

Improving Safety of Intravenous Prostacyclin Administration to Pediatric Patients With Pulmonary Hypertension

Julia McSweeney, MSN, RN, CPNP
Emily Rosenholm, MSN, RN, FNP
Katherine Penny, MSN, RN, WOCN, CPNP
Mary P. Mullen, MD, PhD
Thomas J. Kulik, MD

BACKGROUND Pulmonary hypertension is a rare, life-threatening disease with limited therapeutic options and no definitive cure. Continuous intravenous prostacyclin therapy is indicated for treatment of severe disease. These medications have a narrow therapeutic index and a brief half-life; therefore, administration errors can be lethal.

OBJECTIVE To reduce medication errors through an inpatient program to improve, standardize, and disseminate continuous intravenous prostacyclin therapy practice guidelines.

METHODS Data were collected from the electronic safety reporting system of a single hospital to determine the number and types of continuous intravenous prostacyclin therapy errors that were reported over an 8-year period. A clinical database and hospital pharmacy records were used to determine the number of days on which hospitalized pediatric patients received the therapy.

INTERVENTIONS A nursing-directed quality improvement initiative to enhance the safety of continuous intravenous prostacyclin therapy for pediatric patients was begun in January 2009. Efforts to improve safety fell into 4 domains: policy, process, education, and hospital-wide safety initiatives.

RESULTS The number of therapy errors per 1000 patient days fell from 19.28 in 2009 to 5.95 in 2016. Chi-square analysis was used to compare the result for 2009 with that for each subsequent year, with *P* values of .66, .35, .16, .09, .03, .12, and .25 found for 2010 through 2016, respectively.

CONCLUSIONS The trend in reduction of continuous intravenous prostacyclin therapy errors suggests that proactive processes to standardize its administration, emphasizing both policy and education, reduce medication errors and increase patient safety. (*Critical Care Nurse*. 2019;39[4]:e1-e7)

CE 1.0 hour, CERP B

This article has been designated for CE contact hour(s). The evaluation tests your knowledge of the following objectives:

1. Identify 2 high risks associated with continuous intravenous (IV) prostacyclin therapy.
2. List 2 errors associated with continuous IV prostacyclin therapy.
3. Describe 3 methods to standardize continuous IV prostacyclin administration and improve patient safety.

To complete evaluation for CE contact hour(s) for test C1943, visit www.ccnonline.org and click the "CE Articles" button. No CE fee for AACN members. This test expires on August 1, 2022.

The American Association of Critical-Care Nurses is an accredited provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation. AACN has been approved as a provider of continuing education in nursing by the State Boards of Registered Nursing of California (#01036) and Louisiana (#LSBN12). ©2019 American Association of Critical-Care Nurses doi:<https://doi.org/10.4037/ccn2019651>

Pulmonary hypertension is a rare, life-threatening disease with limited therapeutic options and no definitive cure. The condition is characterized by elevated pulmonary artery pressure, resulting in right-sided heart failure and premature death.¹ Continuous intravenous prostacyclin therapy (CIPT), including epoprostenol and treprostinil, is indicated for treatment of advanced disease.² These prostacyclin analogues are potent vasodilators that promote vascular remodeling and inhibit platelet activation.³ Because they have a narrow therapeutic index and a brief half-life, their abrupt discontinuation may result in life-threatening rebound pulmonary hypertension. Continuous intravenous prostacyclin therapy uses nonstandardized concentrations (because of weight-based dosing combined with ongoing dose titration and a fixed volume of infusate that can be routinely delivered on an outpatient basis), and the con-

Prostacyclin administration errors represent a considerable safety risk, particularly in tenuous pediatric patients, in whom even small errors can have serious hemodynamic consequences.

tinuous nature of the infusion poses a challenge as the patient is cared for

through the primary, secondary, and tertiary care settings. Prostacyclin administration errors are common and represent a considerable safety risk, particularly in tenuous pediatric patients, in whom even small errors can have serious hemodynamic consequences.⁴ A previous survey of 97 providers indicated that 68% of patients experienced prostacyclin errors, with 29% of errors resulting in serious adverse events, including 9 deaths.⁵

Authors

Julia McSweeney, Emily Rosenholm, and Katherine Penny are nurse practitioners, Cardiology Program, Boston Children's Hospital, Boston, Massachusetts.

