Improving the Timeliness of Chemotherapy Administration in the Bone Marrow Transplant Unit

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Abstract

Patients undergoing hematopoietic stem cell transplantation (HSCT) are often admitted to the hospital the day they are due to begin their conditioning regimen. Timely initiation of chemotherapy during regular work hours is important for patient safety, because during the night shift fewer physicians and pharmacists are available for urgent or unexpected matters. A review of the data at our institution from October 2017 to August 2018 showed that approximately one-third of our chemotherapy was started during the night shift (after 19:00), and the average time from admission to start of chemotherapy was over 8 hours. There are currently no well-defined benchmarks for timeliness of chemotherapy initiation. The aim of this quality improvement initiative was to increase the percentage of patients who start chemotherapy in the bone marrow transplant unit before 19:00 from 65% to >80% by March 31, 2019. We identified barriers to timely initiation of chemotherapy through process mapping and analysis of failures. The primary barriers were late admissions (after 12:00 pm) and time from admission to preparation of chemotherapy. We addressed mechanisms to mitigate these barriers through Plan-Do-Study-Act testing. Interventions included providing families specific admission times and their rationales and process for notifying pharmacy of admissions immediately on arrival. We used standardized control charts to measure the impact of the interventions on change. We also monitored medication errors before and during the intervention. From September 2018 to March 2019 the percentage of patients who started preparative chemotherapy before 19:00 increased from 65% to 85%, the percentage of patients who were admitted after 12:00 remained similar before (31%) and after the
interventions (33%), and the average time from admission to start of chemotherapy decreased from 8.6 hours (513 minutes) to 6.4 hours (382 minutes). Medication errors were similar before (n = 50) and after the interventions (n = 43). Using standardized processes, we demonstrated a substantial decrease in the percentage of HSCT patients starting their preparative regimen after 19:00 without a concurrent increase in errors. We believe these interventions and measurements can be used in all transplant centers and have the potential to influence patient safety and outcomes.

**Keywords**
Chemotherapy safety; Quality improvement; Patient safety; Pediatrics; Stem cell transplant

**INTRODUCTION**

There is growing attention on the rates of medical errors. In 2000 the Institute of Medicine Report, “To Err is Human,” brought focus to the errors in healthcare, with rates of preventable adverse events exceeding 50% in some areas [1]. Medication errors are the most common cause of adverse events in the inpatient setting; these errors are largely due to prescribing and administration errors [2,3]. Children are at a unique risk because of varying dosage forms, concentrations, and formulations that must be reconstituted from powder and weight-based dosing, with error rates per patient-days greater in pediatric intensive care units [1,4,5]. The most frequently involved classes of drugs in medication errors are antibiotics and antitumor agents [6–8]. Infused medications are at particular risk given their complex preparation and administration processes [9]. A prospective study in pediatrics found a medication error rate of 5.7% and that 19% of adverse drug events were preventable [2]. Factors associated with an increased risk of prescribing error include drugs ordered from 4 to 8 am and moderately to severely ill patients [10]. In a survey of nurses regarding reporting of medication errors, distractions and interruptions, nurse-to-patient ratios, many medications per multiple patients, and long shifts were among reasons cited for medication administration errors [11].

Thus, pediatric hematopoietic stem cell transplant (HSCT) poses a particularly at-risk patient group, because these patients are often very ill, receive large numbers of medications with narrow therapeutic windows, and receive medications with significant adverse effect profiles. Timely initiation of high-dose chemotherapy during regular work hours is important for patient safety, because during the night fewer physicians are available for urgent or unexpected matters and typically no attending physician is present on the unit. Other vital members such as oncology-certified pharmacists are often not available overnight to help address any unforeseen chemotherapy questions or concerns. There are currently no well-defined benchmarks for timeliness of chemotherapy initiation. Recognizing the significant risk of starting chemotherapy in the evening or overnight, we established a quality improvement initiative to improve preparative regimen start times in patients undergoing HSCT.
Local Problem

Before any intervention, there was not a standardized process for tracking and improving rates of late scheduled admissions and chemotherapy administration times in the bone marrow transplant (BMT) unit. Additionally, nearly 30% of patients admitted to the BMT unit for same-day conditioning chemotherapy began their infusions during the night shift (after 19:00). Delay in chemotherapy initiation was identified by nursing leadership and staff as a potential risk factor for chemotherapy errors.

