Reducing unnecessary nitric oxide use: a hospital-wide, respiratory therapist-driven quality improvement project

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Previous Presentations

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Abstract

Objective: Evaluate institutional use of inhaled nitric oxide (iNO) and create a pathway to reduce waste using the Institute for Healthcare Improvement's model for improvement. Our SMART aim was to reduce the use of iNO by 20% within 8 months.

Setting: Quaternary care, children's hospital intensive care units.

Design: Prospective, respiratory therapist-driven quality improvement project**.** We implemented a hospital-wide iNO utilization protocol that was developed by neonatology, pediatric critical care and cardiac critical care, and respiratory therapy. iNO use and respiratory therapist input for protocol 'failures' were derived from the electronic medical record and used to generate improvement opportunities. Monthly total hospital hours use of iNO was used as primary outcome measure. Median hourly use per subject (evaluated in groups of 7 subjects) was used as secondary outcome measure. New sildenafil dosing was tabulated for pre- and post-iNO weaning protocol intervention as a balancing measure.

Subjects: All subjects in the hospital who were given iNO therapy during the specified time-frame.

Interventions: Novel hospital-wide, respiratory therapist-driven iNO utilization protocol

Measurements and Main Results: Hospital-wide total hours were reduced from 1515 hours/month to 930 hours/month. This hospital-wide reduction of 39%, equates to a cost-avoidance of approximately $912,000 per year based on 2018 costs of $130 per hour. Median hours of iNO per subject decreased from 88 hours to 50 hours. Sildenafil was started on 18 of 98 subjects (18%) in the pre-intervention period and 12 of 109 subjects (11%) in the post-intervention period, p=0.27.

Conclusions: A hospital-wide, multi-professional initiative can be implemented and lead to reduction in unnecessary iNO use resulting in decreased subject exposure and associated cost-avoidance.

Introduction

Inhaled nitric oxide (iNO) is a potent vasodilator that critical care teams leverage to reduce pulmonary vascular resistance. There are a multitude of clinical conditions in which reducing pulmonary vascular resistance may augment pulmonary blood flow and optimize ventilation/perfusion matching and improve oxygenation.[1] For over two decades now, multiple studies have attempted to show improved outcomes in pediatric subjects with heart and/or lung diseases including acute respiratory distress syndrome, bronchopulmonary dysplasia, and pulmonary hypertension who were treated with iNO.[2-7]

Despite the lack of conclusive evidence regarding its efficacy for certain conditions, iNO is commonly used in intensive care units. iNO is an expensive medication that does have toxicity associated with its use.[8,9] For these reasons, quality improvement initiatives have been created and implemented protocols for the initiation and weaning of iNO.[9-13] While there is no nationally accepted and validated weaning protocol, many of these studies showed that implementing a weaning protocol was safe, and effectively decreased the duration of nitric oxide therapy and decreased its associated costs. These studies were performed in single, isolated neonatal, pediatric, or cardiac intensive care units and were often physician-driven.

The aim of this multi-professional, respiratory therapist-driven, hospital-wide quality improvement project was to reduce iNO use by 20% within 8 months after protocol implementation.

Materials and Methods

Study Setting and Subjects

This study was performed at a large, academic, quaternary children's hospital, Riley Children's Hospital at Indiana University Health, Indianapolis, Indiana, USA. The study was reviewed and exempted by the Indiana University institutional review board as a quality improvement project prior to implementation. The study was implemented in the neonatal ICU, pediatric PICU, and pediatric cardiac ICU. Each of the units has a separate intensive care physician group and respiratory therapy team, although some members of the respiratory therapy team do overlap unit coverage. ECMO can be performed in all three intensive care units if needed. Any subject regardless of age or underlying condition that was started on iNO therapy in any of the ICUs was eligible for the RT-driven iNO weaning protocol. All subjects received acute iNO therapy through an endotracheal tube while mechanically ventilated or with a heated, humidified, high-flow nasal cannula system as the iNO delivery method.