Mary P. Mullen is Associate Director, Pediatric Pulmonary Hypertension Program, Boston Children's Hospital, and Assistant Professor of Pediatrics, Harvard Medical School, Boston.

Thomas J. Kulik is Director, Pediatric Pulmonary Hypertension Program, Boston Children's Hospital, and Assistant Professor of Pediatrics, Harvard Medical School.

Corresponding author: Julia McSweeney, MSN, RN, CPNP, Boston Children's Hospital, 300 Longwood Ave, Boston, MA 02115 (email: julia.mcsweeney@cardio.chboston.org).

To purchase electronic or print reprints, contact the American Association of Critical-Care Nurses, 101 Columbia, Aliso Viejo, CA 92656. Phone, (800) 899-1712 or (949) 362-2050 (ext 532); fax, (949) 362-2049; email, reprints@aacn.org.

Medication errors are the most common type of medical error and cost the United States approximately \$4 billion annually.⁶ According to the Agency for Healthcare Research and Quality, adverse drug events result in more than 770 000 injuries and deaths each year and cost up to \$5.6 million per hospital.⁷ The Joint Commission designated safe use of medications as a 2017 national patient safety goal.⁸ Errors that are most likely to result in serious outcomes include those involving intravenous medications, medications given in specialty areas (such as intensive care units), and medications with complex dosing regimens^{7,9}; CIPT meets all of these criteria. In addition, because pulmonary hypertension is a rare disease, particularly in the pediatric population, critical care nurses, prescribers, and pharmacy staff often have limited experience with both the medication and the associated ambulatory infusion pump.¹⁰

Given the frequency of prostacyclin errors and the considerable risk they pose to pulmonary hypertension patients, we sought to standardize and disseminate CIPT practice guidelines in an effort to reduce medication errors and increase patient safety. This initiative was spearheaded by the Pediatric Pulmonary Hypertension Program nurse practitioner staff in response to critical care nurses' request for greater knowledge regarding prostacyclin administration.

Methods

Data on CIPT errors reported during an 8-year interval (January 1, 2009-December 31, 2016) were collected from a computerized safety event reporting system (SERS). The SERS users (hospital staff directly or indirectly involved with patient care) anonymously submitted reports of errors and adverse drug events. Data reported included medication, patient location, and details of the error event. Data adequacy was ensured by SERS mandatory informational domains. Patient identifiers such as name, date of birth, and hospital identification number were not included, eliminating any ethical concerns about the quality improvement initiative. Events were classified as nonpreventable, possibly preventable, or definitively preventable.

The Pediatric Pulmonary Hypertension Program clinical database was used to determine the number of days on which hospitalized pediatric patients received CIPT from January 1, 2009, to December 31, 2010, as electronic medical records did not exist for this interval.

Pharmacy records were used for dates ranging from January 1, 2011, to December 31, 2016.

Interventions

Efforts to improve safety fell into 4 domains: policy, process, education, and hospital-wide safety initiatives.

Policy

Policies on CIPT administration were standardized, with separate policies developed for epoprostenol and treprostinil. Policies addressed processes including initiating medication, titrating dosage, and transitioning from epoprostenol to treprostinil. We also included recommendations on preferred intravenous access, method of infusate reservoir change, and patient monitoring. Common side effects and adverse reactions were noted. Supplies specific to each CIPT pump, including infusate reservoir, battery, extension tubing, filter, and central venous catheter cap, were listed. A clinical reference tool standardizing the process of safely switching a CIPT infusion between vascular access devices (eg, from peripheral intravenous catheter to central venous catheter and vice versa) was created, with separate tools for epoprostenol and treprostinil. Policies were reviewed every 2 years, and relevant changes were made with the approval of the hospital's Cardiovascular and Critical Care Policy and Practice Committee.

A clinical algorithm was created for management of febrile pulmonary hypertension patients receiving CIPT by means of a chronically indwelling central venous catheter. Additionally, a clinical reference tool intended for emergency department staff was developed to standardize the care of patients receiving CIPT with central venous catheter dysfunction.

