3 Days Vs 7 Days Course of Intravenous Antibiotics for Probable Neonatal Sepsis

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I.   Introduction:

Duration of appropriate antibiotic therapy for neonatal sepsis does not have evidence-based guidelines. The current recommendations have never been scientifically evaluated. Untested approaches could result in the unnecessary use of antibiotics leading to prolonged hospitalization, mother infant separation, emergence of drug resistant strains and increase cost of care. In uncomplicated probable neonatal sepsis, prolonged antibiotic therapy effect bacterial colonization and immune activation after birth which could have implications later risk of allergy and asthma.

Objectives

To compare 3 days v/s 7 days course of antibiotics for probable neonatal sepsis.

II.   Methodology

The study was conducted in NICU, Department of Paediatrics, Old Government General hospital, Siddhartha medical college, Vijayawada. From June 2018-march 2019

Type Of Study: randomized control trail (computerized randomization)
Source Of Data:neonates who were admitted in NICU for probable sepsis (clinical signs of sepsis, positive sepsis screening) who were on antibiotic therapy with sterile blood culture at third day.

Inclusion criteria:

Neonates of > 34 weeks of gestation and > 2000 grams at birth with probable sepsis who present with following clinical features
a)   Hypothermia or fever
b)   Lethargy, poor cry, feeding difficulty.

Positive Septic Screening – presence of two of the following namely
a)   TLC (< 5000 / cumm or > 15000/cumm)
b)   Immature to total neutrophil ratio of >0.2
c)   Absolute neutrophil count < 1800/cumm
d)   C – reactive (CRP) > 1mg/ dL (immunoturbidimetric method)
Exclusion Criteria:
a)   Babies with major malformations
b)   Severe birth asphyxia
c)   Bone, joint or deep – seated infection
d)   Who are already on antibiotics before coming to NICU?
e)   Babies undergoing surgery
f)   Babies who diagnosed as proven sepsis (culture positive sepsis)
g)   Culture negative but sick neonates

Sample Size:

Sample size for the present study was calculates as 75 in each group, so total of 150, assuming 15% difference in improvement rate between two methods and 95% improvement in one of the methods.

Method of Collection of Data:

Babies admitted with in NICU with sepsis symptoms were investigated (septic screening) and blood culture was sent. At the end of 72 hours if culture was negative with positive septic screening then the cases were included in this study, eligible babies were allocated to one the two groups according to computerized randomised numbers.

Group 1: these subjects did not receive further antibiotics after receiving the sterile culture report.

Group 2: these subjects received a total of 7 days of antibiotics

Neonates of the group 1 were observed in NICU or in the mother's ward for 24 hours following the discontinuation of antibiotics prior to discharge and were re- examined as out patients at two days after discharge and followed up after one week.

At each visit information regarding episodes of illness at home after discharge was recorded, if any subject did not come for follow up they were contacted by telephone. Parents were asked to report to our unit for any episode of illness till 15 days.

Therapy was considered to be successful when there was weight gain, no apparent signs of sepsis as found on clinical examinationand nore-hospitalisation for sepsis.

Investigations Performed :
a) CRP (IMMUNOTURBIDINETRICMETHOD)
b) CBC:
1) Total leukocyte count
2) Absolute neutrophil count
3) Immature to total neutrophil ratio
c) Blood culture
d) Chest X ray
e) CSF analysis and culture
f) Urine examination and culture.

Statistical Analysis
Applied statistical methods:

Descriptive analysis was done by calculating mean, standard deviation (SD), proportions. inferential statistics was done by chi – square test, independent t test. $P < 0.05$ is considered statistically significant. All calculations are done by SPSS software.

III.   Results:

150 neonates were randomised to receive 3 day or   7day course (n=75). Baseline variables were balanced in two groups. There was no significant difference in the improvement or relapse between the two groups.