Plan-Do-Study-Act (PDSA) Cycles

Using the model for improvement methodology we evaluated institutional use of iNO and created a pathway to reduce waste. The project team began analyzing hospital-wide iNO use in January 2018. Initiation criteria for iNO therapy was left to the treating team with a starting dose of 20 parts per million (ppm). Prior to project initiation, there was no standard for weaning or cessation of iNO. The project team came to two conclusions regarding our institutional use of iNO. First, the largest opportunity to reduce unnecessary iNO use was related to the inconsistencies in the duration and cessation of iNO therapy as weaning was variable with regards to interval and dose. Second, our subject selection for treatment with iNO was appropriate and further efforts to improve this would be of low value. (This determination was made on the basis that there are few true indications for iNO therapy. Regarding the pediatric ICU population, the PALICC guidelines describe iNO therapy as a supplemental therapy for refractory hypoxemia that is not routinely recommended.[14] The neonatal ICU uses iNO therapy

for new patients with congenital diaphragmatic hernia, or severe refractory hypoxemia due to meconium aspiration or persistent pulmonary hypertension of the newborn. The cardiac ICU uses iNO primarily for acute treatment of pulmonary hypertension related to underlying congenital heart disease. The project leadership team, which included members from all three ICUs, concluded that the decision to initiate iNO therapy was not a variable that required further standardization.) Figure 1 shows the key driver diagram for this project. The elements of the project were: (1) start iNO therapy consistently at 20 ppm, (2) institute objective criteria to initiate weaning, (3) follow a set weaning protocol for interval and dose of iNO, (4) have a definitive plan for discontinuing iNO therapy with criteria for re-initiating if the subject did not tolerate discontinuation.

PDSA Cycle 1: Protocol development, staff education, and protocol initiation

Starting July 2018, relevant literature was reviewed to identify safe and effective practices for iNO weaning across neonatal and pediatric populations.[10,15,16] Subjects who were started on iNO and had no perceived benefit could be taken off therapy per clinician discretion and did not necessarily have to follow the weaning protocol. For subjects who had a perceived benefit and remained on iNO therapy, criteria to wean were defined as FiO2 less than or equal to 60% and pulse oximetry meeting subject-specific goals that included inherent flexibility to accommodate for cyanotic cardiac lesions. Subjects had cardiopulmonary monitoring parameters (pulse oximetry, heart rate, systolic, diastolic, and mean arterial blood pressures) established as part of their general ICU care. Subjects were screened every six hours and if criteria were met, then weaning occurred in a stepwise approach (at 12 am, 6 am, 12 pm and 6 pm) as follows: 15 ppm, 10 ppm, 5 ppm, 2.5 ppm, and off (Figure 2). Criteria for wean failure were a decrease in pulse oximetry below goal for more than 10 minutes despite increasing FiO2, a decrease in arterial pressures below goal or increase in central venous/atrial pressure

or pulmonary artery pressures (if applicable) for more than 10 minutes in response to a change in iNO dose. If weaning failure occurred, the subject was placed back on the previously tolerated dose and not necessarily the starting dose of 20 ppm. If failure occurred while weaning to off, iNO was restarted at 5 ppm.

Once the protocol was agreed upon by the project team, it was disseminated to the intensive care physicians by short educational workshops followed by regular interval updates (every 1-2 months). Educational workshops were also done for the respiratory therapy groups in each unit. Once education and small-scale testing were completed, the protocol was initiated in October 2018.

PDSA Cycle 2: Respiratory Therapist Bedside Cards

An audit of the weaning pathway from October and November 2018 showed the majority of failed opportunities were due to poor awareness of the details of the protocol among the clinician and respiratory therapy teams (Figure 3). The project team noted that when more experienced respiratory therapists, or those who were directly involved in the protocol's development were the bedside therapist, there was a higher level of compliance with the protocol. The same was true for the medical teams, with higher compliance by those who were directly involved with the protocol development. Compliance also seemed higher initially in the pediatric ICU and neonatal ICU than in the cardiac ICU. The project team met to discuss ideas to address these barriers. A laminated bedside card that contained the weaning criteria and weaning schedule was placed on each iNO tank as a reminder to the bedside nurse, clinician team, and primarily the respiratory therapist that the subject who is receiving iNO should be on the weaning protocol (Figure 2). These cards were in open view of the respiratory therapist at the time of iNO initiation as a level of reliability 1 intervention. Informal, post-intervention

feedback was that these cards were helpful for the respiratory therapists as a reminder both that the subject should be on the protocol, and how the protocol was to be conducted.

PDSA Cycle 3: Weekly Huddle

In February 2019 we implemented a weekly huddle on Tuesday mornings at 8 am where a representative from the project team would meet with on-service physicians as well as respiratory therapy representatives from the neonatal ICU, pediatric ICU and cardiac ICU teams. During this brief huddle the team discussed subjects who were currently on iNO therapy, if the weaning protocol had been implemented, and if not, barriers for its implementation. This huddle served to provide education for the representatives as to the details and goals of the protocol and to inform the project team what barriers were being encountered.

