JPPT | Review

Implementation Strategies for Baby NINJA (Nephrotoxic Injury Negated by Just-in-Time Action) to Prevent Neonatal Medication-Induced Kidney Injury

Sadie B. Stone, PharmD; Elizabeth Bisaccia, PharmD; Mary Soliman Zakhary, PharmD; Ferras Bashqoy, PharmD; Deborah Wagner, PharmD; and Christine Stoops, DO, MPH

Acute kidney injury (AKI) is a common complication among patients admitted to the neonatal intensive care unit. Nephrotoxic medications (NTMs) are known to increase the incidence of AKI, but the use of these medications is often unavoidable. Baby NINJA (Nephrotoxic Injury Negated by Just-in-Time Action) is a quality improvement (QI) project that may be implemented at individual institutions and aims to systematically identify AKI in neonates and infants receiving NTMs. The purpose of this review is to describe nephrotoxic AKI in the neonatal population, introduce the Baby NINJA QI project and its potential to reduce neonatal AKI, and outline strategies for effective implementation of Baby NINJA.

ABBREVIATIONS AKI, acute kidney injury; AKIN, Acute Kidney Injury Network; ARIMA, autoregressive integrated moving average; AWAKEN, Assessment of Worldwide Acute Kidney Injury Epidemiology in Neonates; AWARE, Assessment of Worldwide Acute Kidney Injury, Renal Angina, and Epidemiology; eGFR, estimated glomerular filtration rate; EHR, electronic health record; ICU, intensive care unit; KDIGO, Kidney Disease: Improving Global Outcomes; NAKI, nephrotoxic acute kidney injury; NICU, neonatal intensive care unit; NINJA, Nephrotoxic Injury Negated by Just-in-Time Action; NTM, nephrotoxic medication; pRIFLE, Pediatric Risk, Injury, Failure, Loss, and End-Stage Renal Disease; QI, quality improvement; SCr, serum creatinine; SPS, Solutions for Patient Safety; UOP, urine output

KEYWORDS acute kidney injury; infant, newborn; intensive care units, neonatal; nephrotoxic medication; quality improvement

J Pediatr Pharmacol Ther 2023;28(4):287–296

DOI: 10.5863/1551-6776-28.4.287

Introduction

Acute kidney injury (AKI) is a pervasive but underestimated comorbidity in the neonatal intensive care unit (NICU). The Assessment of Worldwide Acute Kidney Injury Epidemiology in Neonates (AWAKEN) study described neonatal AKI in the NICU.[1] The incidence of AKI in this study was 29.9%, with 13.9% reaching AKI stage 1; 7.1% reaching AKI stage 2; and 8.9% reaching AKI stage 3. Staging criteria are described in Table 1. Similarly, the Assessment of Worldwide Acute Kidney Injury, Renal Angina, and Epidemiology in critically ill children (AWARE) study, conducted in critically ill patients 3 months to 25 years of age, reported an AKI incidence of 26%.[2] The financial burden is significant with the potential for prolonged hospital admission and long-term associated morbidities.[2–5] Moreover, AKI is an independent risk factor for mortality; therefore, rapid identification and mitigation is crucial.[6,7]

While AKI is often multifactorial, nephrotoxic medication (NTM) stewardship has been suggested as a method for reducing incidence of and complications from AKI.[8] Neonatal and pediatric statements from the 22nd Acute Disease Quality Initiative conference highlight the importance of identifying at-risk populations, stratifying risk based on a set of baseline risk factors and acute exposure, and implementing monitoring and preventive strategies to decrease the incidence of AKI.[9,10] Baby Nephrotoxic Injury Negated by Just-in-Time Action (NINJA) is an ongoing quality improvement (QI) project that targets NICU patients at greatest risk of AKI from NTM, a potentially modifiable risk factor, by monitoring daily serum creatinine (SCr) concentrations while the patient is exposed to NTM until 2 days after end of NTM exposure or end of AKI, whichever is last.[11] Information including days of exposure, rates and incidence of AKI, and census are used to create control charts to monitor key metrics, which are outlined below. The purpose of this article is to describe nephrotoxic acute kidney injury (NAKI) in the neonatal population, introduce the Baby NINJA QI project and its potential to reduce neonatal AKI, and outline strategies for effective implementation of Baby NINJA.

