Reducing Time to First Dose of Antibiotic: The Example of Asymptomatic Neonates Exposed to Chorioamnionitis

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INTRODUCTION

The time of medication delivery from the onset of illness is one of the factors which determines disease outcomes in pediatric and adult populations.1-3 This finding was demonstrated in multiple specialties and care settings, ranging from oncology, endocrinology, and infectious disease to neonatal-perinatal medicine.2,3 In neonatal-perinatal medicine, the importance of timely medication delivery begins with resuscitation in the delivery room and continues throughout the infant’s stay in the neonatal intensive care unit (NICU). An example of this is the concept of the “golden hour,” which began in trauma medicine but is now widely used in neonatology. The focus of the “neonatal golden hour” is on resuscitation, thermoregulation, early administration of antibiotics for suspected sepsis, early intravenous parenteral nutrition, hypoglycemia management, and completed admission within 1 hour of life.4 Several steps occur from the time of diagnosis and/ or time of admission to the delivery of medications in the NICU. Some of these steps include nurses’ admission workflow, computerized physician order entry, order confirmation by nurses and pharmacists, obtaining diagnostic/laboratory samples, and securing medication administration access. Any of these steps can constitute a barrier to prompt administration of medication.5

Kotter’s work proposes how to address barriers to process/quality improvement (QI).6,7 In these landmark articles which describe how to effect change in a system, Kotter outlined the following 8 essential steps to implement change in any system: create urgency, form a powerful coalition, create a vision for change, communicate

Abstract

Introduction: Time of medication delivery from the onset of illness is one factor that determines disease outcomes. In this study, we aimed to reduce the average time from admission to the first dose of antibiotic by at least 30% and increase the percentage of neonates receiving the first antibiotic dose within 1 hour of neonatal intensive care unit arrival to 50% over 12 months in asymptomatic neonates 34 weeks and older estimated gestational age with exposure to maternal chorioamnionitis as a sample population.

Method: This study involved 135 infants 34 weeks and older gestational age exposed to chorioamnionitis. We documented the demographic characteristics of mothers and infants. We monitored time to the administration of the first dose of antibiotics through multiple plan-do-study-act cycles. We identified barriers to timely antibiotic administration and targeted them with multipronged interventions in plan-do-study-act cycles. Process measures were displayed monthly using X-bar/S control charts and P charts. We applied established rules for detecting a special cause. Results: We reduced the meantime to the first dose of antibiotics from 130 to 78 minutes (40% reduction). The percentage of infants who received the first antibiotic dose within 60 minutes rose from 5.8% to 36.3% during the study period. Special cause improvement was seen in all process measures. The most significant improvement seen was in the time to obtain a blood culture and the interval between intravenous access placement and antibiotic delivery.

Conclusion: Multipronged interventions can help improve timely medication delivery to neonates in the neonatal intensive care unit in this example of infants exposed to chorioamnionitis. (Pediatr Qual Saf 2021;6:e407; doi: 10.1097/pq9.0000000000000407; Published online May 5, 2021.)
the vision, remove obstacles, create short-term wins, build on change, and anchor the changes in corporate culture. Although he carried out his studies using the business setting as a model, his approach has been applied to other settings.

In the NICU, there are different clinical situations in which timely performance of a procedure or delivery of medication is vital to the outcome. One of such disease entities in the newborn period for which timely delivery of medication is essential to the outcome is neonatal sepsis. Neonatal sepsis can present with nonspecific signs and symptoms and may progress to shock, multiorgan involvement, and death if not promptly treated. Among survivors, sequelae of neonatal/perinatal infection and inflammation, such as chronic lung disease, white matter injury, and poor neurodevelopmental outcomes, have been well documented in multiple studies. Overall mortality in term and late preterm infants with neonatal sepsis is approximately 2%–4%. A high index of suspicion, coupled with prompt and adequate treatment, is key to limiting morbidity and mortality. Early administration of antibiotic therapy is critical to both containment of infection and optimizing outcomes in newborns.

Several risk factors predispose neonates to early-onset sepsis. There is also a tremendous amount of controversy related to the utility of predisposing factors in determining this risk. One such risk factor for early-onset sepsis is chorioamnionitis, an acute inflammation of the placental membranes and chorion.