Process

Templates for CIPT order sets were created, with separate order sets for epoprostenol and treprostinil. Order set templates included type of pump (CADD-Legacy pump [Smiths Medical], Crono Five pump [InfuSystem], or hospital pump), dosing weight (kilograms), dose (nanograms per kilogram per minute), concentration (nanograms per milliliter), additive dose of reservoir (total number of nanograms per syringe or cassette), and pump rate (milliliters per day or milliliters per hour, depending on pump type). In addition, timing of pump change and requirement for ice packs were noted. In

accordance with the hospital's high-risk medication standard, signatures of 2 nurses were required in the electronic medical record when initiating prostacyclin or changing the infusate reservoir.

A triple-check system was used for admission of patients receiving CIPT on an outpatient basis. The prescriber, pharmacist, and nurse were required to review the CIPT dose and pump settings with the patient and/or family, personally visualize the prostanoid pump to confirm settings, and call the providing specialty pharmacy to verify CIPT information.

Education

Mandatory education on pulmonary hypertension and CIPT was provided to all new incoming cardiovascular nursing staff members. In addition, annual prostanoid pump education and competency evaluation were made mandatory for existing cardiovascular nursing staff. Both verbal and practical prostanoid pump education was provided to nursing staff at least annually, with mandatory annual hands-on prostanoid pump competency evaluation. Written and videotaped resources were created for each intravenous prostanoid pump. These resources

provided **Written and videotaped resources were made readily available to nurses online, in a binder on the inpatient units, and in the medication room by means of printouts.**

by-step directions for programming the pump, preparing the infusate, priming the extension tubing, initiating the infusion, and ending the infusion. Important practical tips were included such as triaging pump alarms, how to check the pump rate with the pump actively infusing, and how frequently to change the batteries. These resources were made readily available to nurses online, in a binder on the inpatient units, and in the medication room by means of printouts for written materials and smartphone QR codes for videotaped materials. These efforts were combined with multidisciplinary education targeting staff members who were likely to encounter CIPT patients.

Hospital-Wide Safety Initiatives

Hospital-wide safety initiatives were also instituted and may have affected CIPT error rates. The pharmacy department implemented unique labels, such as "tall-man"

Table 1 Severity level of continuous intravenous prostacyclin therapy errors

Severity level	Category	Definition	No. of events							
			2009	2010	2011	2012	2013	2014	2015	2016
0	Near miss	An event that was intercepted before reaching the patient	0	0	0	1	0	1	0	0
1	None	No harm; no change in condition; may have required monitoring to assess for potential change in condition; no intervention indicated	4	2	1	1	1	1	1	1
2	Minor	Transient change in condition; not life-threatening; condition returns to baseline; required monitoring; required minor intervention such as holding a medication, obtaining laboratory values, or applying heat/cold	3	1	0	0	0	1	0	0
3	Moderate	Transient change in condition; may be life-threatening if not treated; condition returns to baseline; required monitoring such as a reversal agent, additional medication, or transfer to ICU	0	0	0	0	0	0	0	0
4	Major	Change in condition; life-threatening if not treated; change in condition may be permanent; may have required initial admission or readmission to hospital; may have required transfer to ICU; required monitoring; required major intervention such as invasive procedure, intubation, hemodynamic support, or blood product transfusion	0	0	0	0	0	0	0	0
5	Catastrophic	Death	0	0	0	0	0	0	0	0

Abbreviation: ICU, intensive care unit.

lettering (writing part of a drug's name in capital letters), to reduce confusion surrounding sound-a-like or look-a-like medications. In addition, an electronic barcode medication administration system was successfully executed. Finally, the Red Zone patient safety initiative was employed, in which behavioral and environmental changes were implemented to ensure distraction-free time during all phases of medication preparation and administration.¹¹

Results

Pediatric pulmonary hypertension patients received CIPT for a total of 2326 days while hospitalized from January 1, 2009, to December 31, 2016. There were 469 days of epoprostenol infusion and 1857 days of treprostinil infusion. Twenty-two errors were reported by SERS users, but 3 errors were excluded because of inappropriate classification and insufficient documentation. A total of 19 errors were analyzed and deemed preventable by the SERS reporter, of which 17 were classified as definitively preventable and 2 were classified as possibly preventable. There were 2 "near miss" SERS events, 12 level 1 events, and 5 level 2 events. There were no level 3, 4, or 5 events (Table 1). No error was associated with patient adverse events. One patient complained of chest pain at

the time of an error, but there was no clinical correlate. Although all errors involved pediatric patients, these errors were not unique to the pediatric population and could occur at any adult institution treating pulmonary hypertension patients with CIPT.

