PSNet
PATIENT SAFETY NETWORK

When Looks Aren't All They Appear to Be: A Medication Error in an Uncommon Indication

October 28, 2020
Ton K. When Looks Aren't All They Appear to Be: A Medication Error in an Uncommon Indication . PSNet [internet]. 2020.
https://psnet.ahrq.gov/web-mm/when-looks-arent-all-they-appear-be-medication-error-uncommon-indication

The Case

A 58-year-old female patient with a history of liver cirrhosis and transformed lymphoma was admitted for inpatient administration of her chemotherapy with Rituximab, Ifosfamide, Carboplatin, and Etoposide Phosphate (R-ICE). She reported feeling well without any contacts with any sick individuals upon admission. After three days of her first cycle of therapy, she complained of diffuse abdominal pain that lasted all day with nausea and vomiting. She underwent extensive workup where she was found to have neutropenia, elevated lactic acid, leukopenia, elevated d-dimer, and low fibrinogen. An abdominal CT was consistent with inflammatory colitis with possible cholecystitis involvement. Computed tomography arterial portography (CTAP) was noted to have a neoplastic mass on the anterior abdominal wall. She became hypotensive with systolic blood pressures in the 80s and low oxygen saturations. She was determined to be experiencing septic shock and transferred to the intensive care unit (ICU). In the ICU, she was found to have E. coli bacteremia and colitis secondary to neutropenia. Her condition was made worse by the onset of ongoing hiccups of unknown etiology which lasted more than 48 hours. She was prescribed thioridazine (brand name Mellaril) 10 mg twice daily for the hiccups. The medication was verified, and she received four doses without resolution. This resulted in an increase in the thioridazine dose from 10 mg twice daily to 15 mg for one dose then again to 25 mg twice daily for an additional four doses.

When she was transferred back to the inpatient floor, a pharmacist reviewed the medical record. This review confirmed that the patient had been started on thioridazine and that?she had not received this medication before admission to the hospital. When questioned by the pharmacist, the resident physician confirmed that thioridazine had been prescribed to treat persistent hiccups when chlorpromazine (brand name Thorazine) had been intended.?The medication was discontinued as a result of altered mental status possibly secondary to medications. Ultimately, no Thorazine was needed.

The Commentary

By Kathy Ton, PharmD

Approach to Improving Safety & Patient Safety Target

Medications that are prescribed rarely or for less common diagnoses or indications require more attention during the ordering process. In the case presented above, thioridazine was mistaken for chlorpromazine, also known as Thorazine. This is a prime example of how look-alike sound-alike (LASA) medications can lead to prescribing errors. LASA medications are those that, either spoken or written, may be potentially result in harmful errors if confused for one another.[1] The Institute for Safe Medication Practices (ISMP) currently lists nearly 1,000 LASA medications as of 2019.[2] LASA medications account for almost 30% of dispensing errors and name confusion is a causative factor in nearly 20% of medication errors.[3] Thorazine, a brand name for chlorpromazine, and thioridazine, the generic name of Mellaril, represent such a pair.

Chlorpromazine, brand name Thorazine, is a first-generation antipsychotic. It is a phenothiazine that blocks dopamine receptors in the post-synaptic membrane in the meso-limbic pathway. This antagonism of dopaminergic function represents the mechanism by which chlorpromazine exerts its therapeutic effects in psychotic conditions such as schizophrenia. Besides psychotic disorders, chlorpromazine is also approved by the United States Food and Drug Administration (FDA) for the following indications and uses: nausea and vomiting, agitation or aggression associated with psychiatric disorders, acute intermitted porphyria, and relief or treatment of intractable hiccups.[4] Of note, chlorpromazine is the only medication that has a label indication for the treatment of hiccups. Other medications, including prochlorperazine, gabapentin and baclofen, are sometimes used off label for this indication.[5] Interestingly, the evidence basis for the FDA's label indication began with two small reports published in the 1950s where intravenous (IV) chlorpromazine was administered to patients with hiccups. These reports described various cases where intravenous administration of IV chlorpromazine (25 to 50 mg) to 100 individuals with hiccups of unspecified duration. Cessation of hiccups was seen almost immediately in 81 of these patients.[6-7] Since these documented reports, there have been no randomized controlled trials studying chlorpromazine for hiccups. Although the data are limited, chlorpromazine has been the mainstay of treatment of intractable hiccups for over 50 years.