Comparison of mean age in days when baby presented with sepsis symptoms between two groups

	Group	N	mean	Std. deviation
Age in days when child presented with sepsis symptoms	**Group 1**	**75**	**4.33**	**3.310**
	Group 2	**75**	**3.89**	**2.403**

Mean age (in days) of babies of group 1 was 4.33 days And in group 2 was 3.89 days

Comparision of sex distribution between two groups

| Sex of baby	Group 1	%	Group 2	%
Male	**50**	**66.7**	**45**	**60**
Female	**25**	**33.3**	**30**	**40**
Total	**75**	**100**	**75**	**100**

In group 1 – 66.7 % were male and 33.3% were female compared to group 2 in which 60% were male and 40% were female.

Comparison of symptomatology between two groups

Symptom	Group 1	group 2
Fever	**18 (24%)**	**22 (29.3%)**
Hypothermia	**4 (5.3%)**	**9 (12%)**
Lethargy	**68 (90.7 %)**	**69 (92%)**
Feeding difficulties	**63 (83%)**	**70 (93.3%)**
Poor cry	**28 (37.3 %)**	**31 (41%)**

Comparison of Symptomatology Between Two Groups

Investigations	Group 1	Group 2
Leukocytosis	63(83%)	65(86.5%)
Leucopenia	8(10.6%)	10(13.3%)
I:T ratio	37(49.3%)	36(47.9%)
ANC	6(7.9%)	9(11.9%)
CRP	51(67.9%)	62(82.5%)
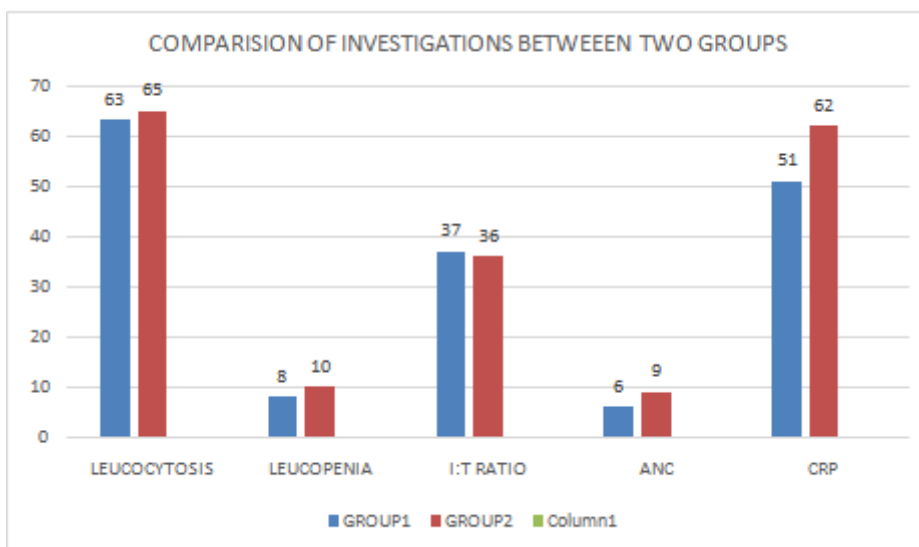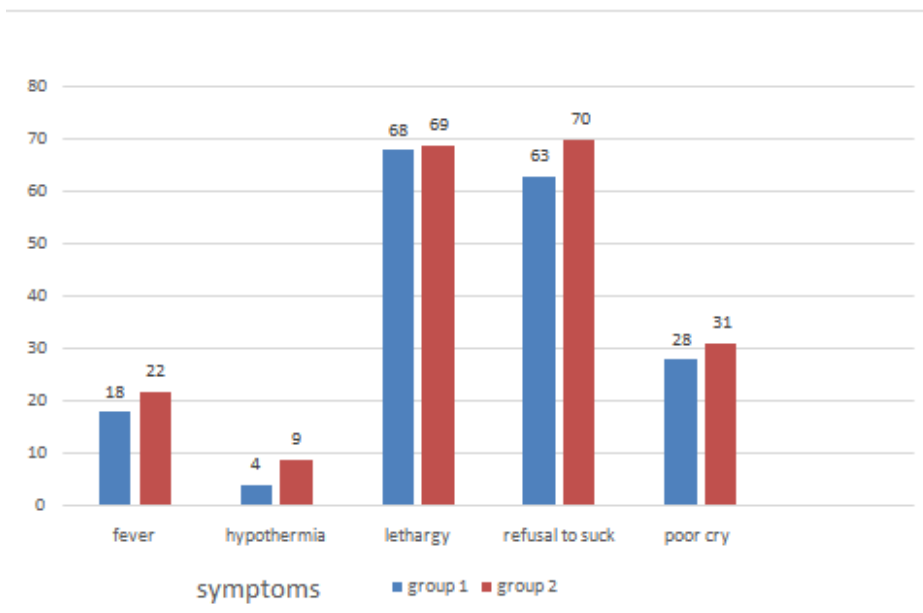
Comparison of outcome between two groups

