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PATIENT SAFETY NETWORK

Is the Admission Drug Dose Too Low?

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The Case

A 72-year-old man with a long history of chronic obstructive pulmonary disease (COPD) was admitted to the hospital with increasing shortness of breath. His admitting diagnoses were COPD exacerbation and pneumonia. Among his preadmission medications, the patient was taking Theo-Dur (extended-release theophylline), 300 mg three times daily. A theophylline blood level, drawn on admission, was 1.2 mg/L (therapeutic range: 10-20 mg/L). The admitting physician ordered Theo-Dur, 600 mg TID. A nurse questioned the order since this was double the patient's usual dosage, but the physician stated that he needed to get the patient's blood level up. The patient received Theo-Dur, 600 mg, at 12:00 AM, 5:56 AM, 11:43 AM, and 11:00 PM.

A theophylline blood level, drawn at 3:22 AM the following day, was 28.7 mg/L. The lab called the "critical result" to the floor at 6:55 AM. The night-shift nurse, a recent hire, had not checked to see if the blood level result was back before giving the patient his next dose of Theo-Dur at 6:05 AM. Later that day, the patient developed atrial flutter with a rapid ventricular response (heart rate in the range of 140 bpm), chest pain, and increased shortness of breath. A repeat theophylline blood level, drawn at 7:08 PM, was 38.1 mg/L, a very dangerous level. The patient was given oral activated charcoal, intravenous digoxin, and a continuous infusion of diltiazem. The patient's heart rate remained elevated for 3 days but ultimately returned to normal.

The Commentary

Medication errors are the most common type of medical error and occur frequently in the inpatient setting.(1) This elderly man with long-standing chronic obstructive pulmonary disease (COPD) suffered a serious cardiac arrhythmia as a result of a series of errors in dosing theophylline, monitoring for side effects, and responding to critical information in a timely fashion.

After presenting with a low theophylline level, the admitting physician could have verified the patient's dose and medication compliance, rather than doubling his reported dose immediately. In addition, when questioned by a nurse, the admitting physician should have performed additional investigative steps, such as comparing the admission theophylline level with previous values obtained during ambulatory care visits. Although the physician did obtain an admission blood level, many factors might cause this level to be an inaccurate reflection of the patient's current medication history. These include inaccurate recollection by the patient, nonadherence, incorrect administration (such as crushing the Theo-Dur tablet), and drug–drug or drug–disease state interactions.

In the inpatient setting, there is often a mismatch between a patient's preadmission dosage and the dosage ordered by the admitting physician. This is the focus of medication reconciliation—a critical safeguard in preventing medication errors. Medication reconciliation is the process of comparing a patient's medication orders to all of the medications that the patient has been taking.(2) This should be done at every transition of care in which new medications are ordered or existing orders are rewritten. A study by Pippins and colleagues found 1.4 unintentional and potentially harmful medication discrepancies per admitted general medical patient in a large tertiary hospital.(3) Of these discrepancies, 72% were due to errors in history-taking, suggesting the importance of verifying patient histories with pharmacists, primary care providers, or electronic health information when available. Apparently, none of these actions were taken in this case. In 2005, The Joint Commission made inpatient medication reconciliation a National Patient Safety Goal, focusing nationwide attention on the issue of inpatient medication errors as patients transition between health care settings.(2)

Within hospitals, ordering errors are the most common type of medication errors. A study of adult inpatients found 5.3 errors per 100 orders, with 6.6% being near misses and 0.9% resulting in actual patient harm.(4) Medications with a narrow therapeutic index, such as theophylline, require a heightened level of attention when prescribed. A study by Aitken and Marten, for example, showed that 65% of toxic theophylline levels received by their toxicology laboratory occurred in patients whose levels were not in the toxic range at admission.(5) In this case, the admitting physician failed to follow appropriate guidelines for dosing and monitoring theophylline. For patients presenting with low theophylline levels, doses should be increased by 25% and then monitored with serum levels.(6) It is also necessary to verify that all doses have been taken for 60 hours prior to blood sampling to ensure that steady state has been achieved and that the level is an accurate reflection of the chronic dosing regimen. If this is not possible, comparing the present blood level to past levels (on the same regimen) may provide a clue as to medication adherence. This elderly patient had additional risk factors for theophylline toxicity that should have resulted in an even more cautious approach to theophylline dosing. Reduced theophylline clearance has been documented in patients older than 55 years, particularly in males and those with chronic lung disease.(6)