Thioridazine, also sold under the brand name Mellaril, is another a first-generation antipsychotic. However, it does not have the label indication for hiccups nor any documentation for use in hiccups.[8] Additionally, it is rarely prescribed present day as it is recommended to be reserved for patients who do not have an acceptable response to other antipsychotics.[9-10] Both chlorpromazine and thioridazine carry cardiac risks such as QT interval prolongation and ventricular arrhythmias. However, thioridazine presents the greatest risk and, thus, has a label recommendation for baseline electrocardiogram (ECG) and serum potassium level (before administration of the first dose).[11] In previous studies, thioridazine was shown to have a greater propensity in altering portions of the ECG compared to chlorpromazine.[12]

As presented above, the patient had very complex clinical picture with various risk factors. Most notable were severe nausea and vomiting due to abdominal pain and chemotherapy leading to dehydration and possibly contributing to her hypokalemia. She was being aggressively treated with two anti-emetic agents, ondansetron and prochlorperazine. Additionally, she was on prophylactic fluconazole to prevent any systemic fungal infections while she was neutropenia. Ondansetron, prochlorperazine and fluconazole are known agents to cause QT prolongation and additive effects with unintended thioridazine further increased her risk of QT prolongation.[13]

Systems Change Needed/Quality Improvement Approach

Research has shown that since the implementation of computerized physician order entry (CPOE), there has been an overall reduction in prescribing errors in the hospital setting.[14] However, pharmacist involvement as well as continuous evaluation and assessment of the clinical decision-making tools integrated into the ordering system are crucial for maintaining safe medication prescribing practices.

This specific case highlights the importance of having a pharmacist as an integral part of patient care team. Prescribing errors are most commonly associated with medication knowledge deficiency.[14] A pharmacist can serve as a resource to provide physician and nursing education on medications used to treat uncommon indications. On the other hand, the pharmacy staff as well as nursing staff should play an active role in ensuring that medications that are ordered and administered to patients are appropriate and question any medication that is not commonly prescribed or administered.

Since most inpatient facilities have now implemented of CPOE, it is necessary to evaluate what information is included in the ordering and verification processes to help with making clinical decisions. For this case, ordering thioridazine did not alert the ordering provider about any details of this medication. It also did not require the ordering provider to specify the indication for therapy. This error prompted changes in the orders to provide consistency and prevent ordering of an unintended medication.

The naming convention was updated to include “tall man lettering” to help differentiate look alike sound alike medications (thioRIDazine). There are a number of studies that suggest that tall man lettering can help to reduce medications errors related to similar drug names through faster detection of dissimilarities, ease of distinguishing between look-alike medication names or increased accuracy of drug name perception.[15-17] There also exists studies that suggest this method of differentiation may not be effective. However, these studies often have limitations where the setting of the studies are not clinical practice settings.[18-20] Although the data may be inconclusive, the ISMP still recommends this technique to reduce errors involved LASA medications and acknowledges that additional research is required.[21]

There were also enhancements made to the clinical decision-making support system for this medication to highlight the cardiac risk and the need to obtain a baseline ECG. Prescribers are now required to select a specific indication for thioridazine from a drop-down menu. Such automated alerts have been shown to provide effective means of communicating essential clinical data about a drug or patient to those who are prescribing and verifying. There is evidence to suggest that hard stops, nearly hard stops and forcing functions in the prescribing process are effective in capturing the prescriber’s attention and getting them to change a prescription.[22] Furthermore, there were some inclusions to the “verify orders” activity for pharmacists to emphasize that thioridazine is a look-alike sound-alike medication and to include the

change in naming convention as well as the order instructions mentioned previously.

Luckily, there was no harm done to the patient in this case as the patient did not have any baseline cardiac comorbidities that may have precipitation harm, and the prescribed dosage was within the safe therapeutic range for both chlorpromazine and thioridazine.

Take Home Points

- Medication errors are among the most common medical errors
- Medication errors are more likely occur with look-alike sound-alike medications
- Institutions should develop their own look alike sound alike medication list based on utilization patterns and internal data about medication errors
- Work with pharmacy colleagues to ensure that less commonly prescribed or ordered medications are done so appropriately and correctly
- All members of the patient care team should be involved in the medication review process especially when a less commonly prescribed medication is ordered
- Implement changes in the computerized physician order entry process that assist in preventing an unintended medication
- For medications that are not commonly ordered, best practice alerts should be programmed into the ordering process to assist with appropriate ordering and order verification to ensure patient safety

Kathy Ton, PharmD
Department of Pharmacy Services
UC Davis Health

References

1. Pharmaceutical Services Division, Ministry of Health Malaysia. Guide on Handling Look Alike Sound Alike Medications. WHO.
2. ISMP: List of Confused Drug Names. Feb 28, 2019. https://www.ismp.org/recommendations/confused-drug-names-list
3. Rahman, Z., & Parvin, R. (2015). Medication Errors Associated with Look-alike/Sound-alike Drugs: A Brief Review.?Journal of Enam Medical College,?5(2), 110-117. https://doi.org/10.3329/jemc.v5i2.23385
4. Chlorpromazine hydrochloride tablets. [package insert]. Bridgewater, New Jersey. Amneal Pharmaceuticals: 2018
5. Polito NB, Fellows SE. Pharmacologic Interventions for Intractable and Persistent Hiccups: A Systematic Review. J Emerg Med. 2017 Oct;53(4):540-549. doi: 10.1016/j.jemermed.2017.05.033. PMID: 29079070
6. Friedgood CE, Ripstein CB. CHLORPROMAZINE (THORAZINE) IN THE TREATMENT OF INTRACTABLE HICCUPS. JAMA. 1955;157(4):309–310. doi:10.1001/jama.1955.02950210005002