Failure mode and effects analysis [12] demonstrated that late starts to chemotherapy on the BMT unit included delays in provider assessment after admission; late admission times; delays in preparation of chemotherapy because of poor communication between the inpatient unit and the pharmacy, such as notifying the pharmacy once a patient is admitted and deemed stable to receive his or her planned chemotherapy so the pharmacy knows to prepare the chemotherapy; and delays in chemotherapy delivery to the floor. These barriers led to a significant time gap between admission and beginning chemotherapy. In addition, we found that chemotherapy that is not started before the nursing shift change at 19:00 is further delayed at least another 2 hours because of the nursing handoff process (Figure 1).

Available Knowledge

With the information that medication administration errors are the most common errors to reach patients, Weiss et al. [4] created a chemotherapy safety working group at a large urban pediatric medical center. They initiated a daily chemotherapy safety huddle that takes place every afternoon and includes charge nurses, fellows, attending physicians, hospitalists, nurse practitioners, care managers, a pharmacist, and a chemotherapy safety officer. This provided a venue to discuss plans for all chemotherapy being administered in the next 24 hours and to review any errors in the past 24 hours. It also included a discussion on planned admissions and bed availability. Other interventions targeted reducing distractions while clinicians ordered chemotherapy, a new workflow to address leaking chemotherapy lines, development of a time-sequencing job aid to determine the correct time of administration for time-sensitive medications, and requirement that chemotherapy is written at least 1 week in advance. With these interventions, they saw a sustained 50% reduction in chemotherapy errors that reached patients [4].

Rationale

Before any intervention we analyzed our chemotherapy initiation times over a 10-month period and found that approximately 30% of patients admitted for same-day chemotherapy had infusions started during the night shift, and 54% of them were admitted after 12:00. Through detailed process mapping we identified 2 primary barriers to timely initiation of chemotherapy: late admissions (after 12:00) and prolonged time from admission to preparation of chemotherapy (Figure 2A). Thirty-two percent of patients admitted for same-day chemotherapy were admitted late. Fifty-four percent of patients admitted late had infusions that started during the night shift. We discussed barriers to timely admission with a group of families which revealed that improved and more specific communication between families and the BMT team regarding admission details may be beneficial toward achieving our goal. The average time from admission to administration of chemotherapy was over 8
Thus, the interventions we identified to mitigate these barriers were providing families specific admission times and their rationales and a process for notifying pharmacy of admissions immediately on arrival (Figure 2B).

**Specific Aims**

The aim of this study was to decrease the percentage of chemotherapy started during the night shift (after 19:00) in patients admitted for same-day chemotherapy in the BMT unit.

**METHODS**

In July 2018 we established a multidisciplinary team consisting of physicians, registered nurses (RNs), and pharmacists. The team reviewed the current process for administering chemotherapy in the BMT unit from the decision to give chemotherapy to the chemotherapy reaching the patient to identify areas for improvement. Using the model of improvement [12–14], we identified reliable interventions to implement and tested our hypotheses through Plan-Do-Study-Act measures.

**Context**

Children’s Hospital Los Angeles is a large, urban pediatric medical center, and the BMT team performs 90 transplants per year. The BMT unit has 14 beds. Patients are frequently admitted for same-day chemotherapy before HSCT. Although all efforts are made to admit all patients receiving HSCT to the BMT unit, some patients receive their BMT care on the regular oncology floor. For this initiative we specifically included patients admitted to the BMT unit to receive same-day conditioning chemotherapy.

**Interventions**

- **Providing specific admission times**—BMT coordinators were already notifying families of general admission times 1 day in advance, largely based on bed availability. With this intervention, coordinators were asked to give more specific times rather than time ranges or approximates. They were also asked to explain the importance of arriving on time (ie, to start chemotherapy earlier in the day rather than overnight when it may interrupt normal sleep cycles). Initially, this process was measured in real time with regular check-ins between the study team and BMT coordinators.

