Patient Safety Tip of the Week

June 12, 2018

Adverse Events in Cancer Patients

Adverse events are common in patients with cancer. Sometimes these are events potentially anticipated as a result of their treatment. But many adverse events in cancer patients are also potentially preventable.

Researchers at Memorial Sloan Kettering Cancer Center recently looked at a sample of cancer patients to see how often they suffered adverse events and how often such were preventable (Lipitz-Snyderman 2017). The sample included 400 randomly selected patients from a population of patients with lung, colorectal or breast cancer. Overall, they found 304 adverse events (AE's), for an overall rate of 2.3 events per 1000 patient days (91.2 per 1000 inpatient days and 0.9 per 1000 outpatient days). Thirty-four percent of the patients had 1 or more AE's and 16% of the patients had 1 or more preventable or mitigable AE's. The AE rate for patients with breast cancer was lower than the rate for patients with colorectal or lung cancer. Sixty-three percent of AE's occurred in the inpatient setting, for a rate of 79.0 AE's per 100 hospital admissions.

Nearly **a third** of all AE's (32%) were deemed **definitely or probably preventable**. The rate of preventable or mitigable AE's for inpatients was 29.9 AE's per 100 hospital admissions. For preventable AE's, the rates were 31.52 per 1000 inpatient days and 0.24 per 1000 outpatient days. For mitigable AE's, the rates were 3.82 and 0.08, respectively. The overall rate of preventable AE's was 0.73 per 1000 patient days, and the rate of mitigable AE's was 0.13 per 1000 patient days.

The AE and preventable or mitigable AE rates by setting differed by cancer type. The largest proportion of preventable or mitigable AE's of the total AE's belonged to lung cancer (47%), followed by colorectal cancer (36%) and breast cancer (20%). Regarding stage of disease, overall AE's and preventable/mitigable AE's occurred more frequently in patients with advanced disease for colorectal cancer, but not for lung or breast cancer.

The study does not go into great detail about the actual adverse events but does provide general categories for them. Infectious events (such as C. diff infection) were the most common AE's. Other frequent types included things like mucositis, hematologic events like thrombocytopenia, and metabolic events like hypokalemia or hypomagnesemia.

Approximately half of all AE's occurred within 3 months of the first treatment.

Regarding **harm**, 6% of overall AE's and 4% of preventable AE's were deemed to have resulted in permanent harm, to have required life-sustaining intervention, or to have resulted in death.

One of the types of adverse event that cancer patients are particularly vulnerable to is medication error. Complex regimens and multiple venues where they receive medications may be contributing factors. In our May 5, 2015 Patient Safety Tip of the Week "Errors with Oral Oncology Drugs" we described many of the other factors involved in such errors. In addition, chemotherapy agents are high-alert medications, meaning that errors related to these drugs have a high potential for causing patient harm.

The Pennsylvania Patient Safety Authority (PPSA) recently reported on over 1000 medication errors from outpatient hematology and oncology clinics reported to the Pennsylvania Patient Safety Reporting System (PA-PSRS) over a two year period (Banasser 2017). High-alert medications were reported in 55.5% of the events, with antineoplastic agents making up 94.3% of those medication errors reported with high-alert medications. (Other high-alert medications in this patient population included opioids and anticoagulants). But chemotherapy pre-medications, colony-stimulating agents, and corticosteroids were other agents involved in reports.

Though errors most frequently involved the prescribing node followed by the administering mode, errors occurred in every step of the medication use process (i.e., prescribing, transcribing, dispensing, administering, and monitoring).

Dose omissions (15.3%) and wrong dose/over dosage (13.1%) were among the most common errors encountered. The medication classes most frequently associated with dose omissions were antineoplastic agents, colony stimulating factors, and systemic corticosteroids.

Drugs involved most often in wrong dose/overdose events were antineoplastic agents and corticosteroids. Fortunately, two-thirds of these events were intercepted before reaching the patient and none resulted in patient harm. But the one-third that did reach the patient required monitoring or interventions to prevent harm.

Because so many of these drugs have dosages calculated based upon variables such as incorrect patient weight, height, body surface area (BSA), or serum creatinine level, it is not surprising that incorrect information about those factors contributed to some of the wrong dose errors. The authors point out that one patient safety intervention designed to prevent errors, i.e. having CPOE systems calculate dosages based upon such variables, will result in error if the underlying patient information is incorrect. We've done several columns on the importance of accurate and up-to-date weights (see list of columns below). Particularly in a cancer patient population, where weight loss may be frequent, it is important to have an up-to-date weight to use in dosage calculations. Some of the errors might also result from not having the most up-to-date laboratory information when dosage calculations or decisions about whether to proceed with a medication are made.

7.8% of errors were “wrong time” events. These were most often due to schedule errors or to delays in treatment.

Wrong drug errors also accounted for 7.8% of the errors. Name confusion was a common theme (for example, confusing PACLitaxel and DOCEtaxel or CARBOplatin and CISplatin). And our old favorite of confusion between morphine and HYDROmorphone was also reported.

Infusion-rate errors, omission of drugs or hydration, and improper preparation of drugs were also reported, albeit less frequently.