7. DAVIGNON A, LEMIEUX G, GENEST J. Le chlorpromazine dans le traitement du hoquet rebelle [Chlorpromazine in the treatment of stubborn hiccup]. Union Med Can. 1955 Mar;84(3):282-4. French. PMID: 14374117
8. Thioridazine hydrochloride [package insert]. Mumbai, India; Sun Pharmaceuticals Inc.: 2016
9. Drugs and Lactation Database (LactMed) [Internet]. National Library of Medicine (US); Bethesda (MD): 2006. Thioridazine.
10. The American Psychiatric Association Practice guideline for the treatment of patients with Schizophrenia, Third Edition. (2020), p. 70
11. Fenton M., Rathbone J., Reilly J., Sultana A. Thioridazine for schizophrenia. Cochrane Database of Systematic Reviews. 2007;1(3, article CD001944) doi: 10.1002/14651858.CD001944.pub2
12. Huston JR, Bell GE. The Effect of Thioridazine Hydrochloride and Chlorpromazine on the Electrocardiogram.?JAMA.?1966;198(1):16–20. doi:10.1001/jama.1966.03110140066019
13. Incidence, Diagnosis, and Management of QT Prolongation Induced by Cancer Therapies: A Systematic Review. Andreu Porta?Sánchez?,?MD MSc?,?Cameron Gilbert?,?MD?,?Danna Spears?,?MD?,?Eitan Amir?,?MD, PhD?,?Joyce Chan?,?PharmD, MSc?,?Kumaraswamy Nanthakumar?,?MD?, and?Paaladinesh Thavendiranathan?,?MD, SM?dinesh.thavendiranathan@uhn.ca
14. Bobb A, Gleason K, Husch M, Feinglass J, Yarnold PR, Noskin GA. The Epidemiology of Prescribing Errors: The Potential Impact of Computerized Prescriber Order Entry. Arch Intern Med. 2004;164(7):785–792. doi:10.1001/archinte.164.7.785
15. DeHenau C, Becker MW, Bello NM, Liu S, Bix L. Tallman lettering as a strategy for differentiation in look-alike, sound-alike drug names: the role of familiarity in differentiating drug doppelgangers.?Appl Ergon. 2016;52:77-84.
16. Filik R, Purdy K, Gale A, Gerrett D. Labeling of medicines and patient safety: evaluating methods of reducing drug name confusion.?Hum Factors. 2006;48(1):39-47
17. Filik R, Price J, Darker I, Gerrett D, Purdy K, Gale A. The influence of tall man lettering on drug name confusion: a laboratory-based investigation in the UK using younger and older adults and healthcare practitioners.?Drug Saf. 2010;33(8):677–87.
18. Schell KL. Using enhanced text to facilitate recognition of drug names: evidence from two experimental studies.?Appl Ergon. 2009;40(1):82–90.
19. Irwin A, Mearns K, Watson M, Urquhart J. The effect of proximity, tall man lettering, and time pressure on accurate visual perception of drug names.?Hum Factors. 2013;55(2):253–66.
20. Zhong W, Feinstein JA, Patel NS, Dai D, Feudtner C. Tall man lettering and potential prescription errors: a time series analysis of 42 children's hospitals in the USA over 9 years.?BMJ Qual Saf. Published Online First: November 3, 2015.
21. Special Edition: Tall Man Lettering; ISMP Updates Its List of Drug Names with Tall Man Letters. Jun 2, 2016.
22. Strom BL, Schinnar R, Aberra F, et al. Unintended Effects of a Computerized Physician Order Entry Nearly Hard-Stop Alert to Prevent a Drug Interaction:?A Randomized Controlled Trial.?Arch Intern Med.?2010;170(17):1578–1583. doi:10.1001/archinternmed.2010.324

This project was funded under contract number 75Q80119C00004 from the Agency for Healthcare Research and Quality (AHRQ), U.S. Department of Health and Human Services. The authors are solely responsible for this report's contents, findings, and conclusions, which do not necessarily represent the

views of AHRQ. Readers should not interpret any statement in this report as an official position of AHRQ or of the U.S. Department of Health and Human Services. None of the authors has any affiliation or financial involvement that conflicts with the material presented in this report. View AHRQ Disclaimers