Although the American Academy of Pediatrics recommends treatment with broad-spectrum antibiotics in symptomatic neonates with chorioamnionitis (CA) exposure, the treatment of asymptomatic neonates exposed to maternal CA remains controversial, with practices varying among the US institutions. At the time of this study, our institution’s policy was to admit all infants exposed to maternal CA to the NICU for suspected sepsis. We managed these infants presumptively for sepsis during the study period by obtaining a blood culture and serial complete blood counts and administering empiric broad-spectrum antibiotics (ampicillin and gentamicin) until blood culture is negative for 48 hours. As multiple studies have shown that early administration of antibiotics contributes to the outcome of neonatal sepsis, the guideline in our NICU at the time of this study was for all neonates, regardless of gestational age or symptomatology, admitted for suspected sepsis to receive the first dose of antibiotics within 1 hour of arrival into the unit. We decided to target the steps from admission to medication delivery in a cohort of asymptomatic late preterm and full-term neonates admitted for antibiotic therapy to improve the timely administration of medications in the NICU.

In this process, improvement initiative, we determined an average baseline time to the first dose of antibiotics in asymptomatic infants 34 weeks and older estimated gestational age (EGA) born to mothers with CA in our NICU.

We hypothesize that prospective and sequential multi-pronged interventions will improve the time to the first dose of antibiotics in this sample population.

SMART Goal
At the end of 12 months, we aimed to reduce the average time from admission to the first dose of antibiotics by at least 30% in asymptomatic neonates 34 weeks and older EGA with exposure to maternal CA. Our secondary aim is to increase the percentage of these neonates receiving the first antibiotic within 1 hour of NICU arrival to 50% during the study period.

METHODS

Human Subjects’ Protection
The Institutional Review Board of Drexel University College of Medicine approved the study and granted an exemption of consent as the project aims to improve patient care quality.

Setting
We performed this process improvement initiative at an academic, urban hospital with an average of 2,000 deliveries per year and 350 admissions to the NICU. On average, 82 infants per year are exposed to CA in our institution. The institution has a 26-bed level III NICU. The hospital uses Cerner (Millenium 2017.1.1.87) for its electronic health record (EHR).

Inclusion Criteria
All asymptomatic neonates greater than or equal to 34 weeks EGA with exposure to maternal CA, as determined by obstetrical documentation.

Exclusion Criteria
All neonates younger than 34 weeks EGA, and all neonates 34 weeks and older exposed to maternal CA who required cardiopulmonary stabilization upon arrival into the NICU.

Planning and Implementation of Interventions

Baseline Data
We performed a retrospective review of the EHR of infants 34 weeks and older EGA admitted to our NICU between March 2015 and October 2015 to determine baseline data. These data included the mean duration to the first dose of antibiotics after NICU admission and the percentage of infants who received their first dose within 60 minutes of NICU admission. Evaluation of these baseline data of 55 infants over the 8 months demonstrated that 5.8% of all babies 34 weeks and older EGA received the first dose of antibiotics within 1 hour of NICU admission, and the average time to the first dose was 130 ± 76 minutes (median of 109.5 min; range of 36–420 min).
Targeted Steps
Following the baseline evaluation, we identified multiple steps that could be targeted for intervention. Contextual elements considered necessary at the outset of introducing the interventions were the care team’s admission workflow, sepsis evaluation laboratory sampling, placement of intravenous (IV) catheter, order entry by the physicians, and order review by the pharmacists and nurses. Steps that took a long time to perform were priority targets as these will help the most to achieve our aim. We found out that the pharmacist’s meantime to order review from the baseline data was 8 minutes; therefore, we dismissed this step as a target for potential intervention. We then developed a key driver diagram using these data (Fig. 1).

Interventions
Implementation of this process improvement initiative occurred sequentially by performing a series of interventions in Plan-Do-Study-Act (PDSA) cycles. Figure 2 demonstrates the timing of each intervention, with new interventions added based on the principal investigator’s real-time review of the trend. The interventions are listed in Figure 2. The team members involved in this process included the NICU nursing staff and the medical team (residents, neonatal nurse practitioners, fellows, and attending physicians).

The investigative team used a Microsoft Excel spreadsheet (Microsoft, Inc. Redman, Wash.) as a data collection tool to record the following information from the EHR: date and time of birth, time of admission into the NICU, time of order entry by physicians, time of blood culture and IV catheter placement, and the start time of administration of the first dose of antibiotics. The principal investigator regularly conducted a real-time review of the process to identify areas of progress and for improvement. We discussed these as team members to plan the next PDSA cycle.