The PPSA paper has numerous recommendations to help avoid medication errors in this patient population and setting:

- Use either electronic or paper chemotherapy templates to standardize chemotherapy orders.
- Require reference(s) of primary literature if ordering chemotherapy outside of the chemotherapy template.
- Define a process to immediately communicate, document, and explain rationale for order changes and clarifications to the patient's healthcare team, including updating orders previously entered or processed when patient information, such as patient weight and serum creatinine levels, change.
- Explicitly write or indicate specific days for chemotherapy drugs (e.g., write as "Day 1, 2, 3").
- Develop policies and procedures that guide healthcare practitioners to identify, verify, and document the current cycle and the day within the cycle of chemotherapy (e.g., cycle 3 of 6, day 3 of 5) against an established treatment protocol before each dose is administered.
- Include the patient-specific dose and the mg/kg, mg/m , units/m, or other dosing method used to calculate the patient-specific dose for all chemotherapy drug orders (e.g., for a 1.67 m patient: 240 mg/m ; dose = 400 mg).
- Create chemotherapy order sets that include appropriate pre- and post-chemotherapy medications (e.g., colony stimulating factors).
- Implement a two-pharmacist independent double check of all chemotherapy orders prior to dispensing.
- Build hard stops that cannot be overridden, as appropriate, in computer systems for orders that exceed established maximum dose limits.
- Enable dose-error reduction software with soft stops and catas trophic or hard stops on electronic ordering systems and smart infusion pumps to intercept and prevent wrong dose/wrong infusion rate errors that can occur when programming pumps, calculating doses, or prescribing medications.
- When double checking prescribed chemotherapy doses, verify the patient's BSA using the patient's height and weight (in metric units) entered into the computer, and recalculate the actual dose (mg/m or mg/kg).
- Incorporate an independent double check of the prescriber's calculated dose for chemotherapy—according to the protocol or treatment plan—that considers the chemotherapy cycle before administering the drug.

- Ensure that independent double checks, whenever required by the organization's policy, are always performed and documented in the CPOE system and electronic health record.
- Institute a time-out immediately before administering the chemotherapy. During this time-out, two licensed healthcare practitioners independently double check the correct patient, compare the drug label to the order/medication administration record, verify the drug, diluent, dose, route, and rate, as well as pump settings, pump channel, and line attachment as applicable.
- Implement bar coding systems to verify drug selection prior to compounding and dispensing chemotherapy and treatment-related drugs (includes robotic dispensing) and at the point of care to verify chemotherapy and treatment-related drug selection prior to administering medications.
- Implement a chemotherapy error policy to direct healthcare practitioners to report and evaluate chemotherapy medication errors.
- Institute a system to review, learn from, and disseminate chemotherapy errors.

One very interesting study was reported at the recent Congress of the Oncology Nursing Society (Sato-DiLorenzo 2018). Laboratory values are typically checked prior to administration of chemotherapy to ensure the chemotherapy can be safely given. The researchers identified many near-misses related to this process and identified contributing causes, including lack of clear treatment criteria, a delay in lab processing, and patients expressing distress due to long wait times. They then developed two interventions to help prevent near-misses or actual adverse events:

- a two-nurse lab check during order verification
- utilization of "display the last day" function in the electronic medical record to limit the lab display

Prior to the intervention there were 4-11 near-misses/week. In the 3 months after the intervention there was only a single near-miss. However, continued surveillance for the next 7 months found 0-3 near-misses/week. They identified barriers to full success, such as returning to past habits and the primary nurse simply telling the second verifying nurse that pre-treatment labs have been verified. They suggest there may be a limit to how human actions alone can produce sustainable changes.

We've done multiple columns on the limitations of **double checks** (see, for example, our Patient Safety Tips of the Week for October 16, 2012 "What is the Evidence on Double Checks?" and April 19, 2016 "Independent Double Checks and Oral Chemotherapy"). Nevertheless, double checks do have an important role when dealing with high-alert medications, like chemotherapy agents. But those must be truly "independent" double checks. That means the second healthcare worker needs to independently verify a dose calculation or lab data prior to discussing results with the other healthcare worker.

Our April 19, 2016 Patient Safety Tip of the Week "Independent Double Checks and Oral Chemotherapy" noted that the number opportunities for double checking is typically far less for oral chemotherapy compared to intravenous chemotherapy. Also, with oral chemotherapy in some settings you may be dealing with community pharmacists who are

less experienced (compared with cancer center pharmacists) with the many complexities of chemotherapy regimens.

Two other issues relate to route of administration. We've done several columns on vincristine administered intrathecally rather than intravenously:

- December 2016 "Standardize 4 Safety and Just Bag It!"
- June 2017 "Just Bag It Campaign Success Story"
- January 2018 "Eliminating Vincristine Administration Events"

The Just Bag It! campaign calls for health care professionals to always dilute vincristine in a 50ml mini-IV drip bag and never in a syringe to minimize the risk of such incidents.

