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Original Article

Paediatrics Section

Reduction of Antibiotics Used in Newborn Babies Admitted to Neonatal Unit: A Quality Improvement Initiative

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ABSTRACT

Introduction: Excess exposure of antibiotics early in life disrupts the developing microbiome in skin and gastrointestinal system of new born which may lead to development of different health conditions. Prolong use of antibiotics in Neonatal Intensive Care Unit (NICU) develops resistance to infection, increases risk of Necrotizing Enterocolitis (NEC) and invasive fungal infection in new born. Studies reported that short course of antibiotics prevent treatment failure, cause reduction of duration of hospital stay, prevent antimicrobial resistance, decrease neonatal mortality and improve neurological outcome.

Aim: This Quality Improvement (QI) study aimed to establish a standard guideline for reduction of antibiotics use in new born unit of a tertiary level health care institution of India.

Materials and Methods: This QI study was conducted in the newborn units of paediatrics department of a tertiary health care center, Odisha, India, from 1st June to 31st July, 2018. Patients, under antibiotic therapy, were enrolled in this study. The data were collected in a predesigned case record form regarding duration, indications (as per the minimal investigation for sepsis, as per minimal risk factor for antibiotics used, as per high index of suspicion) and outcome in terms of cured, death and LAMA (Leave Against Medical Advice). Baseline data regarding the use of antibiotics were collected for one month period and final data for another one month were collected after applying newly formed antibiotic use guideline among neonates. Data were analysed by Chi-square test using Graph pad prism ver. 0.5.

Results: In this study distribution of antibiotic used among hospitalised patients in post-intervention phase was significantly decreased (77%) compared to baseline data (94%). This study result showed that percentage of cases using antibiotics, were not as per risk factors and were reduced significantly, post implementation of guidelines. Antibiotic used, as per the high index of suspicion increased (76%) significantly compared with baseline data (27%) and also as per the systemic sign of sepsis increased significantly in final data (74.04%) over baseline data (48%). Antibiotic use duration was reduced in post-intervention period i.e., ≥3 days over ≥5 days (baseline data) significantly. There was no significant difference in outcomes.

Conclusion: On application of newly formed antibiotic use guideline with reduced antibiotic use strategy, the final data compared with baseline data did not show any significant difference in cure rate as well as death/LAMA/referred.

Keywords: Antibacterial agent, Neonatal sepsis, Quality improvement study

INTRODUCTION

Antibiotic therapy can affect not only the target pathogen but also the commensal inhabitants of the human host. Human micro-biota is normally present in skin and mucus membrane of mouth, nose, GI tract and vagina. It protects human beings from pathogenic organisms by development and maintenance of immune system and helping host to access nutrients in food. Preterm infant's gut micro-biota has reduced microbial diversity coupled with an increase in colonisation with pathogenic organisms [1-3].

In preterm infants, establishment of the gut microbiota is also of importance for key morbidities like Late Onset Sepsis (LOS) and NEC which are significant causes of mortality. Prolonged use of antibiotics leads to adverse effect in newborn brain and behaviour [4].

Excess exposure of antibiotics in early life of newborn disrupts the developing microbiome in skin and GI system which may lead to various morbidities and mortality. Antibiotics use in NICU for a longer period, lead to development of resistance against microorganisms [5] and also increased risk of NEC and invasive fungal infection in new borns [6].

Due to delayed development of the preterm gut microbiome in twins, they are at risk of NEC and sepsis [7]. In NICU, antibiotics are the most prescribed drug to treat infection [8]. A study from India reported that antibiotics are prescribed more in number, there is less use of generic drugs, the absence of latest Essential list of medicine and not in line with culture report in NICU of a tertiary care centre [9]. Short course of antibiotics can prevent treatment failure, reduce duration of hospital stay, and prevent antimirobial resistance, decreases neonatal mortality and neurological outcome [10]. A study found that prolonged antibiotic therapy (≥5 days) started on the 1st day of life was independently associated with LOS alone and the composite outcome of LOS, NEC or death [11].

Neonatal sepsis very often has nonspecific signs and leads to serious consequences. So empirical antibiotics, are usually used in symptomatic infants with suspected sepsis, after obtaining biological material for culture [12]. However, neonates without any signs of infection often receive antimicrobial agents, and such inappropriate antibiotic treatment may have adverse consequences [13].

With this background this QI (quality improvement) study was undertaken to establish a standard guideline for reduction of antibiotics use in new born unit of our institution. The objectives of the study were to assess rate and duration of antibiotic used in pre-intervention phase and after application of reduction method of antibiotic use as per standard guideline.

MATERIALS AND METHODS

This was a QI study conducted in the neonatal unit, casualty, newborn word, Advanced care Research Centre and Special neonatal care unit (ACRC and SNCU) of paediatrics department of a tertiary health care center, Odisha, India, from 1st June to 31st July, 2018. The protocol was discussed in IEC. It was decided as there is no deviation from guideline rather trying to rationalize the antibiotic use, the IEC approval is not mandatory.

