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Drug-Related Problems Detected During Octo-Pills Medication Review by Pharmacists in Singapore: A Case Series

	
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ABSTRACT

Medication review by pharmacists has shown to reduce healthcare costs, improve patient health outcomes and reduce adverse drug events. However, due to the high patient load in the public hospitals, the pharmacists may not be able to conduct a thorough medication review with the patient. Project Octo-Pills is a pharmacist-led community outreach initiative in Singapore wherein older adults were referred from a tertiary hospital to community pharmacy for medication review. Due to the accessibility and strategic locations of community pharmacies in the neighborhoods of Singapore, Octo-Pills was able to provide health care services at a greater convenience to the patient. This case series featured the detection and resolution of four different types of drug-related problems via a synergized collaboration between the hospital and community pharmacists. The involvements of pharmacists in the community setting highlighted the potential bridge to fill the much-needed gap in chronic disease management for community-dwelling older adults.

INTRODUCTION

The economic burden in older adults' health care costs in Singapore is expected to rise tenfold by 2030 to more than US\$49 billion (S\$66 billion) annually¹. Hence, there is a need to explore areas where healthcare can be optimized and cost can be reduced. Adverse drug event is one of the factors that contribute to health care costs². Medication reconciliation and reviews are able to reduce adverse drug events and they can be carried out by healthcare professionals such as pharmacists. Pharmacist-led medication reconciliation and review have been shown to improve patient health outcomes and decrease readmission rates³.

The following series of case reports describe Drug Related Problems (DRPs) obtained from Project Octo-Pills, a pilot practice model in Singapore engaging community pharmacists in medication reconciliation and review for older patients referred from a tertiary hospital. The full protocol of Project Octo-Pills was published by Kheng Yong et al⁴. The high patient load in public hospitals leads to challenges in conducting a thorough medication review and physical medication reconciliation by pharmacists for all patients. A collaborative effort between hospital and community pharmacists to improve safe and effective medication use in the community was explored to overcome this challenge. The DRPs identified were categorized using the DRP classification from Pharmaceutical Care Practice (Table 1)⁵.

This case report entailed the pharmacists' findings during Octo-Pills medication review conducted from September 2015 to April 2016, steps taken to resolve the DRPs, and the non-pharmacological advice provided. In addition, precautions to prevent future occurrence of the respective or potential new DRPs were explored.

Case report 1: Unnecessary drug therapy (therapeutic duplication)

Patient Demographics			
Age	58		
Gender	Female		
Race	Chinese		
Medical History			
Drug allergy	NKDA		
Smoker	No		
Alcohol intake	Never or rarely		
Physical activity	<150 mins per week		
Medical problems	Type 2 diabetes mellitus, hypertension, proteinuria		
Relevant laboratory results	HbA1c 9.1 % three months ago HbA1c 9.4% one month ago Microalbuminuria 148mg/g three months ago Serum Creatinine 57µmol/L		
Current medication list			
	Medication	Strength	Dose/Frequency
1	Enalapril	5mg	1 tab OM
2	Telmisartan/Hydrochlorothiazide	40/12.5mg	1 tab OM
3	Acarbose	100mg	1 tab BD
4	Atenolol/Nifedipine SR	50/20mg	1 tab OM
5	Gliclazide	80mg	2 tab BD
6	Lantus Solostar	100 units/ml	26 units OM
7	Metformin HCl	500mg	2 tab BD

During Octo-Pills medication review, the patient was found consuming enalapril and telmisartan concurrently. The patient revealed that the medications were prescribed by different doctors in the tertiary hospital and her private clinic, respectively. Telmisartan /hydrochlorothiazide was the patient’s regular medication prescribed by her private doctor, while enalapril was added when she was admitted into the tertiary hospital. After discussion with her primary doctor, the patient was advised to stop enalapril and to continue telmisartan/hydrochlorothiazide only as both medications increased the risk of hyperkalemia if consumed concurrently. The patient was further advised on the importance of monitoring

her blood pressure at home, recording the readings and reporting them to her primary doctor. This case demonstrated the importance of medication reconciliation and communication between the various healthcare professionals in detecting therapeutic duplication at all transitions of care. Patients should be educated to identify the indications of their own medication, and bringing an updated medication list for all clinic appointments⁶.

Case Report 2: Dosage too low (possible drug interaction)

Patient Demographics			
Age	84		
Gender	Male		
Race	Chinese		
Medical History			
Drug allergy	NKDA		
Smoker	No		
Alcohol intake	Never or rarely		
Physical activity	<150 mins per week		
Medical problems	Coronary artery disease (triple vessel disease- refused CABG), benign prostate hyperplasia, hyperlipidemia, hypertension and chronic kidney disease stage 4 (CrCl 27mL/min)		
Current medication list			
	Medication	Strength	Dose/Frequency
1	Clopidogrel	75mg	1 tab OM
2	Omeprazole	20mg	2 caps OM
3	Alfuzosin HCl XL	10mg	1 tab ON
4	Atorvastatin	40mg	1 tab ON
5	Bisoprolol	2.5mg	1 tab OM
6	Calcium carbonate/ vitamin D	450mg/200IU	2 tabs OM
7	Ferrous fumarate	200mg	1 tab BD
8	Frusemide	40mg	0.5 tab OM
9	Glyceryl trinitrate	0.5mg	1 tab PRN
10	Hypromellose eye drops	0.3%	1 drop TDS
11	Isosorbide mononitrate SR	60mg	1 tab OM