Table 1. Pediatric and Neonatal AKI Criteria[23–25]

Stage	pRIFLE	AKIN	Modified KDIGO Definition for Neonates
1	**Risk**		
	SCr rise ≥ 1.5× reference SCr (eGFR decrease by 25%)	SCr rise ≥ 0.3 mg/dL within 48 hr or SCr rise ≥ 1.5–2× reference SCr	SCr rise ≥ 0.3 mg/dL within 48 hr or SCr rise ≥ 1.5–1.9× reference SCr within 7 days
	UOP < 0.5 mL/kg/hr for 8 hr	UOP < 0.5 mL/kg/hr for > 6 hr	UOP < 0.5 mL/kg/hr for 6–12 hr
2	**Injury**		
	SCr rise ≥ 2× reference SCr (eGFR decreased by 50%)	SCr rise ≥ 2–3× reference SCr	SCr rise ≥ 2.0–2.9× reference SCr
	UOP < 0.5 mL/kg/hr for 16 hr	UOP < 0.5 mL/kg/hr for > 12 hr	UOP < 0.5 mL/kg/hr for ≥ 12 hr
3	**Failure**		
	SCr rise ≥ 3× reference SCr (eGFR decrease by 75% or < 35 mL/min/1.73 m^2)	SCr rise ≥ 3× reference SCr or SCr ≥ 4 mg/dL (acute increase of 0.5 mg/dL) or receipt of RRT	SCr rise ≥ 3× reference SCr or SCr ≥ 2.5 mg/dL (represents eGFR < 10 mL/min/1.73 m^2) or receipt of RRT
	UOP < 0.3 mL/kg/hr for 24 hr or anuric for 12 hr	UOP < 0.3 mL/kg/hr for ≥ 24 hr or anuric	UOP < 0.3 mL/kg/hr for ≥ 24 hr or anuric for ≥ 12 hr
	Loss of renal function > 4 wk	—	—
	End-stage renal disease > 3 mo	—	—

AKI, acute kidney injury; AKIN, Acute Kidney Injury Network; eGFR, estimated glomerular filtration rate using the Schwartz method; KDIGO, Kidney Disease: Improving Global Outcomes; pRIFLE, Pediatric Risk, Injury, Failure, Loss, and End-Stage Renal Disease; RRT, renal replacement therapy; SCr, serum creatinine; UOP, urine output

Challenges of Defining Neonatal Renal Function and Acute Kidney Injury

Nephrogenesis and Biomarkers of Neonatal Renal Function. Nephrogenesis begins at 5 weeks' gestation and continues through 36 weeks' gestation.[12] Smaller renal volume, fewer nephrons, and immature tubular function are noted when nephrogenesis is interrupted following premature birth.[13,14] Renal development continues in premature neonates after delivery, and once corrected to term, renal function will likely mirror that of term-born peers.[14] Functional improvements will continue to be gained with continued development after term age and potentially reach adult clearance capacity by 2 years of age, assuming no renal insults occur.[15] However, multiple risk factors exist for development of AKI in NICU patients including low gestational age, small for gestational age, intrauterine growth restriction, maternal preeclampsia, hypovolemia, NTM exposure, sepsis, and other comorbidities such as congenital heart disease, including moderate to large patent ductus arteriosus.[16,17]

Interpretation of surrogate markers for renal function can be challenging, especially in the neonatal setting. The 2 most common markers to monitor renal function, SCr and urine output (UOP), have limitations. Serum creatinine values can lag behind real-time kidney injury and are dependent on non-renal factors (e.g., muscle mass, age), which leads to poor sensitivity (0%–40% for days 1–3 post insult) in the setting of AKI.[18] In neonates, this is further confounded by maternal SCr in the first week of life; variability in reabsorption in the proximal tubules, based on degree of prematurity; and small muscle mass.[19,20] Measuring accurate UOP is often cumbersome and inaccurate in patients for whom urine is not measured with each void or if urine is mixed with stool in a soiled diaper. These factors can make it difficult to identify and interpret the true degree of AKI, and clinical correlation is needed for timely recognition.

