signs of respiratory distress or failure till the time of discharge (minimum 72 hours) or death. All neonates discharged home were followed up in neonatal follow-up clinic, post-discharge for signs and symptoms of sepsis.

Data pertaining to various maternal demographic variables like parity, risk factors for sepsis (prolonged rupture of membranes>24 h, intrapartum fever ≥38.0°C, unclean or frequent per-vaginal examination (≥3), clinical chorioamnionitis, maternal UTI), fetal distress (fetal heart rate abnormalities on auscultation or cardiotocography), meconium consistency (thick pea soup or thin watery), mode of delivery, along with neonatal variables like sex, birthweight, gestational age, APGAR score, incidence of non-vigorous

neonates and requirement of endotracheal intubation for positive pressure ventilation was recorded in a pretested proforma. Additional data collected during neonatal hospital stay will include duration and severity of respiratory distress (using Downe's score), requirement and total duration of oxygen therapy, need for and duration of CPAP or mechanical ventilation, and incidence of complications like air leaks or persistent pulmonary hypertension of newborn (PPHN). In addition, any development or progression of hypoxic ischemic encephalopathy (HIE) or involvement of other organ systems and the duration of stay was recorded.

Statistical Analysis

SPSS (Statistical Package for Social Sciences) version 27.0 and Graph Pad (online) for windows was used for data analysis. Mean and standard deviation were descriptive values for quantitative data with median and range for non-normally distributed data. Student's t-test and non-parametric t-test (Mann Whitney test) were used comparing means of two independent groups. Paired t-test and non-parametric paired t-test (Wilcoxon signed rank test) were used for comparing means of two dependent groups. Chi-square – Fisher exact test were the tests for proportion independence. P-value < was considered significant.

Outcome Measures

The primary outcome was defined as the incidence of early (within 72 h of birth) or late onset sepsis (after 72 h of birth), suspected sepsis (clinical symptoms or sepsis screen positive;>2 positive parameters) and confirmed sepsis (positive blood culture).

Secondary Outcome

Secondary outcome measures include the incidence of development of complications (like MAS, HIE, pneumothorax), duration of hospital stay and mortality.

Results

This study is prospective open labeled studies which include 200 neonates admitted in SNCU of department of Pediatrics, MLB Medical College, Jhansi (U.P.) Enrolled neonates were randomized into Group-A and Group-B based on randomization done using random no. table method (Table 1).

Group-A: 100 neonates received prophylactic intravenous antibiotics.
Group-B: 100 neonates not received any antibiotic.

Variable	Group A	Group B	Total (%)	P Value
Sex distribution				0.3
Male (n= %)	65	58	123(61.5%)	
Female	35	42	77(38.5%)	
Total	100	100	200 (100%)	
Type of Admission				0.08
Inborn	47	59	106 (53%)	
Outborn	53	41	94 (47%)	
Total	100	100	200 (100%)	
Gestational age (in wks)				**0.35**
28-32	2	3	5(2.5%)	
33-36	10	9	19 (9.5%)	
37-39	70	69	139 (69.5%)	
40	18	19	37(18.5%)	
Total	100	100	200 (100%)	
Birth weight (in kg)				0.98
<2.5	16	22	38 (19%)	
2.5-3.5	82	76	158 (79%)	
>3.5	2	2	4 (2%)	
Total	100	100	200 (100%)	

Gravida				0.62
Primigravida	54	58	112 (56%)	
Multigravida	46	42	88 (44%)	
Total	100	100	200 (100%)	
Mode of delivery				0.2
NVD	57	48	105 (52.5%)	
LSCS	43	52	95 (47.5%)	
Total	100	100	200 (100%)	
Consistency of Meconium				0.62
Thick	62	58	41 (20.5%)	
Thin	38	42	159 (79.5%)	
Total	100	100	200 (100%)	
Time of onset of respiratory distress				0.66
Absent	2	2	4 (2%)	
Onset <2 hrs	80	75	155 (77.5%)	
Onset 2-6 hr	16	18	34 (17%)	
>6 hr	2	5	7 (3.5%)	
Total	100	100	200 (100%)	
Risk factor of Sepsis			Total (%)	
PROM	9	8	17 (8.5%)	
Intrapartum fever	5	4	9 (4.5%)	
Maternal UTI	5	6	11(5.5%)	
Unclean or frequent (3) PV examination				
	6	5	11 (5.5%)	
Clinical chorioamnitis	4	4	8 (4%)	
No antenatal risk factor	71	73	144 (72%)	

Table 1: Table shows base line variables of the study.

Baseline characteristic For both group A and group B are represented in Table 1, shows no difference between the groups in terms of gender, gestational age, birth weight, mode of delivery and consistency of meconium.