The annual CIPT error rate was determined for 2009 through 2016 and expressed as CIPT preventable errors per 1000 patient days (Table 2). The CIPT error rate decreased by 69% from 2009 to 2016 (see Figure). The nadir of preventable errors occurred in 2013, when the CIPT error rate was 80% lower than in 2009, the first year of the program to enhance CIPT safety. The CIPT error rate appeared to rise appreciably in 2016, but in fact only 1 error occurred that year. The higher rate was due to a drop in the total number of inpatient CIPT days because of increased use of inhaled, subcutaneous, and oral prostacyclin in our pediatric patients.

Chi-square analysis was used to determine the statistical significance of the results, comparing 2009 with each subsequent year, with *P* values of .66, .35, .16, .09, .03, .12, and .25 found for 2010 through 2016, respectively. The variability of the statistical significance throughout the 8 years analyzed was due largely to the inconsistency and relatively low numbers of CIPT days. The largest

Table 2 Continuous intravenous prostacyclin therapy: preventable errors

Year	Total CIPT days	No. of errors	Preventable errors per 1000 patient days	Patient location at time of error				
				Emergency department	Interventional radiology	Cardiology ward	Cardiac ICU	Medical-surgical ICU
2009	363	7	19.28	0	0	4	2	1
2010	210	3	14.29	0	0	0	2	1
2011	137	1	7.30	0	0	0	0	1
2012	302	2	6.62	1	0	0	1	0
2013	265	1	3.77	0	0	0	1	0
2014	646	3	4.64	0	1	0	1	1
2015	235	1	4.26	0	0	1	0	0
2016	168	1	5.95	0	0	1	0	0

Abbreviations: CIPT, continuous intravenous prostacyclin therapy; ICU, intensive care unit.

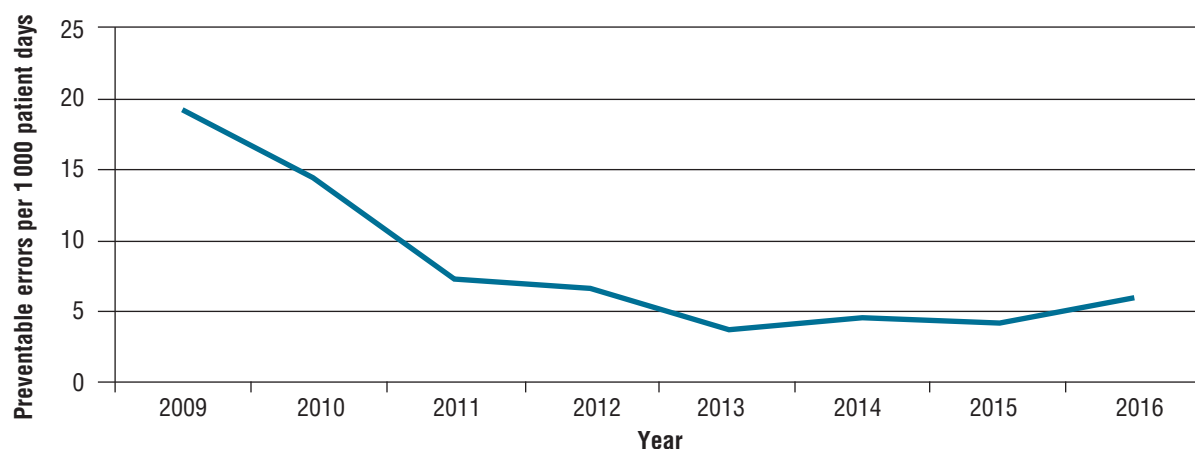


Figure Preventable continuous intravenous prostacyclin errors.

number of CIPT days was in 2014, close to the error rate nadir, with a statistically significant *P* value of .03.