Owing to the clinical and practical limitations of SCr discussed above, several novel urinary biomarkers are under investigation in neonates and infants to aid in earlier identification of AKI. Commonly investigated biomarkers include cystatin C, urine neutrophil gelatinase-associated lipocalin, liver-type fatty acid–binding protein, interleukin-18, and kidney injury molecule-1.[7,21,22] Further studies are needed to determine the clinical utility and feasibility of these biomarkers in the neonatal population.

Defining and Staging Acute Kidney Injury in Newborns. The 3 most commonly used criteria for estimation of renal function include the modified Kidney Disease: Improving Global Outcomes (KDIGO) criteria for neonates; Pediatric Risk, Injury, Failure, Loss, and End-Stage Renal Disease (pRIFLE) criteria; and AKI Network (AKIN) criteria.[16,23–25] All 3 classification systems vary in the scoring and staging of AKI, and each system has benefits and limitations (Table 1). Briefly, the pRIFLE system classifies patients on the basis of estimated glomerular filtration rate (eGFR) or UOP.[24] For the AKIN scoring system, increase in SCr is classified rather than decrease in eGFR.[25] Lastly

the modified KDIGO recommendations use the same staging recommendations as AKIN but add an eGFR of 10 mL/min/1.73 m^2 or less in their stage 3 criteria for neonatal patients, which differs from the breakpoint of 35 mL/min/1.73 m^2 or less used for this stage when KDIGO criteria are applied to pediatric patients.[23] These AKI staging systems have been compared with one another by several authors to determine the most appropriate method of assessing kidney function, with conflicting findings.[26,27] The Neonatal Kidney Collaborative recommends that the neonatal modified KDIGO definition be used as the standard until newer definitions are validated in large multisite trials and correlated with long-term outcomes.[16,28,29]

Acute Kidney Injury Secondary to NTM

In the pediatric inpatient setting there is a correlation between use of NTM and development of AKI, with increased risk associated with exposure to intravenous aminoglycosides and/or 3 or more NTMs.[30,31] Aminoglycoside use for 5 or more days is responsible for AKI in 19% to 31% of cases owing to the direct mechanism of injury and concern for accumulation-related long half-life.[31] When the use of NTM is required owing to clinical indication, increased SCr monitoring allows for more accurate and earlier detection of NAKI.[32] Unfortunately, the ramifications and effect of NAKI can persist for many patients. Menon and colleagues[33] found that 6 months after an episode of NAKI that occurred during hospitalization, 70% of pediatric patients had evidence of residual kidney damage. Further, in 10% to 49% of pediatric patients with AKI, the condition progresses to chronic, irreversible kidney damage, indicating that prevention of AKI could also reduce rates of chronic disease.[30]

For multiple reasons AKI remains an underreported morbidity in the intensive care unit (ICU) setting, particularly in the NICU. Neonatal kidney function is inherently incomplete and underdeveloped, which places this population at increased risk for NAKI.[12] Also, exposure to NTM is high in the NICU. Rhone and colleagues[34] reported up to 87% of very low birth weight infants in the NICU had exposure to at least 1 NTM after which about one quarter of patients developed AKI. Additionally, infants with AKI received more NTMs per day than infants without AKI (0.24 vs 0.15, $p = 0.003$).[34] The NTMs evaluated in this study were acyclovir, amikacin, amphotericin B, gentamicin, ibuprofen, indomethacin, iohexol, tobramycin, and vancomycin.[34] Because NTM exposure is a commonly present and potentially modifiable risk factor, implementation of a NAKI surveillance program has the potential to decrease the incidence of AKI in this vulnerable population.

History of the NINJA and Baby NINJA QI Projects

Exposure to NTM is a common cause of AKI in pediatric hospitalized patients. To address this, a multicenter QI project named NINJA that aims to prevent AKI through early identification was created.[35] Initially, only pediatric patients who were not admitted to the ICU who met NTM exposure criteria were included. Medication exposure was defined as patients who received either vancomycin or aminoglycosides for more than 3 days, or immediately if receiving 3 or more NTMs in a 24-hour period. Owing to their long half-life, some medications (i.e., amphotericin B, cidofovir, iohexol) resulted in a patient being considered "exposed" for a full 7 days following the last dose of the medication.[36] A comprehensive list of NTMs as defined by NINJA, most recently updated August 1, 2017, is included in Table 2.[11,37] Patients were evaluated for development of AKI, using the KDIGO criteria. Systematic automation of the NINJA project resulted in a 42% reduction in NAKI per 100 days.[35,36] Collaborators in the NINJA project across 9 different centers found a 23.8% reduction in NAKI rate through autoregressive integrated moving average (ARIMA) modeling and statistical process control analysis.[37] The success of the project was the result of the systematic, prospective monitoring of SCr coupled with the clinical and cultural drive to change prescribing practices amongst at-risk populations.