PDSA 4: Electronic medical record order link

The iNO order set had been built during the planning phase prior to the protocol implementation. A pitfall in the iNO order set was discovered that when the iNO was ordered it was not automatically linked with order to initiate the weaning protocol. There was a lack of awareness among the medical providers about the need to simultaneously order the iNO medication and the weaning protocol. Contemporaneous with PDSA 3, PDSA 4 was a designed level of reliability 2 intervention linking the ordering of iNO to the order to start the iNO weaning protocol in the electronic medical record. This eliminated provider error and oversight.

Study Measurements and Statistical Analysis

Pre-implementation data was obtained retrospectively from January to September 2018, and post-implementation data was obtained prospectively through manual electronic chart review from October 2018 to August 2019. Project data was collected and managed using REDCap,[17,18] database electronic data capture tool hosted at Indiana University and included subjects' total hours of iNO use, primary diagnosis necessitating iNO therapy, ICU in which the subject received care, and sildenafil use. Monthly total hospital hours of iNO was used as the primary outcome measure. To account for varying numbers of subjects using iNO per month, median hourly use per subject (evaluated in groups of 7) was used as a secondary outcome measure. The study goal was a reduction of iNO total hospital use by 20% within 8 months of protocol implementation. Both outcome measures were evaluated using statistical process control charts created using QI Macros add-in for Excel Version 2018.09 (KnowWare International, Denver, CO). The upper control limit and lower control limit were calculated as three-sigma above and below the center line. Shift in the center line was performed when there were eight consecutive points above or below the center line. New sildenafil dosing was tabulated for pre- and post-iNO weaning protocol implementation as a balancing measure, and the proportions were compared using a chi-squared test. Project updates were given at regular intervals to different ICU quality and safety committees, as well as during physician faculty meetings.

Results

Ninety-seven subjects were included in the pre-implementation analysis. The protocol was implemented and data collected on 110 subjects. Table 1 shows the breakdown of patient demographics, diagnoses, and subject location. Following protocol implementation, the mean total hospital iNO use decreased from of 1515 hours per month to 930 hours per month (Figure 4). The per subject mean iNO use decreased from 88 hours/subject to 50 hours/subject (Figure

5). There was a period of special cause variation in the median use group that occurred at the end of August 2018. Upon review of the subjects at that time, there were 3 subjects admitted within several days of each other to the NICU with severe congenital diaphragmatic hernia. Contemporaneously, the CVICU had 2 subjects with severe pulmonary hypertension. All 5 of these subjects had prolonged use of iNO. The total iNO hours and number of subjects receiving iNO did not meet special cause variation during this time.

Safety data was obtained regarding mortality and hospital length of stay both prior to protocol implementation and following protocol implementation. The median hospital length of stay prior to protocol implementation was 35 days, and post protocol implementation was 36.5 days, which was not significantly different (p= 0.87). The mortality rate in our population prior to protocol implementation was 18.56% (18/97), and following protocol implementation was 18.18% (20/110), which was not significantly different (p=0.99). These comparisons illustrate that no increase in mortality or hospital length of stay was seen following protocol implementation.

The monthly number of subjects receiving iNO did not change over the course of the project (Supplemental Figure 1). Based on our results, the actual reduction of total hospital iNO use was 39% within 9 months of protocol implementation. When adjusting for the total number of subjects utilizing inhaled nitric oxide, the actual reduction of iNO hours use per subject was 43%. Regarding the balancing measure, new sildenafil use did not change after protocol implementation; 18% (18 of 98 subjects) compared to 11% (12 of 109 subjects) (p=0.27), respectively.

During the time of this study, the hospital charge was $130 per hour of iNO use. Based on the pre-implementation data, a total charge of $196,950 per month is calculated for iNO use. Using the post-implementation data, a total charge of $120,900 per month is obtained. Extrapolating this data to a yearly amount results in a yearly hospital charge savings of

$912,600. At the per subject level, the average charge prior to protocol implementation was $11,440 compared to $6,500 post-implementation, resulting in an average savings of $4,940 per subject.

Discussion

The specific aim of this project was to decrease the utilization of iNO in our institution by 20% within 8 months of protocol initiation. We ultimately achieved a decrease of 39% within 9 months of protocol initiation. At 8 months' time we lacked the statistical ability to shift our center line, thus we stretched our data collection to 9 months. To our knowledge, this is the first standardized iNO weaning protocol to be applied to an entire hospital's intensive care units. The creation of this protocol had unique challenges inherent to such a widespread application. The subject populations which are typical recipients of iNO varied greatly across the ICUs. Neonatologists treating subjects with severe bronchopulmonary dysplasia, or congenital diaphragmatic hernias and pulmonary hypoplasia had a culture and personal experience in utilizing iNO that was slightly different that the general pediatric intensivists who utilized iNO primarily for subjects with severe ARDS. Adding the pediatric cardiac intensivists who utilized iNO mainly for pulmonary vasodilation in subjects with congenital cardiac lesions or pulmonary vascular abnormalities brought another layer of complexity. This heterogeneity added complexity to the creation and design of the protocol and precipitated several face-to-face meetings with unit leadership to identify the needs of each separate unit and establish buy-in by unit leadership. Even with these efforts in place prior to protocol implementation, there were several steps required to improve adherence to the process.

