Medication Incidents Associated with Patients with Renal Impairment: A MULTI-INCIDENT ANALYSIS

Grant Fuller, PharmD Candidate[1,2]
Kendra Carroll, HBSc, PharmD Candidate[2,3]
Alan Ho Lun Li, BPharm Candidate [4]
Certina Ho, RPh, BScPhm, MISt, MEd, PhD[2,3]

[1] School of Pharmacy, University of Waterloo
[2] Institute for Safe Medication Practices Canada
[3] Leslie Dan Faculty of Pharmacy, University of Toronto
[4] School of Pharmacy, The Chinese University of Hong Kong

INTRODUCTION

The kidneys are one of the main organs responsible for eliminating drugs from the body. Decreased renal function may lead to reduced drug clearance and a subsequent increase in plasma drug concentration. If dosing adjustments are not made based on a patient's renal function, increased exposure to the medication may put the patient at risk of side effects, serious harm, or death.[1]

As our population ages and requires an increasing number of medications, situations of inappropriate medication use in patients with reduced renal function may become more frequent.[2] Renal impairment, regardless of the cause, introduces further complexity and opportunity for errors within the medication-use process. The likelihood of medication incidents involving this population is particularly high in communities when healthcare practitioners have limited access to patient medical records and lab values. Despite these challenges, pharmacists are responsible for providing safe and effective care to patients. Acknowledging the limitations of our current health care system will help us implement feasible improvements in the medication-use process.

To protect patients with renal impairment, many medications must be dose-adjusted according to the patient's renal function. A list of common medications requiring dose adjustment or avoidance in renal impairment is presented in **Table 1**. The objective of this multi-incident analysis is to examine medication incidents involving patients with renal impairment within the community pharmacy setting. Common themes and potential contributing factors are provided as well as recommendations to improve the care of these patients (**Tables 2-5**).

Table 1. Examples of Top 100 prescribed drugs that must be considered for dose adjustment or avoidance in renal impairment[3,4]

• Gabapentin	• Duloxetine
• Pregabalin	• Escitalopram
• Ciprofloxacin	• Venlafaxine
• Valacyclovir	• Alendronate
• Gliclazide	• Risedronate
• Glyburide	• Rosuvastatin
• Metformin	• Spironolactone

Disclaimer: *This list is not comprehensive of all medications requiring dose adjustment in renal impairment. Refer to the Ontario Renal Network and other resources as appropriate to confirm dose adjustments or contraindications in renal impairment.*

METHODS

A total of 172 incident reports were extracted from the ISMP Canada Community Pharmacy Incident Reporting (CPhIR) program database from June 2014 to May 2019. The CPhIR program aggregates medication incident data from different provinces, including incident reports from jurisdictions where pharmacists have access to patient lab values.* A collection of broad renal-associated search terms including but not limited to: "GFR", "dialysis", "kidney" and "renal" were used to capture incidents involving patients with renal impairment. Thirty-eight incidents were excluded, as they did not involve the target patient population. A total of 134 incidents met the inclusion criteria and were evaluated in this qualitative incident analysis. Two independent analysts conducted a multi-incident analysis of the data, identifying common

themes, subthemes, contributing factors, and recommendations to improve patient safety.

Of note, 86 of the 134 incidents analyzed were classified by reporters as "near misses" that were caught before reaching the patient. Therefore, many of the following incident examples should be interpreted as demonstrating best practices by pharmacy professionals, rather than errors that should be avoided. Where applicable, we will differentiate mitigating factors or best pharmacy practices in preventing medication harm from potential contributing factors to medication incidents in **Tables 2 to 4** below.

**Note: While incident examples included in this article are not specific to Ontario, we believe that the shared learning and experiences from these near misses and medication incidents are still beneficial to pharmacy professionals in Ontario.*