In 2015, NINJA was adapted to the NICU.[11] Named "Baby NINJA," this was the first implementation of the NINJA QI program in the ICU setting. With some adaptations for the neonatal population, Stoops et al[11] showed reductions in NTM exposures from 16.4 to 9.6 per 1000 patient-days ($p = 0.03$), incidence of NAKI 30.9% to 11% ($p < 0.001$), and AKI intensity 9.1 to 2.9 per 100 susceptible patient-days ($p < 0.001$). Additionally, it was estimated that 100 AKI episodes were prevented during the 18-month sustainability era. Published NINJA and Baby NINJA studies are summarized in Table 3.

Implementation of Baby NINJA

Successful implementation of Baby NINJA to reduce NAKI in neonates requires the collaboration of multiple key stakeholders. First, motivated program leaders representing neonatology and pediatric nephrology must be identified to co-lead the initiative, because each service has a unique role in the program. A pharmacist motivated to initiate Baby NINJA at their institution could help with identifying physician leaders to spearhead the initiative. Strengthening the relationship between neonatology and nephrology promotes awareness of neonatal AKI for better identification of infants at risk. Promoting dialogue between these 2 specialties can support innovative decision-making discussions and help identify at-risk infants who may need more specific monitoring in the NICU and/or post-discharge follow-up with nephrology.

Additionally, leadership involvement and endorsement of Baby NINJA at the administrative level can

Table 2. NTMs Included in the NINJA Project[11,37*]

Acyclovir[§]	Ioxilan[‡]
Amikacin[†]	Ketorolac[§]
Amphotericin B (conventional)[‡,§]	Lisinopril
Amphotericin B (liposomal)[‡]	Lithium
Aspirin[§]	Losartan
Captopril[§]	Mesalamine
Carboplatin	Methotrexate
Celecoxib	Mitomycin
Cidofovir[‡]	Nafcillin[§]
Cisplatin	Naproxen
Colistimethate	Pamidronate disodium
Cyclosporine	Pentamidine
Deferasirox	Piperacillin
Diatrizoate meglumine	Piperacillin/tazobactam[§]
Diatrizoate sodium	Polymixin B
Enalapril[§]	Sirolimus
Enalaprilat[§]	Sulfasalazine
Foscarnet	Tacrolimus
Ganciclovir[§]	Tenofovir
Gentamicin[†,§]	Ticarcillin/clavulanic acid
Ibuprofen[§]	Tobramycin[†,§]
Ifosfamide	Topiramate
Indomethacin[§]	Valacyclovir
Iodixanol[‡]	Valganciclovir[§]
Iohexol[‡]	Valsartan
Iopamidol[‡]	Vancomycin[†,§]
Iopromide[‡]	Zolendronic acid
Ioversol[‡]	Zonisamide
Ioxaglate meglumine and ioxaglate sodium[‡]	

NINJA, Nephrotoxic Injury Negated by Just-in-Time Action; NICU, neonatal intensive care unit; NTMs, nephrotoxic medications

* Implemented August 1, 2017.
† Counted as 1 of the 3 NTMs for 7 days following last exposure secondary to long half-life.
‡ Single medication that triggers NINJA exposure after 3 days.
§ Medications commonly used in the NICU population.

facilitate technical and QI support. This may include adding individuals such as chief clinical officers and medication safety officers to the development and implementation team. Clinical pharmacists and clinical informaticists should be involved in discussions of logistics prior to initiation of the program. Additionally, discussion with the antimicrobial stewardship program should occur because prescribing shifts to fewer NTMs, which may occur following implementation of Baby NINJA, must be evidence based and balanced with the institution's antibiogram. Each stakeholder is integral in the development of an institution-specific system for identifying at-risk patients, ordering laboratory tests, documenting results, discussing AKI events, and creating a clinical plan. The roles of each stakeholder in these steps of Baby NINJA are unique to each center and can vary.