The other has to do with both the route and method of administration. The complex nature of some chemotherapy, involving multiple drugs and cycles, also contributes to medication errors in cancer patients. One type of chemotherapy adverse event we have been particularly concerned with is that in which a **chemotherapy drug intended to be infused over several days gets infused much more rapidly** (see our Patient Safety Tips of the Week for September 11, 2007 "Root Cause Analysis of Chemotherapy Overdose", April 6, 2010 "Cancer Chemotherapy Accidents" and September 15, 2015 "Another Possible Good Use of a Checklist"). In those columns on home infusion chemotherapy we noted no one seemed to be asking "what is the highest dose that a patient could tolerate in one day (or less) if there was inadvertent administration of the infusion?". A safety culture would design the protocol with sublethal dosages that would protect the patient in the event of "what can go wrong will go wrong". It also would not put the healthcare workers at the "sharp end" in a situation none of us would want to be in. The same question should apply to oral chemotherapy regimens and be "What would be the highest aggregate dose a patient could tolerate over a specified period?" and avoid prescribing more than that inadvertently. Yes, the patient might be inconvenienced by having to do another physician or clinic visit to get a prescription for the next cycle or the second part of a complex regimen. But isn't that preferable to receiving a chemotherapy overdose due to an avoidable error?

Then, there is also the issue of different doses of drugs depending upon the **indication** for the drug. There are some drugs, such as methotrexate, that are used for treating both cancer and other conditions. However, the dose and dosing frequency regimens are usually quite different when used for these conditions. We've frequently discussed the problem where methotrexate intended to be given on a twice weekly bases for an autoimmune disease erroneously gets given daily, resulting in toxicity for the patient. The opposite can also occur, where methotrexate is given only twice weekly for a cancer that merits daily administration.

And there is always yet the problem of **patient misidentification**. A recent report identified several factors that contributed to such an incident (Schulmeister 2018): "In a busy outpatient registration area, a recently hired clerk followed the facility's procedure and entered the name printed on the patient's driver's license. She clicked the first name in the list that appeared on her computer screen and created a wristband, unaware that other patients with the same name existed in the system. The clerk asked the patient if the

information on the band was correct, and he said yes. In court testimony later, he stated that he was not wearing his glasses at the time and was relying on the hospital staff to apply the correct wristband. The patient was sent to the busy infusion area at noon for his second chemotherapy treatment. A registered nurse asked him if his name was John Jones (name changed here for privacy) and if his birthday was the date that she read from his wristband. He nodded yes. But an error was made. The patient received the chemotherapy intended for another patient who had the same name but a different birthdate." The problem of patient misidentification, of course, is not unique to cancer patients. But, given that chemotherapy agents are high-risk drugs, the consequences of such misidentifications in an oncology setting are likely to be particularly devastating.

Lastly a recent review of interventions to improve oral chemotherapy safety and quality shows we still have lots of room for improvement (Zerillo 2018). A literature search strategy identified almost 8000 abstracts in the peer-reviewed literature but only 16 full-text articles met inclusion criteria and the overall quality of the literature had shortcomings. Even those studies that had positive findings may not be generalizable because they were single institution studies or focused primarily on specific drugs or diseases. Many of the interventions and studies focused on adherence to chemotherapy. But among those that focused on safety/toxicity there was a trend toward lower toxicity profile in those interventions that focused on increased monitoring. Telephone calls, usually by an oncology nurse or pharmacist, shortly after initiation of a chemotherapy regimen were the most successful intervention. But the optimal frequency of calls and how long such calls should be continued are unknown. Drug diaries and pharmacist education on adverse effects were also noted to be useful interventions.

Our prior columns related to chemotherapy safety:

- September 11, 2007 "Root Cause Analysis of Chemotherapy Overdose"
- April 2010 "Medication Incidents Related to Cancer Chemotherapy"
- April 6, 2010 "Cancer Chemotherapy Accidents"
- July 2010 "Methotrexate Overdose Due to Prescribing Error"
- July 2011 "More Problems with Methotrexate"
- May 7, 2013 "Drug Errors in the Home"
- May 5, 2015 "Errors with Oral Oncology Drugs"
- September 15, 2015 "Another Possible Good Use of a Checklist"
- February 2016 "Avoiding Methotrexate Errors"
- April 19, 2016 "Independent Double Checks and Oral Chemotherapy"
- June 21, 2016 "Methotrexate Errors in Australia"
- December 2016 "Standardize 4 Safety and Just Bag It!"
- June 2017 "Just Bag It Campaign Success Story"
- January 2018 "Eliminating Vincristine Administration Events"

Some of our other columns on errors related to patient weights:

- March 23, 2010 "ISMP Guidelines for Standard Order Sets"
- September 2010 "NPSA Alert on LMWH Dosing"
- August 2, 2011 "Hazards of ePrescribing"
- January 2013 "More IT Unintended Conseequences"
- December 8, 2015 "Danger of Inaccurate Weights in Stroke Care"
- May 2016 "ECRI Institute's Top 10 Patient Safety Concerns for 2016"
- September 2017 "Weight-Based Dosing in Children"
- June 2018 "Incorrect Weights in the EMR"

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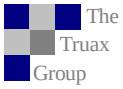

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