- **Notifying the pharmacy of admissions**—Previously, once patients were admitted and evaluated, the bedside RN or charge RN would fax the signed orders to the pharmacy to prepare that patient’s chemotherapy. However, both bedside and charge RNs actively participate in morning rounds. Thus, if patients were admitted during morning rounds, there may have been a long delay between admission time and preparation of chemotherapy. Unit secretaries and patient care technicians are typically the first providers to be notified of patient admissions. With this intervention the secretaries or patient care technicians were asked to notify the pharmacy once patients arrived.
Study of the Improvement

For all patients admitted for same-day chemotherapy before HSCT, we measured the percentage of patients admitted before 12:00, the average time from patient admission to chemotherapy administration, and the percentage of patients who started preparative chemotherapy before 19:00.

We followed medication errors in the BMT unit before and after implementation of the interventions. Medication error rates were calculated as the number of medication errors per 1000 line days. Additionally, we classified and described medication errors before and after implementation of the intervention as per the National Coordinating Council Medication Error Reporting and Prevention Index [15]. Medical errors are classified from Category A (circumstance that has the capacity to cause error) to Category I (an error occurred that may have contributed to or resulted in the patient’s death) [15].

Data Collection

Data were collected in 2 ways. First, data were collected by chart review by a team member on a weekly basis. This log included patient admission time, chemotherapy approval time, and time of first chemotherapy administration. Data were also collated on a monthly basis with a log generated by our pharmacist including chemotherapy regimen, route of administration, time of patient admission, and time chemotherapy was administered. Because chemotherapy orders are both written and entered into the electronic medical record, we evaluated the time of first and second pharmacist verification of chemotherapy (for electronic orders), time of chemotherapy transcription (for written orders), and time chemotherapy was prepared.

Analysis

Statistical process control methods were used to monitor changes in care processes. We established a mean, illustrated as the centerline on all control charts with upper and lower control limits. Statistical process control criteria were used to determine if observed changes in measures were chance random variation (common cause variation) or caused by a specific assignable cause, in this case the intervention (special cause variation) that signifies statistical significance \((P < .05)\) [16,17].

Human Subjects Protection

The present initiative fell within the Children’s Hospital of Los Angeles Institutional Review Board’s guidance for quality improvement projects and was deemed exempt.

RESULTS

The study period was from October 2017 through March 2019. Eighty-two patients were admitted for same-day chemotherapy before HSCT during the time period. Baseline data were obtained in patients admitted before any intervention (October 2017 through August 2018, \(n = 46\)). Thirty-six patients were admitted after the initiation of the interventions (September 2018 through March 2019).
**Percentage of Patients Admitted Before 12:00**

Before any intervention 67% of patients (31/46) were admitted to the hospital before 12:00. Baseline data demonstrated initial Plan-Do-Study-Act testing on detailed family notification of admission times occurred in September and October 2018. From September 2018 through December 2018 late admissions decreased from 31% to 13%. However, from January through March of 2019 the percentage of late admissions increased, largely because of bed availability, and thus the overall percentage of late admissions during the study period remained stable at 33% (24/36).

**Average Time from Admission to Chemotherapy Administration**

After implementation of the interventions, the average time from admission to start of chemotherapy decreased from 8.6 hours (513 minutes) to 6.4 hours (382 minutes) (Figure 3A). Additionally, the standard deviation decreased from 210 minutes to 131 minutes (Figure 3B). The initial decrease in the time of the start of chemotherapy was seen in July of 2018, at the time of team formation and initial analysis of the existing system. This decrease has been sustained through the end of March of 2019.

**Percentage of Patients Who Started Preparative Chemotherapy before 19:00**

From September 2018 through March 2019 the percentage of patients who started preparative chemotherapy before 19:00 increased from 65% to 85% (Figure 4). Similar to the average time from admission to chemotherapy administration, the initial decrease in the time of the start of chemotherapy was seen in July 2018, at the time of team formation and initial analysis of the existing system.

From January through August 2018, before the intervention period, the average monthly all-cause medication error rate in the BMT unit (ie, medication prescribing, dispensing, administration, communication, patient monitoring, and equipment issues) was 16.2 errors per 1000 line days (50 errors). Forty-nine were Category B to D (error occurred, no patient harm), and 1 was Category E (an error occurred that may have contributed to or resulted in temporary harm to the patient and required intervention). From September 2018 through March 2019, during the intervention period, the error rate was 18.2 errors per 1000 line days (43 errors). One error was Category A, 41 errors were Category B to D (error occurred, no patient harm), and 1 was a Category E error (this involved an outpatient medication error that resulted in inpatient admission).