Securing buy-in from stakeholders can improve the implementation process, improve sustainability of the program, and is achieved through open communication regarding perceived drawbacks to the program.[38] A common concern of NICU prescribers is the blood volume limitations unique to this population. However, Gavigan and colleagues[39] demonstrated no correlation between blood transfusion rates and SCr monitoring rates. Education is indicated for staff prior to implementation of Baby NINJA, emphasizing that daily SCr screening needed for the program should be combined with regular daily laboratory testing and that access to central lines solely for SCr can be deferred to avoid increased risk of central line–associated bloodstream infection. Additionally, nonpharmacologic methods to reduce blood waste include strategic timing and coupling of laboratory tests when clinically appropriate.[40]

Following the adoption of NAKI as a Solutions for Patient Safety (SPS) hospital-acquired condition, the Baby NINJA QI criteria were adjusted to align with the SPS criteria to exclude infants <72 hours or <3 days of life, allowing for how each NICU defines date of birth (day of life 0 vs day of life 1).[41] These infants were excluded owing to elevation of creatinine in the immediate postnatal period secondary in part to the presence of maternal creatinine.[42] Further, a systematic approach for determining baseline SCr values was needed for patients with prolonged NICU admissions. Various factors must be considered including maternal SCr level, gestational age, and definition and timing to baseline SCr (the latter of which varies widely amongst NICUs). For Baby NINJA, criteria stipulate identifying the lowest SCr value in the preceding 3- to 6-month period, allowing for center-specific flexibility. Similarly, the decision to use UOP as part of AKI criteria is deferred to each NICU, because there are known challenges to consider such as timing of postnatal diuresis and accurate measurements of voids.[11] The Baby NINJA program chose not to use UOP as a criterion owing to these variables.[11] However, some programs have chosen to use UOP; for instance, if ≥75% of urine volume has been quantified, the UOP is included. Regardless of the approach,

Table 3. Summary of NINJA Studies

Citation	Population	Intervention	Comparator	Outcome	Adaptations to NINJA
Goldstein 2013[35]	Non-critically ill pediatric patients	Pharmacists manually screened Monday to Friday to assess for patients with high NTM (initial screening was manual until an automated EHR-generated screening report was developed) Daily SCr with substitution or therapeutic drug monitoring when possible	Evaluated project for 1 yr Phase 1 (6 mo manual screening), phase 2 (6 mo automated)	N = 21,807 patients included with n = 729 NTM patients (945 total events) AKI prevalence rate 25% Rate of patient with high NTM exposure 31% AKI intensity rate decreased by 42% with intervention When automated screening implemented, captured more compared with manual screening (11.6 vs 7.6 rate of exposure per 1000 patient-days)	Original definition (aminoglycosides ≥ 3 days or ≥ 3 NTMs within 24 hr) pRIFLE criteria used
Goldstein 2016[36]	Non-critically ill pediatric patients	Additional 3-yr follow-up to assess if improvement was sustained	Compared with *a priori* standard of 8 consecutive weekly metric rates below the baseline rate (investigators assumed that initial baseline exposure rates would have persisted without project implementation)	N = 1749 patients with 3243 episodes of NTM exposure and N = 575 AKI occurrences Exposure rate decreased by 38% and the AKI rate decreased by 64% N = 633 exposures and 398 AKI episodes were avoided	KDIGO criteria used
Goldstein 2020[37]	Non-critically ill pediatric patients at 9 centers	Automated screening report to identify patients' NTM exposure Daily SCr during high NTM exposure and for 2 days post exposure or post-AKI resolution, whichever occurred last		N = 638,695 patients with 4513 episodes of NTM exposure and N= 746 AKI occurrences Observed a significant and sustained 23.8% decrease in AKI in patients with high NTM exposure	KDIGO criteria used

(Table cont. on page 292)

it is important to establish these criteria, as well as any exceptions to obtaining daily SCr measurement, before program implementation to ensure standardized data collection and avoid systematic bias.