Group	Total	improved	Improvement rate
Group 1	75	69	92
Group 2	75	72	96
Total	150	141	94

Group1 92% of cases improved compared to 96% in group 2

Comparison Of Outcome According To Age Of Onset Of Sepsis At Presentation Between Two Groups

In group 1, 32 cases were presented with EOS among which 30 (93.8%) improved compared to Group 2 where 38 cases were presented with EOS in which 36 (94.7%) improved.

In group 1, 43 cases were presented with LOS among which 39 (90.7%) improved compared to Group 2 where 37 cases were presented with LOS in which 36 (97.3%) improved.

There is no statistically significant difference among two groups with respect to age of onset of presentation.

	Group 1(3 days)			Group 2(7 days)		
	n	Improved	Rate	n	Improved	Rate
EOS	32	30	93.8	38	36	94.7
LOS	43	39	90.7	37	36	97.3
Total	75	69	92	75	72	96
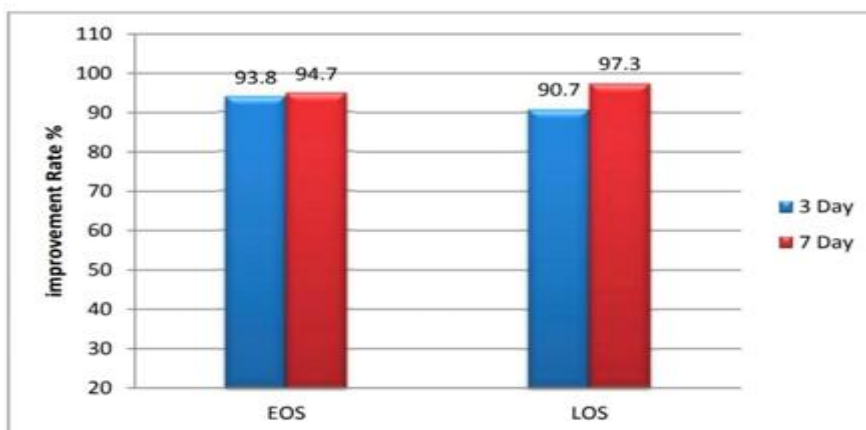
Comparison of Relapse Between Two Groups

Group	Total	Relapse (%)
Group1 (3 day)	69	4 (5.8)
Group2 (7 day)	65	3(4.6)
Total	134	7 (5.2)

In group 1, out of 69 improved cases 4 (5.8%) babies had relapse compared to group 2 in which out of 65 improved cases 3(4.6%) babies had relapse with sepsis symptoms.

Rate of relapse observed in group which received 3days antibiotic treatment is not significantly different compared to group which received 7 days of antibiotics.
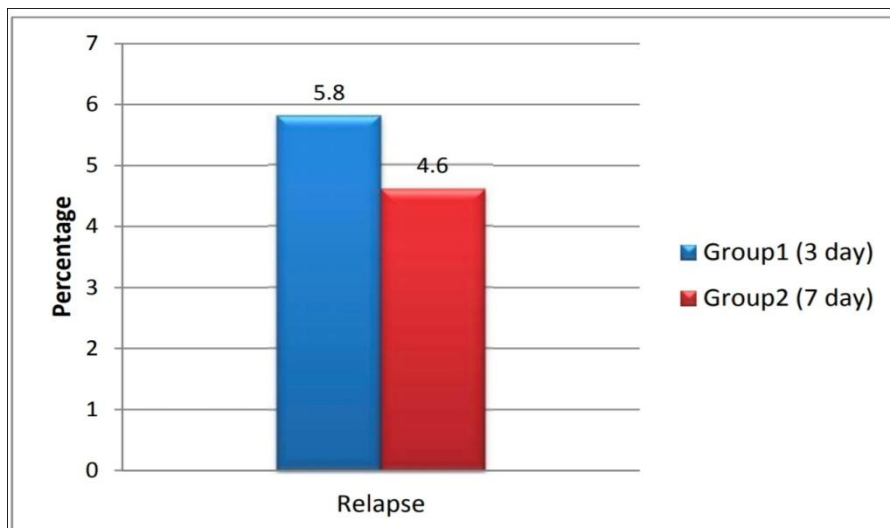
Mean Duration Of Stay In Hospital Among Two Groups