This study was conducted in three phases: 1) Baseline data collection phase/pre-intervention phase (1 month); 2) Intervention phase: training and sensitisation of senior and junior faculties, post graduates and paramedical staffs in the form of CME, group discussion poster reflection in work places as per smart antibiotic policies for sepsis for 1 month); and 3) Final data collection during the period of discharge from hospital. The detailed explanation is given below under study procedure.

For this study a QI team was constituted by including 1 associate professor (team leader), 2 assistant professors, 4 post graduate students, 4 nursing staffs in charge of different sections of newborn unit. A total of 71 cases in pre-intervention phase and 131case in intervention phase were included in the study. Sample size was not calculated. All the neonates under antibiotics during that period were included.

New born cases 0-1 month of age, all sexes receiving antibiotic therapy were included in the study. Patients >1 month of age and not under antibiotic therapy were excluded from this study.

Study Procedure

At the beginning of study there was a discussion among senior faculties with team leader based on their experience in their facility to prioritising the problem on four important points such as important to patient outcome, affordable in terms of time and resources and easy to measure vide POCQI (Point of Care Quality Improvement) facilitator's manual [14].

Data Collection Procedure

Data were collected in a predesigned format from hospital record. The baseline data regarding various aspect of antibiotic therapy like whether antibiotics were recommended as per antibiotics guidelines protocol [15] or not (2 +ve risk factor, 1 high index of suspicion 1, any specific organ involvement). The supportive antibiotic therapy with sepsis cases to be instituted after sepsis screen 2+ve was done or not. Culture and sensitivity study of blood or urine were done or not. The duration of antibiotics therapy was also recorded. Lastly, outcome in form of discharge or LAMA or death were documented.

The antibiotic utilisation was evaluated as per the smart policy of antibiotic use guideline as follows:

Risk factor of sepsis: If >2 of the following high risk factors present, antibiotic therapy is indicated.

EOS (Early Onset Sepsis): Low birth weight <2500 gm, febrile illness of mother within 2 weeks prior to delivery, foul smelling liquor and MSAF, PROM >24 hours, more than 3 vaginal examination during labour, prolong and difficulty delivery with instrumentation and, Perinatal asphyxia (Apgar score <4 at 1 minute or age) or difficult resuscitation).

LOS (Late Onset Sepsis): NICU admissions, low birth weight, prematurity, invasive procedures, parenteral fluid therapy, ventilation and use of stock solutions, poor hygiene, poor cord care, bottle-feeding and prelacteal feeds. Breast-feeding, on the other hand, prevents infection in neonates.

High index of suspicion:-any one

Bradycardia/Tachycardia/Respiratory distress/Apnea and gasping/Hypoglycaemia/Hyperglycaemia/Metabolic acidosis.

Specific systemic features as per which antibiotics given:

- CNS: Bulging AF, blank look, high pitched cry, excess irritability, not arousable, comatose, seizure, neck retraction (suspicion of meningitis)
- Cardiac: Hypotension, poor perfusion, shock
- Gastrointestinal: Feed intolerance, vomiting, diarrhea, abdominal distension, paralytic ileus, enterocolitis

- Hepatic: Hepatomegaly, direct hyperbilirubinemia
- Renal: Acute renal failure
- Haematological: Bleeding, petechie, purpura
- Skin: Multiple pustules, abscess, sclerema, mottling skin, umbilical redness and discharge

Supportive antibiotic therapy with sepsis to be instituted after minimum rated investigation should be undertaken:

- Blood culture
- Sepsis screening: any two present
- Neonatal gastric aspirate >5 polymorph/HPF (suspicion of Chorioamnitis)
- Lumbar puncture: when strong suspicion of meningitis
- Radiology: CXR, Abdominal x-ray, Trans-fontanel ultra-sonogram (TFUSG)
- Urinary Culture

After fish bone analysis of baseline data the QI team discussed about existing practice of antibiotic use and possible barriers in implementing the suggested strategy. Then how to implement the new strategy to improve the quality care was finalised. After the baseline phase the training of the team members was conducted.

PDSA (Plan, Do, Study, Act) cycle was followed involving team members on 5 points like, duration of antibiotic therapy to be reduced from the existing practice, given as per the risk factor, high index of suspicion of sepsis, specific systemic signs of organ involvement, with minimum supporting investigation prior to starting of therapy etc., persons involved in follow-up, place, duration of study and expected outcome. Training material was prepared by the QI team. The written materials (protocols on antibiotics initiations in sepsis) were widely circulated among other doctors and nurses for implementation. Posters regarding new protocol were displayed at several selective places to aware doctors and nursing staffs about the new strategy regarding antibiotic use.

Finally, following changes were made in the system: 1) Training of doctors and neonatal nurses; 2) Finalising the new protocol; 3) Supervising by QI team members; 4) Displaying the guidelines for antibiotic use at different places of New born unit; 5) Assigning the team members to collect data regarding various aspect of antibiotic use in a predesigned case record form prepared by team members.

Post-intervention/final data collection phase dealt with data collection from the hospital record regarding discharge/death or LAMA. QI team met every week to collect feedback from all stakeholders and review each important aspects of feedback and decide to bring any changes in the system, if necessary.