As the Baby NINJA program has evolved, the role of the clinical pharmacist has grown substantially. Clinical pharmacists are well positioned to accurately identify patients exposed to NTM, define baseline SCr values,

Table 3. Summary of NINJA Studies *(cont.)*

Citation	Population	Intervention	Comparator	Outcome	Adaptations to NINJA
Stoops 2019[11]	Level IV NICU (neonates and infants)	Automated screening report to identify patients with ≥3 NTMs within 24 hr or ≥4 calendar days of an IV aminoglycoside Daily SCr during high NTM exposure and for 2 days post exposure or post-AKI resolution, whichever occurred last	Pre-implementation (6 mo) vs sustainability (18 mo) with 1-mo washout period	N = 476 individual NTM exposure events with incidence of AKI 19.7% (n = 94/476) Systematic identification and daily SCr screening in high risk patients prevented 100 AKI episodes in 18-mo period Reduction in NTM exposures from 16.4 to 9.6 per 1000 patient-days (p = 0.03), reduction in percentage of NTM-AKI from 30.9% to 11% (p < .001), and reduction in AKI intensity from 9.1 to 2.9 per 100 susceptible patient-days (p < .001) while maintaining a high SCr surveillance rate.	Extension of IV aminoglycoside from 3 days to 4 or more days Definition of baseline SCr (first 14 days of life follow trends, after 14 days of life compare with lowest previous value) Semi-automated reporting system KDIGO criteria used
Newton 2021[32]	Cystic fibrosis patients (0 to 21 yr)	Automated screening report to identify patients with ≥3 NTMs within 24 hr or ≥4 calendar days of an IV aminoglycoside or vancomycin SCr screening 3 days a week in patients at high risk	Pre-implementation (4 mo) vs sustainability (4 mo) with no washout period	N = 19 patients with 25 NTM exposure events Increased SCr monitoring uncovered more episodes of AKI in the post-implementation phase	Used the pRIFLE criteria SCr screening 3 times weekly (Monday, Wednesday, Friday)

AKI, acute kidney injury; EHR, electronic health record; IV, intravenous; KDIGO, Kidney Disease: Improving Global Outcomes; N, number of patients; NICU, neonatal intensive care unit; NINJA, Nephrotoxic Injury Negated by Just-in-Time Action; NTM, nephrotoxic medication; pRIFLE, Pediatric Risk, Injury, Failure, Loss, and End-Stage Renal Disease; SCr, serum creatinine

closely monitor renal function as defined by the program, provide proactive therapeutic interchanges for infants with AKI, collaborate in multidisciplinary settings, and are proficient at analyzing complex health systems and electronic health records (EHRs).[43] To that end, early involvement of clinical pharmacists in Baby NINJA can aid in creating a systematic approach tailored to each unit's needs and work culture while increasing sustainability of the program. Further, the goals and outcomes of Baby NINJA overlap with antimicrobial stewardship programs. The primary goal of antimicrobial stewardship is to optimize clinical outcomes while minimizing unintended consequences of antimicrobial use. Additional benefits include improving susceptibility rates to targeted antimicrobials and optimizing resource use.[44] Some antimicrobial medications are also

nephrotoxic. The NINJA program's vision statement is that children should only get the NTMs they need for the duration they need them in order to avoid AKI, an unintended but real consequence of NTM.[30] These mutually beneficial initiatives feature clinical pharmacists in substantial roles with the opportunity to provide positive clinical resultsfor this at-risk population.

Use of the EHR for Baby NINJA can improve accuracy of identifying NTM exposure, reliably audit SCr, and potentially identify AKI events. Integration into the EHR can allow for screening to occur when core staff are not present, that is, nights and weekends. EHR documentation has also been used for communicating diagnoses and sharing recommendations. The Institute for Safe Medication Practices notes that implementation of information technology in medication use systems is widely accepted as a method of reducing human error but cautions that thoughtful implementation is required to provide appropriate support to end users.[45] Systematic automation is considered one of the top interventions for medication error reduction because screening is "hardwired" in the EHR to screen and identify.[46] Further, these benefits can increase buy-in from important stakeholders by reducing the time required for performing data collection.[47] When automation is not possible, empowering pharmacists to order SCr tests for Baby NINJA through a collaborative practice agreement leads to improved compliance in monitoring.[48] EHR tools such as pharmacy consult notes and pop-up alerts may be used to communicate to prescribers that patients have qualified for inclusion in Baby NINJA and provide staging information if AKI is identified. These tools can facilitate knowledge sharing amongst team members.[47,48] It is important for nursing staff to be educated on which medications are nephrotoxic, as well as patient-specific indications for use and intended duration of each NTM prior to administration. Their assistance is vital, because they can encourage adherence to these goals and prevent unwarranted administration of NTMs.