Primary Outcome

All the babies in both group A and B were evaluated for the development of suspected or confirmed sepsis. The incidence of suspected sepsis (positive sepsis screen) was found to be 7% (n=7) in group A and 11% (n=11) in group B. Overall incidence of suspected sepsis (positive sepsis screen) in group A and Group B was 9%. The difference however was not found to be statistically significant. (p=0.03229 and chi-square value is 0.9768). Total no. of neonates who developed confirm sepsis in both groups were very few and comparable, being 5% (n=5) and 7% (n=7) respectively in group A and Group B. There was no statistically significant difference between two groups. (P value 0.3546 and chi square is .551515). Antibiotics were continued beyond 3 days or changed in the Group A or added in Group-B based on clinical condition of the baby and sensitivity pattern as per decision of treating team (Table 2).

Outcome	Group A	Group B	P value
Suspect sepsis	7	11	0.33
Confirmed sepsis	5	7	0.35

Table 2: Primary outcome- Incidence of sepsis.

Secondary Outcome

Respiratory distress was present at birth in 31 and 33 babies in Group-A and Group-B respectively which settled

within 48 h in both group A and B. Requirement of CPAP and mechanical ventilation was also comparable and no significant difference was found in both group A and B. Development of complications like pneumothorax, HIE, MAS and duration of hospital stay was also found statistically not significant. Total 8 babies were expired in group A and B, 5 babies in group A and 3 babies in Group-B. Which was statistically insignificant? Causes include respiratory failure, PPHN, HIE and septic shock (Table 3 & 4).

Duration of oxygen requirements	**Group – A**	**Group – B**	**Total (%)**	**P value 0.66**
<48 hrs	22	25	67 (33.5%)	
>48 hrs	9	8	17 (8.5%)	
Not required	69	67	136(68%)	
Total	**100**	**100**	200 (100%)	
Requirement of CPAP	Group – A	Group – B	Total (%)	P value 0.44
Yes	28	33	61(30.5%)	
No	72	67	139 (69.5%)	
Total	100	100	200 (100%)	
Requirement of mechanical ventilation	Group – A	Group – B	Total (%)	P value 0.55
Yes	7	5	12 (6%)	
No	93	95	188 (94%)	
Total	100	100	200 (100%)	
Incidence of MAS	Group – A	Group – B	Total (%)	P value 0.7
Yes	18	16	34 (17%)	
No	82	84	166 (83%)	
Total	100	100	200 (100%)	
Severity of MAS	Group – A	Group – B	Total(%)	P value 0.59
Mild	9	9		
Moderate	3	4		
Severe	6	3		
Complication	**Group – A**	**Group – B**	**Total (%)**	
Pneumothorax	1	0	1 (0.5%)	
PPHN	1	2	3 (1.5%)	
HIE				
HIE-I/II	12	12	24(12%)	
HIE-IIII	1	2	3 (1.5%)	
Oliguria	1	0	1 (0.5%)	
Azotemia	1	0	1 (0.5%)	
Diarrhea	0	4	4 (2%)	
ICH	0	1	1 (0.5%)	
Total babies	17	21		

Table 3: Secondary outcome measures-respiratory outcomes.

Final outcome	**Group – A**	**Group – B**	**Total %**	**P value 0.47**
Discharge	95	97	192 (96%)	
Expire	5	3	08 (4%)	
Total	100	100	200 (100%)	

Table 4: Final outcome of MSAF babies.

Discussion

This study shows that there is no role of routine prophylactic antibiotics administration in management and outcome of neonates born through meconium stained amniotic fluid. Patients clinical profile, the incidence of development of infection, nature of complication during hospitalization and outcome were similar in both group A and Group B. In both the groups we upgraded or added antibiotics in patients who developed complication as it would have been unethical to do otherwise. The routine addition of Broad spectrum antibiotic did not prevent development of infection or serious complication and the overall mortality and morbidity of such neonates is also not affected. In a retrospective analysis by Singh, et al. [10] positive blood culture was obtained only in 2.5% of neonates born with meconium aspiration syndrome. Similarly Krishnan, et al. [11] in their retrospective review, found no significant difference in the incidence of septicemia, between infants intubated for intratracheal suctioning of meconium compared to non-intubated infants. These studies reveal that incidence of sepsis is not significantly high in meconium stained neonates. Studies evaluating the role of antibiotic found no difference in infections with meconium aspiration morbidity in babies with meconium aspiration syndrome, treated with or without antibiotics, in the studies by Shankar, et al. [12] and Lin, et al. [13]. Similarly the incidence of sepsis in MAS reported by Basu, et al. [14] was 4% in the antibiotic and 2.7% in no antibiotic group.