STATISTICAL ANALYSIS

Both baseline data and final data were compiled and analysed by using statistical software, Graph pad prism version.5. The categorical data were analysed by descriptive analysis and expressed in frequency and percentages. The comparison between base line data and final data were done by Chi-square test.

RESULTS

It is evident from [Table/Fig-1], that distribution of antibiotic used among hospitalised patients in post-intervention phase significantly decreased (77%) in comparison with baseline data (94%). It was observed in the study that the use of antibiotics without any risk factor (52%) in baseline data, reduced (46%) in final data, but was statistically not significant. The use of antibiotics as per the high index of suspicion, use of antibiotics as per the systemic sign of sepsis, the use of antibiotics as per the minimal investigations for sepsis increased significantly in post intervention period compared to the baseline data. The antibiotic usage duration was reduced. However, there was no

Parameters	Baseline data (n=71) N (%)	Final data (n=131) N (%)	χ^2 value/ df	p-value
Distribution of antibiotics used				
Yes	67 (94%)	101 (77%)	11.66/ 1	<0.001**
No	4 (6%)	30 (23%)		
Minimum investigation				
Yes	34 (48%)	93 (71%)	10.98/1	<0.001**
No	37 (52%)	38 (29%)		
Risk factors				
Yes	34 (48%)	71 (54%)	0.7203/1	>0.05 NS
No	37 (52%)	60 (46%)		
High index of suspicion				
Yes	19 (26.76%)	100 (76%)	48.06/1	<0.0001***
No	52 (73.24%)	31 (24%)		
Systemic signs				
Yes	34 (48%)	97 (74.05%)	10.98/1	<0.001**
No	37 (52%)	34 (25.95%)		
Antibiotic used duration				
<3 days	16 (23%)	66 (50%)	17.87/1	<0.0001***
≥3 days	55 (77%)	65 (50%)		
Outcome				
Cured	65 (92%)	120 (92%)	0.000/1	>0.05 NS
Not cured (death, LAMA and referred)	6 (8%)	11 (8%)		

[Table/Fig-1]: Evaluation of antibiotics use: baseline data vs final data after intervention with antibiotic use guideline.
Data expressed in N (%); Analysed by chi-square test; **; *** indicates statistical significance

significant change in cured and discharged case between the post and pre-intervention phase i.e., 92% in both the cases.

DISCUSSION

We observed in this study that baseline data prior to intervention of QI strategy showed 94% neonates admitted to the NICU received antibiotics which were significantly reduced in final data i.e., 77% after implementation of QI plan.

Antibiotics were used in neonates without assessment of risk factors for sepsis in highest percentage (52%) of cases in baseline data, whereas in final data the percentage of cases was significantly reduced to 48%. That means risk factor assessment was done in more number of cases prior to institution of antibiotic therapy in post-intervention phase than pre-intervention phase.

Antibiotics were prescribed at base-line, as per the high index of suspicion, in 26.76% of cases whereas it was significantly increased in the final data i.e., 76%. This happened as the newly implemented guideline was followed.

As per the antibiotic use guideline, antibiotics can be given to neonates on the basis of systemic signs for sepsis [9]. However, in this present study, the baseline data showed it was only in 29% cases which were significantly lesser than final data i.e., 79%. Antibiotics should be given after doing certain minimal number of investigations. While, it was very less frequent in baseline data i.e., 29% and increased significantly in final data, up to 77% as it was done as per new guideline.

Duration of antibiotics used at baseline i.e., >3 days (5-7 days) was found to be significantly in more number of cases compared to the final data which was ≤3 days. In a systemic review, half of the 30 centers administered antibiotics of more than 3 days duration in ≥50% of the infants with sterile cultures which suggested that the duration of empirical antibiotic therapy in infants among culture negative cases is not dictated by clinical indicators of sepsis [16].

The outcome in terms of cured and discharged, LAMA and death were compared between baseline data and final data and had no significant difference.

Excess use of antibiotic in early age may alter intestinal microbiota and contribute to the pathogenesis of NEC and Antibiotic-Associated Diarrohea (AAD) [17]. This study result also showed there is no such harmful effect by reducing the duration of antibiotic use in sick newborn.

Every treating physician should follow a standard antibiotic use guideline, specifically prepared for the institution. Antimicrobial Stewardship Programme should be implemented in every teaching institution – which will perform periodic monitoring of the rational use of antibiotic. Periodic Orientation Programme/ CME should be conducted among teaching faculties, SR and PG students. Emphasis should be given for rational use of antibiotics during the UG and PG teaching programme. Government should take some steps and give importance to advocate rational use of antibiotics in health care system.

LIMITATION

This was a short duration study. The study subjects, who received antibiotics, were selected for this study. The outcome of the antibiotics used could not be evaluated according to signs and symptoms of infection and evaluating laboratory parameters like leukocyte count and estimation of c-reactive protein, etc.

CONCLUSION

On the basis of the result found, it could be concluded that the antibiotics were used more rationally after intervention. The antibiotics were used in less number of cases for shorter duration without causing any significant change in outcome. Implementing this strategy, we can reduce the antibiotic related side effect, resistance, cost of the treatment and duration of hospital stay as well as optimise the utilisation of hospital resources.

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