Preventable Medication Errors: Solid Oral Dosage Forms of Diltiazem

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Objectives

- Hypertension is a significant risk factor for cardiovascular diseases such as stroke and heart attack, making blood pressure control an important priority in preventing these events.[1]
- Available in a wide range of formulations, generics and doses, diltiazem plays a role as a non-dihydropyridine calcium channel blocker (non-DHP CCB), which is used to control blood pressure as a first or second line agent,[2,3] with other approved indications including stable angina and coronary spasms.[4] However, if used incorrectly, it may lead to negative consequences including heart block and heart failure, and compromised patient safety.[2]
- The objective of this multi-incident analysis was to examine potential contributing factors of medication incidents involving solid oral dosage forms of diltiazem, and provide recommendations with the aim to enhance medication safety.

Methodology

- Reports of medication incidents involving diltiazem were extracted from the Institute for Safe Medication Practices Canada (ISMP Canada) Community Pharmacy Incident Reporting (CPhIR) Program[5] from January 2010 to April 2016. A total of 358 incidents were retrieved; 184 incidents met the inclusion criteria and were included in the qualitative, multi-incident analysis.
- Due to the nature of voluntary reporting, we might not have captured all incidents related to diltiazem in pharmacy practice. Also, the "Incident Examples" provided here were limited by what was inputted to the "Incident Description" field of the CPhIR program by the reporters.

Results

- The incident reports were analyzed and categorized into two main themes and their associated subthemes (Table 1). Contributing factors were categorized as either non-modifiable or modifiable (Tables 2 and 3). Recommendations were offered according to the Hierarchy of Effectiveness in Error Prevention Principles (available upon request).[6]

Table 1: Themes and Subthemes

THEMES

DILTIAZEM-SPECIFIC

SUBTHEMES

1. Different Formulations and Generics
2. Wide Dosing Ranges
3. Oral Dosage Forms
4. Drug Interactions
5. Non-DHP CCB Role in Drug Therapy

MEDICATION-USE PROCESS

1. Prescribing
2. Prescription Order Entry
3. Prescription Preparation/Dispensing

Table 2: Theme 1 – Diltiazem-Specific

SUBTHEME 1: Different Formulations and Generics

Diltiazem is available through different formulations and also different generics for each formulation Diltiazem can be dosed anywhere from once a day in the evening to four times a day.

INCIDENT EXAMPLE:
A prescription was written for Tiazac® 240 mg. This was entered and filled as Tiazac® XC 240 mg, when it should have been diltiazem ER 240 mg, which is the generic of Tiazac® 240 mg. The patient also had a long history of being on diltiazem ER 240 mg.

INCIDENT EXAMPLE:
A pharmacist dispensed the wrong formulation of the medication. The release rate was different. The patient phoned to question her medication after experiencing side effects.

Note: The medications in the incident were Tiazac® XC and diltiazem TZ, which are not interchangeable.

POSSIBLE CONTRIBUTING FACTORS

Non-Modifiable:
- Multiple formulations and generics available
- Similar strengths across different formulations and generics

Modifiable:
- Unfamiliarity with interchangeability of diltiazem products
- Confirmation bias
- Issue with system alert to flag similar drug dispensed

Comments:
There is no generic of Tiazac® XC and it was designed to be dosed at bedtime to maximize anti-hypertensive effects in the morning.[4]

SUBTHEME 2: Wide Dosing Ranges

Diltiazem is available in different strengths, ranging anywhere from 30-360 mg.

INCIDENT EXAMPLE:
Tiazac® XC 360 mg was being dispensed. A bottle of 300 mg was grabbed instead of 360 mg.

POSSIBLE CONTRIBUTING FACTORS

Non-Modifiable:
- Look-alike bottles
- Multiple strengths supplied for each formulation

Modifiable:
- Confirmation bias
- Not performing independent double checks

Comments:
Tiazac® XC is available in the following dosages: 120 mg, 180 mg, 240 mg, 300 mg and 360 mg.

SUBTHEME 3: Oral Dosage Forms

Diltiazem is also available in tablets and capsules.

INCIDENT EXAMPLE:
The wrong brand of diltiazem was filled and they were tablets. It was supposed to be capsules. This was caught when checking the DIN.

Note: The medications in the incident were Tiazac® XC and diltiazem TZ, which are not interchangeable.

POSSIBLE CONTRIBUTING FACTORS

Non-Modifiable:
- Similar strengths across different formulations and generics

Modifiable:
- Unfamiliarity with tablet and capsule formulations

Comments:
The formulations available as tablets are Cardizem® with its generics and Tiazac® XC only. All others are capsules.

SUBTHEME 4: Drug Interactions

Diltiazem is a major CYP3A4 substrate.[4]

INCIDENT EXAMPLE:
An interaction with diltiazem was flagged while filling a prescription for clarithromycin. This could lead to possible drop in blood pressure or acute renal failure. The doctor was unaware of the problem. The prescription was switched to azithromycin because it does not interact with diltiazem.