Statistical Analysis
We created the Statistical Process Control Charts ($\bar{x}$-, S-, and P charts) using Microsoft Excel QI charts (Scoville Associates, 2007) to determine whether there was an improvement after each intervention. We applied established rules for detecting special cause variation from common cause variation per Benneyan, Lloyd, and Plsek.19 We performed other data analyses using Microsoft Excel and Statistical Package for the Social Sciences (SPSS) version 15.0 (IBM Corporation Business Analytics, Armonk, N.Y.). Results were expressed as mean ± SD and percentages. Differences between categorical variables were calculated using Chi-Square and a $t$ tests to determine differences between continuous variables. Statistical significance was established at $P < 0.05$.

RESULTS
Six hundred sixty-one neonates were admitted during the study period (March 2015–October 2016). We included 135 infants who met the inclusion criteria in the final analysis. There were 55 in the preintervention group and 80 in the postintervention group. There were 58 females and 77 males during the baseline and intervention periods, and 8 of the infants were late preterm, while 127 were term neonates. Table 1 shows other patient characteristics for the preintervention and the postintervention groups.

The demographic variables between the 2 groups were similar. Following interventions, there was a significant increase in the proportion of full-term infants who received antibiotics within 60 minutes of NICU arrival (6% versus 38%, $P = 0.00001$). There were no late preterm infants in the

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Fig. 1. Key driver diagram showing suggested interventions targeted as essential drivers for achieving the goal.
Reducing Time to First Dose of Antibiotic

The x-bar chart showed a drop in the meantime to the first antibiotic dose (blue line) following the first intervention. This improvement was maintained during interventions 2–6. The solid black line demonstrated the special cause variation. The red line is the goal set before the intervention. The UCL and LCL are 3 SDs above and below the mean, respectively. The S chart showed a time range during the same period. CL, centerline; LCL, lower control limit; UCL, upper control limit.

Table 1. Patient Demographics

| Patient Characteristics | Preintervention (n = 55) | Postintervention (n = 80) | P     |
|-------------------------|--------------------------|---------------------------|-------|
| Sex                     |                          |                           |       |
| F                       | 27                       | 31                        | 0.233 |
| M                       | 28                       | 49                        |       |
| Mean GA (wks)           |                          |                           |       |
| All                     | 39.2 ± 1.6               | 39.3 ± 1.4                | 0.701 |
| ≤60 min                 | 39.7 ± 0.6               | 39.4 ± 1.3                | 0.699 |
| >60 min                 | 39.2 ± 1.6               | 39.2 ± 1.5                | 1.000 |
| Groups                  |                          |                           |       |
| LP                      | 5                        | 60                        | 0.270 |
| FT                      | 50                       | 77                        |       |
| Birth weights (g)       |                          |                           |       |
| All                     | 3380.6 ± 522.9           | 3328.7 ± 402.7            | 0.516 |
| LP                      | 2724.0 ± 672.6           | 2350.0 ± 307.5            | 0.409 |
| FT                      | 3446.3 ± 464.8           | 3366.8 ± 356.0            | 0.279 |
| Time to antibiotic      |                          |                           |       |
| FT                      |                          |                           |       |
| ≤60 min                 | 3 (6%)                   | 29 (37.7%)                | <0.0001|
| >60 min                 | 47 (94%)                 | 48 (62.3%)                |       |
| LP                      |                          |                           |       |
| ≤60 min                 | 0 (0%)                   | 0 (0%)                    | 1.000  |
| >60 min                 | 5 (100%)                 | 3 (100%)                  |       |

GA, gestational age; FT, full term; LP, late preterm.

≤60 minutes category in either the preintervention or the postintervention groups.

The x, S, and the P charts in Figures 2 and 3 demonstrate the improvement in the average time to the first dose of antibiotics and the percentage of neonates who received the first dose within 60 minutes, respectively. Special cause variation was demonstrated both in the average time to the first dose of antibiotic and the percentage of infants who received the first dose within 60 minutes of NICU arrival. We reduced the time from admission to medication delivery from a mean of 130 ± 76 minutes (median of 109.5 min; range of 36–420 min) to 78 ± 34 minutes (median of 72 min; range 4–180 min) postintervention. Table 2 demonstrates a 40% reduction in the average time to the first dose of antibiotics, with the percentage of neonates receiving their first dose of antibiotics within 60 minutes increasing from 5.8% to 36.3%. The most significant impact was on the time from IV catheter placement to medication, admission to blood culture, and admission to order placement with 57.9%, 44.9%, and 39.7% reduction from preintervention to postintervention, respectively.