Communication is integral in any ICU and is important for the success of Baby NINJA. First, communication of infants at risk for AKI or those with an AKI diagnosis is imperative. Sharing a list of patients "on NINJA watch" proved challenging at the inception of the program. Physical alerts, including patient bed or door frame identifiers, are useful QI tactics; however, poor adherence to doors, loss of magnets or clings, and "sign fatigue" are barriers to effectiveness. Pharmacy consult notes recorded in the EHR can alert the medical team that NTMs are in use; daily SCr measurements will be obtained for inclusion in the Baby NINJA project, and the prescriber will be alerted if AKI is identified. These notes are helpful when this documentation is accessed, but this method requires active participation on the part of the prescriber(s). The most effective and sustainable communication found by the original Baby NINJA investigators was direct communication, with the aforementioned tactics used as adjunctive support. To encourage this, "Baby NINJA" was included in the daily checklist to review during nursing-led, multidisciplinary clinical rounds. Pharmacists who attend those rounds provide their formal recommendations, and any follow-up needed is directly communicated to the on-service advanced practice provider and/or physician. Second, updates from the overall QI program are important to support commitment amongst stakeholders. The NICU clinical practice team includes representatives from nursing, pharmacy, and the physician staff that play critical roles in patient care, while the Division of Neonatology provides administrative guidance and support for QI initiatives that involve frontline staff. Monthly updates should be provided to both groups to confirm validity of data, review QI metrics, examine outliers, formulate any clinical practice changes, and update institution-specific Baby NINJA goals. Program participants should be particularly attuned to other clinical practice or QI programs in the NICU that may have an effect on Baby NINJA, such as antimicrobial stewardship programs, analgesia initiatives, or other QI programs in which AKI is a factor of interest.

With increased screening for potential AKI events, prevalence is often found to be underestimated with an initial increase in rates following implementation of the Baby NINJA program.[11] While the Baby NINJA program does not dictate any clinical practice changes, appropriate therapeutic interchanges should be considered by the multidisciplinary team. Initial tactics include ensuring daily weights and volume of intake and output are accurately recorded, increasing the frequency of blood pressure monitoring, and/or initiation of near-infrared spectroscopy monitoring. The next step would be to create a formalized approach to mitigate the risks of NTMs, when clinically feasible, that is in congruence with a center's antibiogram and prescribing guidelines. For example, proactive inclusion of a stop date for NTM, timely removal of NTM based on culture sensitivities, increasing frequency of therapeutic drug monitoring, and/or changing to a less nephrotoxic agent. These methods, when used as part of a multidisciplinary approach, can potentially decrease the risk of NAKI or mitigate AKI severity. A step-by-step approach to Baby NINJA implementation is described in Table 4.

Conclusion

Neonatal AKI is a pervasive problem with potential for long-lasting clinical effect on patients. A modifiable risk factor for AKI in this patient population is exposure to NTM. Accurate identification of AKI events is needed to establish accurate AKI prevalence, quantify AKI risk level for each patient, and create follow-up