**DISCUSSION**

We describe a multidisciplinary team-based approach to improve the timeliness of chemotherapy administration in a single unit. Implementation of our approach resulted in a 20% increase in the percentage of patients initiating chemotherapy before the night shift. We also saw a significant decrease in the time from admission to the initiation of chemotherapy. Both of these measures were sustained despite barriers to admission before 12:00, which was impacted by bed availability and room turnover. To improve sustainability, lead RNs are regularly communicating with patient care technicians to ensure they are notifying the pharmacy on patient arrival to the BMT unit. Pharmacy clinical specialists prepare orders,
perform stock checks, and provide communication to frontline staff of all upcoming admissions to improve throughput. Chemotherapy processes are discussed during weekly hematology, oncology, and BMT pharmacy staff huddle sessions. The entire BMT team, including coordinators and physicians, meets weekly to discuss upcoming admissions and strategies to optimize timely admission. The roles and responsibilities entailed in this initiative can be applied to most BMT units and more broadly to oncology floors where there is a large volume of planned patient admissions and a multidisciplinary team coordinating patient care.

Inherent in quality improvement initiatives, there are limitations to the generalizability of our results to other institutions. This study was limited by the lack of patient or family surveys before or after our intervention. In addition to improving patient safety with timely administration of chemotherapy when there are more resources available, another objective is to improve patient satisfaction and quality of life by not requiring frequent overnight assessments while chemotherapy is administered. Also, factors outside of the study team’s control, such as whether beds were available for patients to be admitted early and if patients had to attend previously scheduled appointments or procedures before admission, delayed admission and thus chemotherapy administration time. Finally, we saw improvement in our process measures before broad implementation of the interventions, likely secondary to a Hawthorne Effect. Despite these limitations, we found a significant and sustained decrease in the rate of late infusion start times in admitted patients who were starting same-day chemotherapy without suffering a concurrent increase in errors in the BMT unit.

Our future work will use methods associated with decreasing medication errors, including decreasing device-related infusion errors, decreasing distractions while ordering chemotherapy, requiring chemotherapy orders to be prepared at least 1 week in advance to allow time for careful review, and daily chemotherapy huddles to help decrease rates of chemotherapy errors that reach patients [3–5,9]. We believe that administering chemotherapy during a time of available increased resources, including nursing leadership, chemotherapy pharmacists, and attending BMT physicians, allows team members to focus on their specific responsibilities without added distractions, ultimately improving patient safety. Further, effective communication via daily multidisciplinary huddles may help to reinforce specific roles and responsibilities and improve timeliness of chemotherapy [9,18].

Ensuring that orders are prepared and reviewed in advance should help decrease errors in prescribing and improve timeliness on the day the chemotherapy is due. As described by Maxwell et al. [19], the working environment is dynamic, and thus programs to assess providers’ abilities to effectively communicate, prescribe medications, and manage adverse drug reactions may also contribute to patient safety. Future initiatives should focus on these additional contributory factors to medication errors, specifically in this vulnerable, at-risk population.

In conclusion, using the model for improvement we reduced the percentage of patients starting chemotherapy after 19:00 by 20%. We believe these measures can be used in all transplant centers to increase chemotherapy administration during the daytime when optimal resources are available, ultimately influencing patient safety and outcomes.
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Squire 2.0 Guidelines were used in the writing of this manuscript [20].

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Figure 1.
Failure mode and effects analysis of the preintervention.
Figure 2.
Detailed pre- and postintervention process maps for written orders. (A) Detailed preintervention process map. (B) Detailed postintervention process map of chemotherapy delivery in patients admitted to the BMT unit to start the preparative regimen on the same day as admission. EMR indicates electronic medical record.
Figure 3.
Time from admission to the start of chemotherapy. (A) Average time from admission to start of chemotherapy by month. (B) Standard deviation of the time from admission to the start of chemotherapy.
Figure 4.
Percentage of patients who started preparative chemotherapy before 19:00.