In this study incidence of positive sepsis screen was 7% and 11% respectively in Group A and Group B and overall incidence was 9% in both species and incidence of culture proven sepsis was 5% and 7% in both group A and Group B and overall incidence in both group is 6%. Further no difference was noted in severity of respiratory distress and mortality between the two groups. The result of our study was similar to previous studies. Lin, et al. [13] who did a prospective, randomized, controlled clinical trial and compared the infection-related outcome of non-ventilated cases of MAS without perinatal risk factors for infection. There was no significant difference in the duration of tachypnea, oxygen supplementation and nasal continuous positive airway pressure (CPAP) between the two groups. This study though comparable in sample size to our study included only non-ventilated cases of meconium aspiration syndrome with no perinatal risk factor for sepsis. In this study we included both ventilated and non-ventilated cases and found no statistically significant difference in requirement of oxygen therapy (p-value 0.886), requirement of CPAP (p-value 0.443) and mechanical ventilation (p-value 0.5515).

Shankar, et al. [12] in a randomized clinical trial found that mean duration and severity of respiratory distress at 24 and 48 hours were similar in the two groups of MAS treated with or without antibiotics. in this study sample size was very small excluded neonates with maternal risk factor for neonatal sepsis and did not define sepsis based on blood culture positivity.

Basu, et al. [14], in their study of infants with meconium aspiration syndrome excluded all infants with any risk factor of sepsis and those who develop early onset sepsis within 24 hr of life. Moreover they randomized the subject of 24 hrs of life thus compromising generalizability of study. No followup was done in both of these studies.

Our study has comprehensively included all meconium stained neonates irrespective of risk status for sepsis and yet the results shows that there is no role of antibiotic in their management. Routine use of antibiotics in an NICU gives rise to the emergence of drug- resistant strains of bacteria which is a matter of concern, particularly in a developing country with a shortage of funds and where neonatal mortality is high.

Hence, we recommend the avoidance of empirical use of antibiotics in such neonates born through meconium stained amniotic fluid without documented evidence of infections.

Conclusion

This study shows that there was no statistically significant difference in the incidence of development of infection, complication and final outcome in neonates born through meconium stained amniotic fluid when treated with or without antibiotics.

References

1. Cleary GM, Wiswell TE (1998) Meconium-stained amniotic fluid and the meconium aspiration syndrome. An update. Pediatr Clin North Am 45(3): 511-529.

2. Wiswell TE (2001) Advances in the treatment of the meconium aspiration syndrome. Acta Paediatr Suppl 90(436): 28-30.

3. Wiswell TE, Tuggle JM, Turner BS (1990) Meconium aspiration syndrome: have we made a difference? Pediatrics 85(5): 715-721.

4. Moses D, Holm BA, Spitale P, Liu M, Enhorning G (1991) Inhibition of pulmonary surfactant function by meconium. Am J Obstet Gynecol 164(2): 477-481.

5. Whitsett JA, Pryhuber GS, Ward R (1999) Rice, Acute Respiratory Disorders: Meconium aspiration syndrome. In: Avery GB, et al. (Eds.), Neonatology: Pathophysiology

and Management of the Newborn. 5th(Edn.), Lippincott Willams & Wilkins, Philadelphia, pp: 496-497.

6. Basu S, Kumar A, Bhatia BD (2007) Role of antibiotics in meconium aspiration syndrome. Ann Trop Pediatr 27(2): 107-113.

7. Lin HC, Su BH, Tsai CH, Lin TW, Yeh TF (2005) Role of antibiotics in management of non-ventilated cases of meconium aspiration syndrome without risk factors for infection. Biol Neonate 87(1): 51-58.

8. Shankar V, Paul VK, Deorari AK, Singh M (1995) Do neonates with meconium aspiration syndrome require antibiotics? Indian J Pediatr 62(3): 327-331.

9. Vain NE, Szyld EG, Prudent LM, Wiswell TE, Aguilar AM, et al. (2004) Oropharyngeal and nasopharyngeal suctioning of meconium-stained neonates before delivery of their shoulders: multicentre, randomised controlled trial. Lancet 364(9434): 597-602.

10. Ghidini A, Spong CY (2001) Severe meconium aspiration syndrome is not caused by aspiration of meconium. Am J Obstet Gynecol 185(4): 931-938.

11. Bhutani VK, Chima R, Sivieri EM (2003) Innovative neonatal ventilation and meconium aspiration syndrome. Indian J Pediatr 70(5): 421-427.

12. Shankar V, Paul VK, Deorari AK, Singh M (1995) Do neonates with meconium aspiration syndrome require antibiotics? Indian J Pediatr 62(3): 327-331.

13. Lin HC, Su BH, Tsai CH, Lin TW, Yeh TF (2005) Role of antibiotics in management of non-ventilated cases of meconium aspiration syndrome without risk factors for infection. Biol Neonate 87(1): 51-55.

14. Basu S, Kumar A, Bhatia BD (2007) Role of antibiotics in meconium aspiration syndrome. Ann Trop Paediatr 27(2): 107-113.