DISCUSSION

The baseline data from this QI project revealed that it took over 60 minutes in this NICU for neonates with maternal CA exposure to receive their first dose of antibiotics. Only 5.8% received their first dose within 60 minutes. We observed significant improvements after implementing the ongoing education of the NICU staff members and formulating a suggested timeline for the practice in this area. These sequential multipronged interventions helped improve the timely delivery of antibiotics for this study population. This finding is similar to previous process improvement studies demonstrating that sequential multipronged interventions are key to improving outcomes in different pediatric settings.1,2,5,20
The average time of 130 ± 76 minutes to the first dose of antibiotic in this study was similar to the findings of mean duration to the antibiotic from the arrival of 136 ± 132 minutes in patients with bacterial meningitis and 184 ± 222 minutes in those with no meningitis in the study by Schuh et al. Other studies in different age groups and clinical settings also highlighted similar delay to prompt treatment of suspected infections in different age groups and care settings. Therefore, applying the process improvement principles highlighted in this study will be useful in other pediatric care settings to mitigate the delay to prompt medication administration.

Weiner et al demonstrated an improvement in the time to first dose of antibiotics from 1 hour of physician order and 2 hours of baby’s birth time from a baseline of 28% and 19% to a postintervention value of 87% and 92%, respectively. Although our study demonstrated improvement in all the measured outcomes, it did not reach the set goal of at least 50% of neonates receiving their first dose of antibiotics within 60 minutes of NICU arrival (reaching 36.3% during the study period). This failure may be due to the low percentage of timely antibiotic administration at baseline in this QI project and the shorter duration of the intervention (12 compared to 20 mo in the Weiner study). Besides, Weiner et al implemented a strict policy change of administering the antibiotic via the intramuscular route if there was a delay in securing IV access. We did not implement this intervention in our study, although it should be considered in future PDSA cycles.

The practice in our NICU for asymptomatic neonates with maternal CA exposure at the time of the study was to evaluate and treat empirically with antibiotics until 48 hours of negative blood culture and no clinical signs of sepsis. At the time of the study, this practice varied among NICUs across the United States. It differed from the current American Academy of Pediatrics recommendation for the management of asymptomatic neonates with CA exposure. However, this process improvement initiative aimed to identify barriers to prompt delivery of any medication and target such steps to effect improvement. Therefore, this process analysis and targeting can be applied in different settings, patient populations, and diagnoses.

Employing multipronged sequential interventions that worked together to achieve the demonstrated improvements in this QI study was in line with the 8-point change model advocated by Kotter. The application of this process helped foster teamwork among the varied health care providers during this project, remove obstacles, and create awareness among all providers on the need to complete all needed procedures promptly before medication administration.

Three factors played critical roles in the improvement demonstrated in this study. The first factor is a proposed timeline within which to accomplish all necessary procedures performed before administering antibiotics. This timeline helped create the urgency needed and shorten the time it takes to remove the “barriers” to the early administration of the medications. These are two of the essential steps to change proposed by Kotter and Schlesinger. Unfortunately, this timeline was not strictly followed throughout the project. The reason given for this by some team members was the need to teach less experienced team members the admission processes and procedures. As it is a teaching hospital.

The second key factor was the selection of nurse champions for this initiative. These champions empowered the nursing team to take “ownership” of the project. In previous QI initiatives, multidisciplinary collaboration with resultant “ownership” by the nursing team was identified as integral in achieving the outcome.
The third key factor was intensive education in the form of monthly reminders to all stakeholders. As in other QI initiatives, we realized early in the project that culture change would not be easy.5,23 However, the use of continuous reminders was consistent with Kotter’s eighth step to help anchor this change in our staff. The mild degradation in our improvement toward the end of our study may be related to the employment of several new staff members during the study period.

The limitations of the study include the small sample size and the project execution at a single center. These limitations may have overestimated the initiative’s demonstrated improvement, and the approach may not be directly applicable to other units with different practices and sizes. However, this quality initiative highlights barriers to process in a setting, building a coalition of team members and champions, developing process standardization, and executing a sequential, multipronged approach to implement the desired change.

In conclusion, the study showed that with a sequential, multipronged approach, there was a decrease in the average time to the first dose of antibiotic by 40% (exceeding the preintervention goal of 30% decrease, and an increase in the percentage of infants receiving the first dose of antibiotic within 60 min of NICU arrival to 36.3% from 5.8% during the baseline period). Future directives are to continue using this change model of interprofessional teamwork and constant education/reminder to further the progress and sustain this critical process improvement and apply this approach to the timeliness of other medications for this vulnerable population.

DISCLOSURE
The authors have no financial interest to declare in relation to the content of this article.

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