Other factors in this case also contributed to the adverse drug event experienced by this patient. Theo-Dur is usually dosed twice daily, although this physician ordered the medication three times a day. Despite the TID order, it was administered at inconsistent intervals such that the patient received four doses of the drug in less than 24 hours. A "critical result" that was called to the floor was not appropriately acted upon, perhaps secondary to nursing inexperience, a transition between day and night teams, and maybe even a suboptimal critical test reporting system. Finally, there was likely no urgent need to achieve a theophylline blood level within the therapeutic range in the setting of an acute COPD exacerbation. A position paper

published in 2001 by a Joint Expert Panel on Chronic Obstructive Pulmonary Disease stated that methylxanthines are not beneficial for treating an acute COPD exacerbation and in fact can be harmful given their potential serious side effects.(7)

Preventing future similar errors requires not just individual physician and nurse education, but also systematic solutions to safeguard against potential harm. Increasing the availability of medication history information at the point of care through the use of multiple interventions, including information technology (IT) applications, would be helpful. In this case, as the patient had a long history of COPD, a call to the patient's outpatient pharmacist or the primary care physician might have confirmed the patient's previous theophylline doses and levels as well as adherence history.(8) Pharmacy benefit manager data and/or electronic ambulatory clinical data at the point of care could be of great assistance in clarifying issues as well.(9) The implementation of interoperable electronic health records, as stipulated by the American Recovery and Reinvestment Act, may be very helpful in creating this type of access to medical information across multiple settings.(10)

Optimizing the critical result reporting system may also have proven useful in this case.(11) This might include a protocol for reporting the laboratory result if the ordering physician cannot be reached, requiring a "read-back" mechanism verifying the information, employing laboratory-based surveillance by clinical pharmacists, and monitoring internal and external laboratory turnaround time.

This patient's experience helps to illustrate several key lessons about improving medication safety for hospitalized patients:

- Check, then double-check the medication history prior to writing medication orders.
- When a patient is admitted with a low or high dose (or blood level) of a medication, especially those with a narrow therapeutic index, consider a triple check.
- Gather the medication history from multiple sources—patient report, other health professionals, primary care providers, visiting nurses, pharmacists, and health records.
- Perform medication reconciliation at all transitions of care.
- Employ systematic solutions to improve medication ordering, including information technology applications.

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References

1. Kohn LT, Corrigan JM, Donaldson MS, eds. To Err is Human: Building a Safer Health System. Committee on Quality of Health Care in America, Institute of Medicine. Washington, DC: National Academies Press; 2000. ISBN: 9780309068376.

2. The Joint Commission. Using medication reconciliation to prevent errors. Sentinel Event Alert. January 25, 2006. [Available at]

3. Pippins JR, Gandhi TK, Hamann C, et al. Classifying and predicting errors of inpatient medication reconciliation. J Gen Intern Med. 2008;23:1414-1422. [go to PubMed]

4. Bates DW, Boyle DL, Vander Vliet MB, Schneider J, Leape L. Relationship between medication errors and adverse drug events. J Gen Intern Med. 1995;10:199-205. [go to PubMed]

5. Aitken ML, Martin TR. Life-threatening theophylline toxicity is not predictable by serum levels. Chest. 1987;91:10-14. [go to PubMed]

6. Theophylline (May 2009). In: DrugPoints® System [Internet database]. Greenwood Village, CO: Thomson Reuters (Healthcare) Inc. Updated periodically.

7. Snow V, Lascher S, Mottur-Pilson, C; Joint Expert Panel on Chronic Obstructive Pulmonary Disease of the American College of Chest Physicians and the American College of Physicians-American Society of Internal Medicine. Evidence base for management of acute exacerbations of chronic obstructive pulmonary disease. Ann Intern Med. 2001;134:595-599. [go to PubMed]

8. Ko Y, Malone DC, Skrepnek GH, et al. Prescribers' knowledge of and sources of information for potential drug-drug interactions: a postal survey of US prescribers. Drug Saf. 2008;31:525-536. [go to PubMed]

9. Kaushal R, Dhopeshwarker R, Gottlieb L, Jordan H. User experiences with pharmacy benefit manager data at point of care. J Eval Clin Pract. 2010;16:1076-1080. [go to PubMed]

10. American Recovery and Reinvestment Act of 2009. Pub L No. 111-005. [Available at]

11. Kuperman GJ, Teich JM, Tanasijevic MJ, et al. Improving response to critical laboratory results with automation: results of a randomized controlled trial. J Am Med Inform Assoc. 1999;6:512-522. [go to PubMed]

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