

Rational use of antibiotics in preterm neonates

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Abstract

Objectives: 1) To manage low infection risk preterms without antibiotics and determine their outcome. 2) To find out relation between maternal risk factors, gestational age and birth weight with regard to need for antibiotics. **Materials and Methods:** **Setting:** NICU, BVDUMC and H, Sangli **Study Design:** Prospective Analytical Study. **Study Period:** 8 months **Methods:** Inborn Preterm babies with low risk factors for infection were closely monitored without antibiotics. Babies were started on antibiotics only when sepsis was considered. Detailed maternal history with regard to obstetric risk factors was recorded. Gestational age and birth weight were correlated with need for antibiotics. Babies were followed up till discharge or death. **Results:** Of 296 babies admitted in NICU during study period, 74 eligible preterms were enrolled. Sixty two (83%) out of 74 did not require antibiotics. There was statistically significant difference in mean birthweight (1.765 ± 0.37 kgs) between neonates who required antibiotics and those who did not. (p -value < 0.001). There was no significant association of gestational age with need for antibiotics. Maternal obstetric risk factors had significant association with need for antibiotics in the babies (p -value = 0.025). Three babies (4%) who received antibiotics developed NEC as against none in the non-antibiotics group. Only 2 (16.3%) out of the 12 babies in antibiotic group had positive blood cultures. Mortality was 4.1% **Conclusion:** Preterms with low risk factors can be managed without antibiotics. Need for antibiotics is strongly associated with maternal obstetric risk factors and low birth weight.

Key Words: antibiotics, preterm neonates.

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Received Date: 17/10/2017 Revised Date: 14/11/2017 Accepted Date: 09/12/2017

DOI: <https://doi.org/10.26611/1012432>

Access this article online

Quick Response Code:



Website:

www.medpulse.in

Accessed Date:
12 December 2017

INTRODUCTION

Neonates in particular are in high risk of developing blood stream infections because of their immature immune system^{2,3}. This is more in case of low birth weight and preterms who are at a higher risk than full term newborns¹. Hospital acquired infection is one of the reasons for neonatal mortality and morbidity. The first microbial colonization in new born occurs during delivery during passage from birth canal. Therefore early onset sepsis is based on most common organisms detected at

birth⁵. Risk factors for infections are maternal fever during delivery, PROM, Maternal infections^{3,6}. It is common practice amongst pediatricians to administer antibiotics to at risk neonates without evidence of clinical or microbiologically proven sepsis. The American Academy of Pediatrics in 1997, suggested prophylactic use of antibiotics to all at risk infants, whereas, Lopez in 2001, recommended against it⁶. Kuppala, Venkata S. *et al.* in 2011 stated that prolonged administration of empirical antibiotics to premature infants with sterile cultures in the first week of life is associated with subsequent severe outcomes. Judicious restriction of antibiotic use should be investigated as a strategy to reduce severe outcomes for premature infants⁹. There is not enough evidence to prove that, prophylactic antibiotics should be administered to neonates⁷. For early onset sepsis, administration of intrapartum antibiotics doesn't provide a solution either because it too, results in resistant strains and change in etiology.

MATERIAL AND METHODS

Setting: Neonatal Intensive Care Unit, Bharati Vidyapeeth Deemed University Medical College and Hospital, Sangli

Study Design: A Prospective Analysis

Study Period: 8 months (August 2015 to March 2016)

Inclusion Criteria: All Inborn Preterm neonates without risk factors for infection admitted to Neonatal Intensive Care Unit (<37 weeks gestational age)

Exclusion Criteria

1. Any symptomatic preterm
2. Babies requiring respiratory support (CPAP, Mechanical Ventilation)
3. Babies requiring umbilical venous catheterization
4. Congenital anomalies
5. Babies already on antibiotics
6. Outborn babies
7. Birth asphyxiated babies
8. Maternal risk factors :
9. PROM / Chorioamnionitis
10. APH
11. Maternal fever

Work Plan

1. Inborn Preterm babies without any risk factors were admitted in NICU
2. Detailed maternal history was noted
3. No antibiotics were started in these babies
4. TPN was started in few babies as per requirement
5. Feeding was started soon and day of full feeding and fortification was noted
6. Babies were closely monitored for evidence of sepsis
7. Antibiotics were started only when sepsis was suspected
8. Gestational age and birth weight were correlated with need for antibiotics

RESULTS

Out of 296 babies admitted in NICU during 8 months duration (August 2015 to March 2016) 74 eligible preterms were enrolled in the study.

Table 1: Distribution according to birth weight and gestational age

| Parameters | Study group |
|------------------------------|---------------|
| Birth weight (kgs) Mean | 1.76563± 0.37 |
| Gestational age (weeks) Mean | 33.861±1.7 |

Feeding was started on day 1. Full feeds were tolerated by Day 6 (Mean-6.007, SD-2.39) and Mean day of fortification was day 10. Mean duration of NICU stay was 11 days.