Table 4. Step-by-Step Implementation of Baby NINJA

Category	Steps
Secure buy-in from key stakeholders	1. Identify physician co-leaders from neonatology and nephrology. 2. Obtain approval from chief clinical officer and/or medication safety officer. 3. Discuss preliminary logistics with NICU clinical pharmacists and clinical informaticists. 4. Draft aim statements specific to the institution's goals and desired timeline to achieve them. 5. Inform antimicrobial stewardship representatives of plan to implement Baby NINJA. 6. Contact Baby NINJA Collaborative to alert of on-boarding status (scan QR code at right for details and contact information).
Operationalize	7. Select a go-live date. 8. Agree on clinical definitions of baseline SCr, whether UOP will be included, and any exceptions to obtaining daily SCr measurement such as for patients whose goals of care are palliative in nature. 9. Work with clinical pharmacy, clinical informaticists, and EHR representatives to integrate daily SCr ordering and monitoring in EHR if possible. Otherwise, decide who will be responsible for manually ordering daily SCr test. 10. Consider a collaborative practice agreement if applicable to facilitate clinical pharmacy's ability to order SCr test for Baby NINJA. Document this intervention as a Baby NINJA consult note in the EHR. 11. Determine whether data will reside in an Excel Spreadsheet (Microsoft) or RedCap (Research Electronic Data Capture; Vanderbilt University, Nashville, TN) and finalize data collection tool. 12. Launch Baby NINJA program.
Educate NICU staff	13. Provide nursing education regarding the importance of adhering to daily SCr screening, combining with regular daily laboratory tests and avoiding excessive accessing of central line, and blood waste reduction strategies. 14. Facilitate clinical pharmacists' understanding of data collection roles and responsibilities. 15. Distribute information to NICU prescribers regarding appropriate documentation of Baby NINJA qualification and/or development of AKI and escalation of concerns related to Baby NINJA. 16. Standardize communication strategies for clinical pharmacists to alert prescribers of Baby NINJA qualification and development of AKI.
Maintain	17. Monitor the process metric of SCr compliance and the 4 outcome metrics: NTM exposure prevalence rate, AKI prevalence rate, rate of NAKI (%), and AKI intensity rate. 18. Frequently communicate with stakeholders to determine how data collection, buy-in, etc., can be improved. 19. Provide monthly updates to the involved services to facilitate on-going dialogue regarding trends. 20. Continue to communicate with the Baby NINJA Collaborative for troubleshooting and ideas. 21. Create algorithmic approach to NTM-exposure reduction with clinical pharmacy and antimicrobial stewardship representatives.

AKI, acute kidney injury; EHR, electronic health record; NAKI, nephrotoxic acute kidney injury; NICU, neonatal intensive care unit; NINJA, Nephrotoxic Injury Negated by Just-in-Time Action; NTM, nephrotoxic medication; SCr, serum creatinine; UOP, urine outputs

plans for infants at risk of a subsequent episode of AKI. While limiting NTM exposure is the ideal solution, use of these medications may be required to achieve optimal clinical outcomes. Implementation of a comprehensive monitoring system for NAKI in the NICU, such as Baby NINJA, can positively affect kidney health among these vulnerable patients.

A multidisciplinary approach is needed to achieve success. Neonatal clinical pharmacists, in collaboration with neonatology and nephrology, play a key role in

this QI project. Further, pharmacists are well suited to provide consistent monitoring of renal function, offer therapeutic alternatives to NTM, recommend dosage adjustments when AKI is identified in this population, and provide the continuity required to conduct prospective research. EHR integration is a very useful tool that can improve accuracy of Baby NINJA data, increase efficiency, and improve integration of Baby NINJA into daily tasks. With the proper engagement and thoughtful use of available tools, Baby NINJA can be a highly effective strategy for mitigating AKI in the NICU.

Article Information

Affiliations. Department of Pharmacy (SBS), Children's of Alabama, Birmingham, AL; Department of Pharmacy (EB), Advocate Aurora Health, Park Ridge, IL; Clinical Operations Department (MSZ), Med Communications, Inc, Memphis, TN; Department of Pharmacy (FB), Hassenfeld Children's Hospital at NYU Langone Health, New York, NY; Department of Pharmacy (DW), Michigan Medicine, Ann Arbor, MI; Department of Pediatrics (CS), University of Alabama at Birmingham, Birmingham, AL

Correspondence. Sadie B. Stone, PharmD; sadie.stone@childrensal.org

Disclosure. The authors declare no conflicts or financial interest in any product or service mentioned in the manuscript, including grants, equipment, medications, employment, gifts, and honoraria.

Ethics Approval and Informed Consent. Given the nature of this study, the institution board/ethics committee review was not required.

Acknowledgment. The authors would like to acknowledge the hard work and dedication of all institutional members of the Baby NINJA Collaborate, led by Children's of Alabama, and the NINJA Collaborative, led by Cincinnati Children's Hospital. The authors would also like to acknowledge the hard work of NICU providers and nurses working in hospitals across the country to ensure this program is implemented and monitored successfully in our smallest patients.

Submitted. January 31, 2022

Accepted. December 27, 2022

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