	Duration of stay	
Group	**Mean**	**SD**
Group1 (3 day)	4.4	1.72
Group2 (7 day)	7.6	1.31

Mean duration of stay in group 1 was 4.4 days compared to 7.6 days in group 2 which is statistically significant.
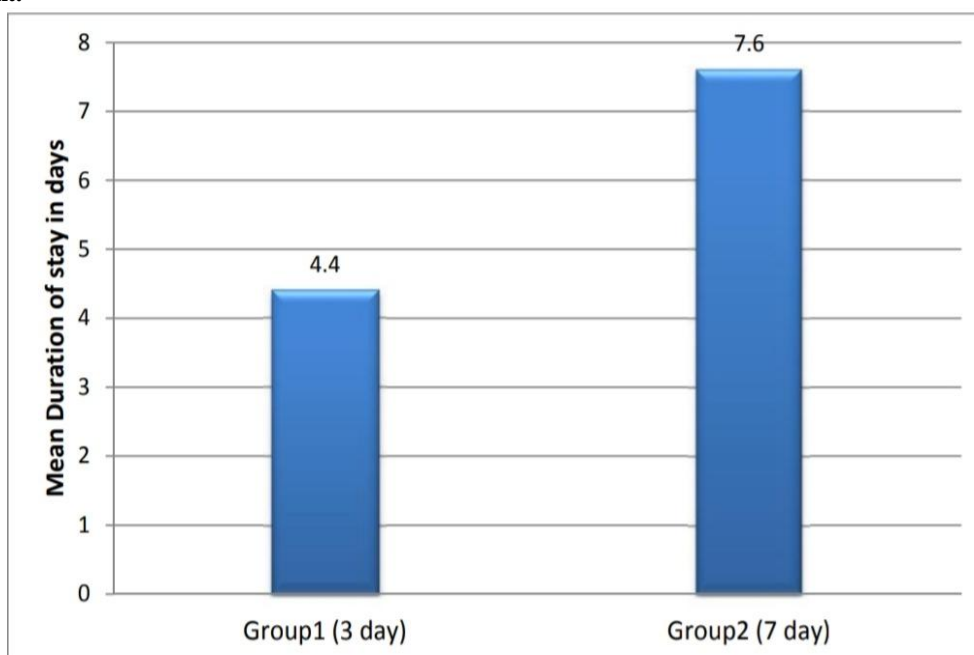
IV. Discussion:

In this study there was no significant difference in the treatment failure rates with 3 days vs 7 days of antibiotics for probable neonatal sepsis similar observations made by Saini et al Kaiser et al and Isaacs D et al …..In the present study 63.3% cases were males compared to study done by Saxena et all where it was 60 %, Gupta et all ,64 %

In our study improvement was assessed clinically in contrast to study done by Lee et al where serial CRP done to stop antibiotics

This study showed,by following 3 days of antibiotics for probable sepsis we can significantly reduce the duration of hospital stay similar to study done by Lee et al and Saini et al .

In the present study there is no significant difference in both early and late onset sepsis cases and term vs pre term babies and vaginal vs caesarean section delivered babies in both groups similar to Saini et al and Lee et al studies.

V. Conclusions:

- 3 day course of antibiotics is enough to treat probable neonatal sepsis
- In both early and late onset probable sepsis 3 day course of antibiotics is enough
- We can significantly reduce the duration of hospital stay by following 3 days course of antibiotics for probable neonatal sepsis

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