RESULTS

Table 2. Main Theme 1 – Recognition of Renal Impairment

Subtheme 1 – Checking/Availability of Lab Values		
Incident Examples	**Contributing Factors**	**Commentary**
• Physician gave Nitrofurantoin to a patient without checking their CrCl, which was very low. Patient's renal function was checked by the pharmacist when filling prescriptions and medication was changed to something more appropriate.	• Lab values unavailable to healthcare practitioners • Lab values available to practitioners, but not checked	• Healthcare providers should always check or obtain lab values whenever high-alert medications are ordered/dispensed for patients with renal impairment.
Subtheme 2 – Patient-Related Factors		
Incident Examples	**Mitigating Factors / Best Practice in Preventing Medication Harm**	**Commentary**
• Physician gave patient Metoclopramide 10 mg QID. Based on a conversation with the patient, we discovered their renal function has been decreased, therefore patient requires a dosage reduction. Contacted the physician and explained the situation. Physician stated to decrease the dose to 5 mg QID. • A prescription was phoned in from the physician for Amoxicillin/Clavulanic acid 875 mg twice daily. Pharmacy knew the patient has renal function issues, so they called the kidney clinic. Patient had a CrCl of 16 mL/min, which means dose should be reduced to 250 to 500 mg twice daily. Pharmacy faxed physician and had dose changed.	• Medical conditions discussed during patient counselling • Practitioner familiarity with patient • Recognizing patients with increased risk of having renal impairment • Interprofessional collaboration within the circle of care	• The familiarity that comes with longstanding patient-provider relationships can draw attention to inappropriate medication prescribing. This includes medications, which have not been dose-adjusted being prescribed to patients with renal impairment.
Subtheme 3 – Drug-Related Factors		
Incident Examples	**Mitigating Factors / Best Practice in Preventing Medication Harm**	**Commentary**
• Prescription was written for Trimethoprim-Sulfamethoxazole DS once daily PO x 7 days. Prescription was filled as Trimethoprim-Sulfamethoxazole DS 800/160 mg - take one tablet by mouth twice daily for 7 days, dispense 14 tablets. Pharmacist caught error when checking prescription. Trimethoprim-Sulfamethoxazole DS is normally dispensed BID, but due to the patient's poor renal function, the physician decided to give DS dosing once daily as opposed to single strength dosing BID. • Physician wanted to prescribe Rivaroxaban for a patient but had not ordered a renal panel. We phoned the physician about checking patient's kidney function first. Renal panel came back and the dose had to be adjusted from 20 mg daily to 15 mg daily.	• Pharmacist's recognition of atypical medication dosing • Pharmacist's recognition of high-alert medications in renal impairment	• Pharmacists, as medication therapy experts, play a key role in recognizing atypical medication dosing and high-alert medications.
Subtheme 4 – Documentation and Computerization		
Incident Examples	**Mitigating Factors / Best Practice in Preventing Medication Harm**	**Commentary**
• Pharmacy had patient's medical conditions documented in patient profile; we knew patient had severe kidney dysfunction and should not be on that dose for that duration. We called physician and discovered that the wrong dose had been ordered; dose was ordered for 3 months instead of 3 days. • The computer system picked up an interaction with Levofloxacin and the patient's medical condition, renal failure.	• Documentation of patient's renal status • Presence of computer alerts/prompts regarding patient's renal status	• Computer system alerts can prompt providers to recognize potentially inappropriate drug therapy (e.g. drug-disease interaction alerts, dosage warnings).

Table 3. Main Theme 2 – Additional Safeguards for Patients With Renal Impairment

Subtheme 1 – Additional Renal-Specific Care Providers		
Incident Examples	**Mitigating Factors / Best Practice in Preventing Medication Harm**	**Commentary**
• A prescription for the patient was written for one tablet twice a day. The patient requires blister packs and previously had received one tablet twice a day on non-dialysis days: Tuesday, Thursday and Saturday. However, the dose was changed to one tablet twice a day everyday. The patient went to the dialysis unit at the hospital and the pharmacist noticed that Candesartan was missing on dialysis days. The hospital pharmacist contacted the community pharmacy and corrections were made.	• Disease specific knowledge and experience • Presence of an independent double check	• Patients being monitored by specialized care providers (e.g. renal pharmacists and nephrologists) have an additional safeguard against the inappropriate use of highly specialized medications. The use of medication reconciliation processes is recommended to detect and resolve potential medication incidents.
Subtheme 2 – Additional Education Provided to Renal Patients		
Incident Examples	**Mitigating Factors / Best Practice in Preventing Medication Harm**	**Commentary**
• Patient was counselled by both the physician and pharmacist to take only one tablet BID due to their decreased kidney function. Upon opening the prescription bag at home, the patient discovered the label said take one tablet QID and the quantity was double what it should have been. Patient contacted pharmacy at once.	• Care providers communicate dosing changes/rationale to patient • Patient knowledge of drug therapy/disease state	• Communication of drug dosing changes/ rationale to the patient and providers within the circle of care is highly recommended. • Patients with renal impairment often receive additional education regarding their medication therapy and disease state. These discussions empower patients to detect near misses or medication errors and act as an independent double check of their medication therapies.