Table 2: Distribution on the basis of maternal risk factors

| Maternal risks | Number | Percent |
|-----------------|-----------|------------|
| NO risk factors | 40 | 54.0 |
| CKD | 1 | 1.4 |
| Oligohydramnios | 1 | 1.4 |
| PIH | 27 | 36.4 |
| Polyhydramnios | 3 | 4.0 |
| RH NEGATIVE | 1 | 1.4 |
| RVHD | 1 | 1.4 |
| Total | 74 | 100 |

Twenty seven mothers (36.4%) had Pregnancy Induced Hypertension.

Table 3: Distribution on the basis of Birth weight and need for antibiotics

| Need for antibiotics after admission | No | Mean | SD | SEM | t value | P value |
|--------------------------------------|----|---------|----------|----------|---------|---------|
| Yes | 12 | 1.43333 | 0.264002 | 0.076211 | - | <0.001 |
| No | 62 | 1.85078 | 0.351877 | 0.046204 | 4.684 | |

There is statistically significant difference in mean birth weights of neonates needing antibiotics and not needed antibiotics. Neonates, those who needed antibiotics, had less mean birth weight

Table 4: Distribution on the basis of Gestational age and need for antibiotics

| Need for antibiotics after admission | No | Mean | SD | SEM | t value | P value |
|--------------------------------------|----|--------|--------|--------|---------|---------|
| Yes | 12 | 33.083 | 2.1088 | 0.6088 | -1.551 | 0.143 |
| No | 62 | 34.086 | 1.6574 | 0.2176 | | |

There is no statistically significant difference in mean gestational age of neonates needing antibiotics and not needed antibiotics. Those neonates, who needed antibiotics, had smaller gestational age, but not significantly.

Table 5: Distribution on the basis of Need for antibiotics after admission and Maternal risk factors

| Need for antibiotics after admission | Maternal risk factors | | Total |
|--------------------------------------|-----------------------|-----------------|------------------|
| | Absent | Present | |
| No | 37(50%) | 23 (31%) | 60 (81%) |
| Yes | 3(4%) | 11 (14.8%) | 14 (19%) |
| Total | 40 (54%) | 34 (46%) | 74 (100%) |

The chi-square statistic is 5.0052. The p-value is 0.025271. This result is significant at $p < 0.05$ Hence there is significant association between Maternal risk factors and need for antibiotics in Preterm neonates

Table 6: Distribution on the basis of NEC:

| NEC | Number | Percent |
|--------------|-----------|------------|
| No | 71 | 96.0 |
| Yes | 3 | 4.0 |
| Total | 74 | 100 |

Table 7: Distribution on the basis of Need for antibiotics

| Need for antibiotics after admission | Number | Percent |
|--------------------------------------|-----------|------------|
| No | 62 | 83.7 |
| Yes | 12 | 16.3 |
| Total | 74 | 100 |

Table 8: Distribution on the basis of Need for antibiotics and culture proven sepsis

| | Babies who needed Antibiotics | Percentage |
|-----------------------|-------------------------------|------------|
| Culture proven sepsis | 2 | 16.6 % |
| Clinical sepsis | 10 | 83.4 % |

Table 9: Distribution on the basis of Outcome

| Outcome | Number | Percent |
|--------------|-----------|------------|
| DAMA | 2 | 3.7 |
| Death | 3 | 4.1 |
| Discharge | 69 | 93.2 |
| Total | 74 | 100 |

Large number of preterm neonates (83.7%) were managed without antibiotics. Preterms with birth weight ≥ 1.8 kgs did not require antibiotics. Neonates with birth weight ≤ 1.4 kg required antibiotics. Hence, need for starting antibiotics was more in preterms with lower birth weight. There was no significant difference in gestational age of babies needing antibiotics and not needed antibiotics. Preterms with smaller gestational age required antibiotics. Forty Mothers (54%) had no obstetric risk factors. Twenty seven mothers (36.4%) had Pregnancy Induced Hypertension which was the commonest obstetric risk factor. There was a significant relation between maternal risk factors and need for starting antibiotics (p -value= 0.025). Three babies (25%) who were started on antibiotics developed NEC during hospital stay suggesting that use of antibiotics can further predispose to occurrence of NEC. Out of the 12 babies (16.3%) who were started on antibiotics with suspicion of sepsis, only two had positive blood cultures. Sixty nine preterms were discharged successfully of which sixty two babies (89%) did not require antibiotics. Out of the 3 babies who died, 2 of them had birth weight < 1.4 kg and gestational age < 33 weeks and all the 3 babies were on antibiotics and but had no culture proven sepsis.

DISCUSSION

Very few similar studies were conducted in past. In our study, birth weight had significant association with need for starting antibiotics which was consistent with the findings of Labenne *et al.* Wolf in 1976 conducted a

study in neonates whose mother had prolonged rupture of membrane and studied the association with antibiotics. PROM was excluded in our study. We also found that maternal risk factors were associated with need for starting antibiotics and results were consistent with study done by Edmond *et al.* Limitations: There was no control group in our study and our sample size was small.

CONCLUSION

Preterms with low risk factors can be managed without antibiotics. Need for antibiotics is strongly associated lower birth weight, smaller gestational age and maternal obstetric risk factors.

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Source of Support: None Declared
Conflict of Interest: None Declared