POSSIBLE CONTRIBUTING FACTORS

Non-Modifiable:
- Pharmacokinetic property of the medications

Modifiable:
- Unfamiliarity with metabolism of medications
- Lack of comprehensive medication review

SUBTHEME 5: Role in Therapy

Its indications and use are usually chronic, so it can be added, titrated or discontinued. Therefore, updating the correct drug regimen can sometimes be missed.

INCIDENT EXAMPLE:
A patient had been changed from atenolol to Tiazac® XC by a specialist. The family doctor was unaware so [he] re-prescribed atenolol with an indication to increase its dose. The prescription was filled by an incoming pharmacist during a shift change on a busy day. The pharmacist had forgotten to look at the Drug Utilization Review (DUR) notes, and therefore missed the interaction with the current Tiazac® XC. The patient went to the hospital due to a low heart rate and it was discovered that she was taking both Tiazac® XC and atenolol. The patient was admitted to the hospital and the medications were changed accordingly. She was stabilized and discharged. The pharmacy only realized an incident had occurred when the patient came to pick up the discharge medications.

POSSIBLE CONTRIBUTING FACTORS

Modifiable:
- Miscommunication between inter-professionals
- Lack of comprehensive medication review
- Alert fatigue
- Unfamiliarity with drug interactions

Comments:
Changes involving diltiazem (adding, titrating, or discontinuing) and also dosing of diltiazem varies with each patient and it depends on the indication, the patient's disease control, tolerability to the medication, and overall drug regimen.

Atenolol is a beta blocker, which can cause bradycardia or cardio depression when used with a non-DHP CCB.[7]

Table 3: Theme 2 – Medication-Use Process

SUBTHEME 1: Prescribing

Sometimes prescribers order the incorrect formulation or incorrect dose of diltiazem and they may also omit the formulation suffixes of diltiazem.

INCIDENT EXAMPLE:
A doctor wrote a prescription for Cardizem® CD 240 mg and the patient has always been taking Tiazac® XC 240 mg. These are not interchangeable. The doctor was faxed and the order was changed back to Tiazac® XC 240 mg.

POSSIBLE CONTRIBUTING FACTORS

Non-Modifiable:
- Similar strengths across different formulations and generics

Modifiable:
- Unfamiliarity with the interchangeability of diltiazem products
- Incorrect formulation chosen in the prescribing software

SUBTHEME 2: Prescription Order Entry

This includes errors in the pharmacy associated with refilling, copying, entering the incorrect diltiazem dose and/or formulation.

INCIDENT EXAMPLE:
A patient was put on Cardizem® CD in the hospital and had it filled at a community pharmacy. Two months later, he was put on Tiazac® XC by the family doctor, but there was no mention on discontinuing Cardizem® CD. Upon data entry, the technician did not see Cardizem® CD earlier in the profile and did not copy the prescription so the patient was taking both medications concurrently. It wasn't until the patient brought in both empty bottles for refills when the technician noticed the two different versions of diltiazem. The doctor was contacted and there were no issues or side effects from the incident. The patient continued on Tiazac® XC only.

POSSIBLE CONTRIBUTING FACTORS

Modifiable:
- Issues with system alert to flag similar drug dispensed
- Miscommunication between inter-professionals
- Lack of communication between patient and pharmacist
- Unfamiliarity with interchangeability of diltiazem products
- Lack of comprehensive medication review

Comments:
These two formulations are not interchangeable. Tiazac® XC is a tablet, whereas Cardizem® CD is a capsule. The patient may have perceived that they were two different medications, so it was never questioned by the patient.

SUBTHEME 3: Prescription Preparation/Dispensing

This includes errors associated with look-alike bottles from the same manufacturer, improper DIN checking and manufacturer shortages leading to filling of the incorrect formulations.

INCIDENT EXAMPLE:
Two stock bottles of Tiazac® XC were retrieved for prescription filling. The correct strength was 180 mg. One bottle was 180 mg and the other was 120 mg. The incorrect bottle was directly behind the correct one.

POSSIBLE CONTRIBUTING FACTORS

Non-Modifiable:
- Look-alike bottles
- Multiple strengths supplied for each formulation

Modifiable:
- Not performing independent double checks
- Confirmation bias

INCIDENT EXAMPLE:
Diltiazem ER was on back order and the pharmacy had to use the brand name, Tiazac®, in a patient's blister pack. When the generic became available again, it was added back to the blister pack. However, Tiazac® was not removed. This put the patient at risk of double-dosing.

POSSIBLE CONTRIBUTING FACTORS

Non-Modifiable:
- Manufacturer shortages

Modifiable:
- Lack of system alert to flag similar drug dispensed
- Unfamiliarity with the interchangeability of diltiazem products
- Lack of full patient drug profile assessment

Conclusion

It can be challenging to remember all formulations and generics of diltiazem; however, this multi-incident analysis aims to bring awareness that the different formulations of diltiazem do exist. When we encounter diltiazem in practice, we should immediately ask, *"Is this the right formulation for our patient?"*

By analyzing medication incidents, our current medication-use system can be improved in order to increase patient safety. Our recommendations in this multi-incident analysis can be extrapolated and applied to similar medications with multiple formulations and various suffixes available.

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ISMP Canada
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www.ismp-canada.org

CMIRPS
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CPhIR
Community Pharmacy Incident Reporting Program
www.cphir.ca

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