Table 4. Main Theme 3 – Additional Risk Introduced by Renal Impairment

Subtheme 1 – Dialysis		
Incident Examples	**Contributing Factors**	**Commentary**
• Metoprolol was supposed to be placed in blister packaging except for the dialysis days. Medication was placed in the wrong slot in compliance packaging. Pharmacist noticed mistake when checking packages and mistake was corrected. • Prescription was misinterpreted - Cephalexin 500 mg PO daily (give after dialysis on Tuesday / Thursday / Saturday) x 2 weeks. Medication was filled as "dispense 6 tablets for the 3 days of the week indicated x 2 weeks". Patient phoned back and explained that the medication is supposed to be taken every day for 14 days (i.e. after dialysis on the indicated days of the week, so that the medication would not be dialyzed and removed from the patient).	• Ambiguity of prescriptions/lack of indicated changes in therapy • Lack of independent double checks	• Dialysis introduces several additional risks to patient, one of which is potential medication incidents due to scheduling complexities.
Subtheme 2 – Drug Therapy Changes Relating to Renal Function		
Incident Examples	**Contributing Factors**	**Commentary**
• After packaging, the clinical check found that the dosing frequency of Valacyclovir to be inappropriate for the patient's renal function. The order was re-processed and counted, but the original label was not changed and still reflected the incorrect dosing frequency.	• Lack of appropriate follow-up to drug therapy changes	• Drug therapy changes related to patient's renal function should always be documented and followed up properly throughout the medication-use process.

DISCUSSION

Access to patient diagnostic test results (e.g. lab values) should be accessible to all healthcare professionals where access to these results would improve the quality of care they provide to the patient. This includes pharmacists who require access to indicators of patient renal function to evaluate the appropriateness of medication therapy and to recommend suitable alternatives if necessary. Furthermore, healthcare practitioners are encouraged to remind patients to share with them if they have any changes to their medical conditions or medications and if they have any recent blood work done. A resource that pharmacists can share and recommend patients to use is the 5 Questions to Ask About Your Medications handout where patients can learn about common questions that they should ask their healthcare providers regarding their medications at each encounter.

Table 5. Summary of Recommendations

For Pharmacists	For Prescribers
• Ask patients about changes to their medical/medication history at every visit. Document changes prominently in the patient profile • Recognize populations at high risk for renal impairment, for example, the elderly, patients under the care of renal specialists (e.g., nephrologists, renal clinics) and patients with hypertension and/or diabetes • Lab values, if available, should be consulted when prescribing and evaluating medication therapy • Practitioners should recognize and exercise caution with high-alert medications in renal impairment (**Table 1**) • When prescribing, recommending, or evaluating medication therapy, consider the potential for drug-disease interactions	
• Atypical medication dosing may signify that a patient has renal impairment. Unfamiliar medication dosing should be investigated to discover the rationale • If there is uncertainty surrounding a patient's degree of renal impairment, contact the patient or prescriber as appropriate to confirm renal status • Utilize pharmacist's expanded scope of practice (as permitted by provincial legislation) to adapt prescriptions as appropriate, including for patients with renal impairment • Implement a checklist of measures to take when adapting drug therapy (e.g. change SIG, adjust quantity, inform prescriber, inform patient, document changes, etc.) • Consider implementing an independent double check system for medications prescribed to patients receiving dialysis • Discuss patient medical conditions during counselling (for both prescription and non-prescription medications)	• Regularly monitor patients' renal function and communicate relevant changes to the patient and the patient's care team • Include relevant lab values (e.g. CrCl, INR, A1C, etc.) on prescriptions to allow pharmacists to independently assess the appropriateness of drug therapy • Clearly indicate changes in therapy and supporting rationale on prescriptions

CONCLUSION

This multi-incident analysis has highlighted several reasons that patients with renal impairment may be prone to medication incidents. These patients are cared for by multiple providers and they work closely with their healthcare team. Collaboration is needed within this circle of care to prevent errors and provide the best possible care.

ACKNOWLEDGEMENTS

ISMP Canada would like to acknowledge support from the Ontario Ministry of Health and Long-Term Care for the development of the Community Pharmacy Incident Reporting (CPhIR) Program. The CPhIR Program contributes to the Canadian Medication Incident Reporting and Prevention System (CMIRPS). A primary objective of CMIRPS is to analyze medication incident reports and develop recommendations for enhancing medication safety across all healthcare settings.

AIMS PROGRAM REMINDER

Please be reminded that as part of the AIMS program, pharmacy professionals must report medication incidents and near misses in the AIMS Pharmapod platform, as well as document the details of the medication incidents, analyze them to identify causal factors and share the learnings with their team in a timely manner.

REFERENCES

1. Levy, G. Pharmacokinetics in renal disease. *Am J Med.* 1977 Apr;62(4):461-5.
2. Lubran, MM. Renal function in the elderly. *Ann Clin Lab Sci.* 1995 Mar-Apr;25(2):122-33.
3. Ontario Renal Network. *Medications that must be considered for dose adjustment or avoidance.* Available from: https://www.ontariorenalnetwork.ca/en/medicationsafety
4. Paquette A. *Special Report: Top Drugs of 2015.* Canadian Healthcare Network. Available from: http://www.canadianhealthcarenetwork.ca/pharmacists/news/special-reports/special-report-top-drugs-of-2015-36905