Root cause analysis was performed for the 19 CIPT errors reported (Table 3). Inappropriate or missing CIPT orders accounted for 4 of these errors. The most common order error was provider prescription based on the patient's actual weight rather than the standardized CIPT dosing weight. Root cause analysis attributed these errors to prescriber knowledge deficit, and process and education initiatives were undertaken to address this problem. Process improvements included standardization of CIPT orders, which required prescribers to include all essential information in order to appropriately and accurately complete the order. Prescriber education took place in the form of in-service training, targeting prescribing physicians and nurse practitioners, especially those new to the service.

Three errors occurred on hospital units that were unfamiliar with CIPT administration, and the root cause was also attributable to staff knowledge deficit. In one circumstance, intravenous fluids were piggybacked into a vascular access device infusing CIPT. In another, intravenous fluids were administered through a vascular access device that previously infused prostacyclin and had residual medication within the length of the line. Policy and education initiatives targeted this problem. Detailed CIPT administration policies were standardized and made available to all hospital staff. Multidisciplinary education initiatives targeted staff members outside of the Cardiology Program who were likely to encounter CIPT patients. Emergency department staff members received in-service training, and clinical algorithms for CIPT administration were created for them. Medical-surgical intensive care unit nurses and staff members

Table 3 Continuous intravenous prostacyclin therapy (CIPT): error root cause analysis

Year	Type of CIPT error				
	Inappropriate or missing CIPT order	Hospital unit inexperienced with CIPT	Lack of adherence to administration policy	Lack of adequate drug supply	Human error
2009	1	1	0	3	2
2010	0	1	1	1	0
2011	0	0	0	1	0
2012	1	0	0	0	1
2013	1	0	0	0	0
2014	1	1	1	0	0
2015	0	0	0	1	0
2016	0	0	0	1	0
Total	4	3	2	7	3

were trained through slide presentations as part of their education day. Postanesthesia care unit and anesthesia nurses and staff members were educated by means of in-service training.

Two errors were associated with lack of adherence to administration policy. For example, in one case the CIPT reservoir volume was not assessed at the recommended interval, resulting in unintentional disruption of CIPT. Root cause analysis attributed these errors to nurses' lack of awareness that there was a policy, or lack of knowledge regarding the policy specifics. Education emphasizing policy practices was made mandatory for all incoming

The most common order error was provider prescription based on the patient's actual weight rather than the standardized CIPT dosing weight.

cardiovascular critical care nursing staff, with annual education and competency

evaluations for existing staff. Processes were put in place whereby 2 nurse signatures were required for the initiation of CIPT or reservoir change, with a triple-check system used with hospital admission of a patient receiving CIPT, ensuring that a single provider unfamiliar with policy cannot initiate CIPT.

Lack of adequate and timely drug supply accounted for 7 of the reported CIPT errors. Examples of these errors were nurses' not requesting the infusate from the pharmacy department in a timely manner, pharmacists' not preparing the infusate in a timely manner after receiving the request, and the infusate not being readily available for a patient's scheduled CIPT reservoir change. Root cause analysis attributed these errors to inadequate organizational processes. Orders for CIPT did not make note of the time the CIPT reservoir was needed, and the

medication could be processed and prepared by any pharmacy staff member (some of whom were not aware of the time-sensitive nature of prostacyclin orders). Process initiatives targeted these errors. Reservoir changes were standardized to occur during the day (between 7 AM and 7 PM) when possible, and the exact timing of the change was noted on the templated order set. Pharmacy staff were included in the triple-check process for hospital admission of CIPT patients, and a core group of pharmacists familiar with CIPT were given responsibility for its preparation.

Three errors were associated with human error. One such error occurred when an infusion was ordered at a dose of 111 ng/kg per minute, when the correct dose was 11 ng/kg per minute. Computerized autocalculation was introduced to determine medication concentration and infusion rate to minimize risk related to perhaps the most error-prone part of the process of ordering these unusual medications.

It is possible that the trend of CIPT error reduction is attributable not to the described safety initiatives but rather to reporting bias. This is unlikely, however, as the hospital has strongly emphasized error reporting as part of its high-reliability program. Furthermore, there was no appreciable reduction in the number of hospital-wide errors reported during the time frame covered in this report. No error was associated with a serious patient adverse event, and a trend was noted of decreasing event severity level over the 8-year time frame.