As modern healthcare provides increasing amounts and varieties of diagnostic tests and therapeutic interventions, there is also increasing risk of overuse.[19] Overuse of iNO is not only

an expensive waste of hospital resources, but may also adversely impact patient outcomes. Our goal was not to limit the amount of medication provided to subjects who required or benefited from iNO, but to decrease the amount provided to subjects who no longer needed it.

The success of the protocol was demonstrated by the profound reduction in total hospital use, as well as per subject use. The cost avoidance was nearly a million dollars per year. If similar results could be seen in other institutions utilizing this protocol, the widespread cost-savings could be beneficial to national and global healthcare systems as we seek to decrease the large burden of healthcare associated costs. The reduction in practice variation from instituting a protocolized weaning method led to a more efficient process than deciding on a case by case basis.[9-11] The dramatic scale of cost reduction seen in this study is likely due to the scope of the intervention being on a hospital-wide level, as opposed to the individual units on which prior studies were conducted.[9,11,13] Physician providers have a very wide spectrum of responsibilities throughout a hospital workday, and this practice is often amplified in an ICU setting. Allowing the respiratory therapists to take ownership of this process and integrate it seamlessly into their daily workflow is what likely made the largest contribution to the success of the protocol. Previous studies have shown that respiratory therapist-driven protocols and interventions can contribute significantly to the safety and subject flow of an ICU.[19,20] This provides another example of how empowering the entire subject care team can lead to significant improvement in the care of individual subjects.

One concern that we had was the potential for trading decreased use of iNO for increased use of alternative pulmonary vasodilator therapies. Our institutional preference for first line therapy is phosphodiesterase inhibitor (sildenafil), another expensive and potentially toxic therapy. For this reason, we chose sildenafil use as our balancing measure. The general practice for sildenafil use in our institution is variable. The majority of patients receiving it are cardiac ICU patients who have evidence of severe pulmonary hypertension. However, there is

currently no standard in our institution as to which patients receive it. It is decided on a case-by-case basis with input from the institutional pulmonary hypertension team. While the percentage of subjects being started on sildenafil was lower post-protocol, the use of sildenafil was not significantly different on pre- vs. post- analysis. It is possible that the increased emphasis on weaning subjects from iNO therapy actually led to fewer subjects requiring it for a prolonged course, and this may have led to fewer subjects being started on sildenafil for inability to wean iNO. Our institutional use of alternative pulmonary vasodilator therapies such as inhaled, intravenous or subcutaneous prostaglandins and endothelin-1 antagonists is minimal.

There are several limitations to this study. The first is that while multiple ICUs were involved throughout the hospital, it is a single center study that may have center-specific practices that were more or less responsive to the implemented changes than would be seen at other institutions. Another potential limitation is that although our neonatal ICU is a completely separate unit staffed by neonatologists and unit specific respiratory therapists, our pediatric ICU and cardiac ICU are closely tied with attending physicians all under one division and respiratory therapists from one pool that staff both the pediatric ICU and cardiac ICU. This made the education of staff and implementation of the protocol easier than if there were three separate physician and respiratory therapy groups.

Conclusion

A hospital-wide, standardized, respiratory therapist-driven protocol for the use and weaning of inhaled nitric oxide was effectively implemented resulting in a decrease in unnecessary inhaled nitric oxide use. This represents a potential, substantial opportunity for other centers to utilize a similar protocol to achieve a safe and effective means to standardize the use and discontinuation of inhaled nitric oxide therapy.

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Quick Look

Current Knowledge

Inhaled nitric oxide is an expensive therapy used in neonatal intensive care units, pediatric intensive care units, and cardiac intensive care units. While some patients show rapid improvement with this therapy, many are treated for longer than necessary. Previous quality improvement studies have reported success implementing nitric oxide weaning protocols within an intensive care unit.

What This Paper Contributes to Our Knowledge

This paper reports the first hospital-wide inhaled nitric oxide implementation and weaning protocol utilized by all three intensive care units in a large, quaternary pediatric

academic medical center. This utilization protocol was found to be safe for patient care, translatable across separate intensive care units, and resulted in a profound decrease in the amount of nitric oxide used by the hospital.