Conclusion

The initiation of multiple robust processes to standardize and disseminate CIPT practices was associated with a substantial and progressive decline in medication

errors by roughly 69% over the course of 8 years. Of those errors reported, a trend was noted of decreasing event severity level over the 8-year time frame. Examination of errors that occurred from 2009 through 2016 suggests that ongoing safety-improvement efforts are warranted regarding prescriber practices and pharmacy provision of CIPT in a timely manner. Although it is not possible to establish a cause-and-effect relationship between our efforts to improve practice and the reduction in CIPT errors, aggressive proactive processes to standardize CIPT administration at our hospital were associated with a significant reduction in medication errors and increased patient safety. A multifaceted approach emphasizing policy, process, and education may be optimal. **CCN**

Financial Disclosures
None reported.



Now that you've read the article, create or contribute to an online discussion about this topic using eLetters. Just visit www.ccnonline.org and select the article you want to comment on. In the full-text or PDF view of the article, click "Responses" in the middle column and then "Submit a response."

See also

To learn more about pediatric care, read "Long-Term Effects of Saline Instilled During Endotracheal Suction in Pediatric Intensive Care: A Randomized Trial" by McKinley et al in the *American Journal of Critical Care*, November 2018;27:486-494. Available at www.ajconline.org.

References

1. Badesch DB, Abman SH, Simonneau G, Rubin LJ, McLaughlin VV. Medical therapy for pulmonary arterial hypertension: updated ACCP evidence-based clinical practice guidelines. *Chest*. 2007;131(6):1917-1928.
2. Abman SH, Hansmann G, Archer SL, et al. Pediatric pulmonary hypertension. *Circulation*. 2015;132(21):2037-2099.
3. McLaughlin VV, Archer SL, Badesch DB, et al. ACCF/AHA 2009 expert consensus document on pulmonary hypertension: a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association, developed in collaboration with the American College of Chest Physicians; American Thoracic Society, Inc.; and the Pulmonary Hypertension Association. *Circulation*. 2009;119(16):2250-2294.
4. Penny K, Marr C, McSweeney J. Utilization of the Q-Syte Split-Septum needleless access device in pediatric pulmonary patients receiving continuous intravenous prostacyclin therapy. Poster presented at: Northeast Pediatric Cardiology Nurses Association; Restoring Effective Circulation in the Pediatric Patient; Washington, DC; March 16, 2016.
5. Kingman MS, Tankersley MA, Lombardi S, et al. Prostacyclin administration errors in pulmonary arterial hypertension patients admitted to hospitals in the United States: a national survey. *J Heart Lung Transplant*. 2010;29(8):841-846.
6. Food and Drug Administration. Food and Drug Administration Safe Use Initiative Fact Sheet. May 6, 2015. <https://www.fda.gov/media/116625/download>. Accessed March 16, 2016.
7. Duthie E, Favreau B, Ruperto A, Mannion J, Flink E, Leslie R. Quantitative and qualitative analysis of medication errors: the New York experience. In: Henriksen K, Battles JB, Marks ES, Lewis DI, eds. *Advances in Patient Safety: From Research to Implementation*. Vol 1: Research Findings). Rockville, MD: Agency for Healthcare Research and Quality; 2005:131-146.
8. The Joint Commission. The Joint Commission National Patient Safety Goals Effective January 2017. https://www.jointcommission.org/assets/1/6/NPSG_Chapter_HAP_Jan2017.pdf. Accessed March 17, 2017.
9. Hicks R, Cousins D, Williams R. Summary of information submitted to MedMarx in the year 2002: the quest for quality. Paper presented at: US Pharmacopeia; 2003; Rockville, MD. https://www.eurekalert.org/pub_releases/2003-11/up-urf111403.php. Accessed March 17, 2016.
10. Kingman MS. Safety recommendations for administering intravenous prostacyclins in the hospital. *Crit Care Nurse*. 2013;33(5):32-39.
11. Connor JA, Ahern J, Cuccovia B, et al. Implementing a distraction-free practice with the red zone medication safety initiative. *Dimens Crit Care Nurs*. 2016;35(3):116-124.