12	Losartan	50mg	1 tab OM
13	Mecobalamin	500mcg	1 tab BD

The patient was prescribed clopidogrel for the prevention of cardiovascular disease as well as omeprazole for gastro-protection. Patients with risk factors such as the history of gastrointestinal (GI) bleed and advanced age have an increased risk of GI bleeding when taking antiplatelets. Thus, many clinicians prescribe proton pump inhibitors (PPIs) along with antiplatelet therapy for the prevention of GI bleeds⁷.

There is a concern that PPIs may interact with clopidogrel and reduce its effectiveness. PPIs may competitively inhibit the CYP2C19 enzymatic transformation of clopidogrel to its active metabolite⁸. This interaction, especially associated with omeprazole, may reduce the antiplatelet activity of clopidogrel. However, there is currently no consensus on the concomitant use of clopidogrel and omeprazole as some observational trials have shown mixed effects with this combination⁹. Nonetheless, the FDA issued safety concerns and labeling changes that discourage combining clopidogrel with omeprazole¹⁰. Due to the possible drug-drug interaction between clopidogrel and PPIs, the pharmacist recommended switching to a histamine-2 receptor antagonist as the patient has no history of GI bleeds with a single risk factor for due to age (84 years old), this may not require the use of a PPI.

Case Report 3: Adverse Drug Reaction (Drug interaction) and Adherence (Does not understand instructions)

Patient Demographics	
Age	84
Gender	Female
Race	Chinese
Medical History	
Drug allergy	NKDA
Smoker	No
Alcohol intake	Never or rarely
Physical activity	<150 mins per week
Medical problems	Chronic kidney disease Stage 5, non-specific anemia, coronary artery disease, mitral heart regurgitation (EF 45%), hypertension, hyperlipidemia, osteoarthritis (right knee) anterolisthesis, bilateral

		cataracts	
Current medication list			
	Medication	Strength	Dose/Frequency
1	Bisoprolol	2.5mg	0.5 tab OM
2	Frusemide	40mg	1 tab BD
3	Isosorbide dinitrate	10mg	1 tab TDS
4	Nifedipine LA	60mg	1 tab OM
5	Alfacalcidol	1mcg; 0.25mcg	1 tab 1mcg OM and 1 tab 0.25mcg on Tue, Thur and Sat morning
6	Aspirin	100mg	1 tab OM
7	Calcium carbonate	1.25g	1 tab TDS
8	Famotidine	20mg	1 tab BD
9	Ferrous fumarate	200mg	2 tab BD
10	Glyceryl trinitrate	0.5mg	1 tab prn
11	Sennosides	7.5mg	2 tab ON
12	Simvastatin	20mg	1 tab ON
13	Sodium bicarbonate	500mg	2 caps TDS

The patient had many changes to her medications. During her emergency admission two months prior to the Octo-Pills review, the dose of frusemide was reduced from 60mg to 40mg BD, and sodium bicarbonate was increased from 500mg to 1000mg TDS. During a recent hospital appointment one month prior to the Octo-Pills review, nifedipine LA 60mg OM was added. When the pharmacist probed the patient on the dosage for each medication, the patient claimed that she was taking frusemide 60mg BD.

The patient complained that she was experiencing dizziness and fatigue in the morning after consuming her medications, which caused her to be unable to step out of her home. She also admitted that she would skip her medications to avoid the dizziness. The patient monitors her BP at home and her systolic BP usually hovers around 140mmHg.

Dizziness and hypotension are especially common in the elderly due to decreased baroreflex sensitivity and parasympathetic activity¹¹. As the timing of administration does not reduce the efficacy of nifedipine, the pharmacist suggested changing nifedipine to be taken at night instead since most of her BP medications were taken in the morning. Most importantly, the pharmacist also emphasized to the patient the correct dose of frusemide.

Case Report 4: Adherence (patient prefers not to take)

Patient Demographics			
Age	68		
Gender	Female		
Race	Chinese		
Medical History			
Drug allergy	NKDA		
Smoker	3-20 cigarettes/day		
Alcohol intake	Never or rarely		
Physical activity	<150 mins per week		
Medical problems	Type 2 diabetes mellitus, hyperlipidemia, hypertension, thyrotoxicosis		
Relevant laboratory results	FBG 8.0mmol/L 2 weeks ago		
Current medication list			
	Medication	Strength	Dose/Frequency
1	Metformin	250mg	3 tabs BD
2	Atenolol	50mg	1 tab OM
3	Carbimazole	5mg	0.5 tab OM
4	Hydrochlorothiazide	25mg	1 tab OM
5	Lactulose Syrup	667mg/mL	10mL PRN
6	Lisinopril	20mg	1 tab OM
7	Simvastatin	20mg	1 tab ON

During Octo-Pills review, the patient mentioned that she would omit her evening dose of metformin if she does not take a proper meal. The patient was fearful of possible

hypoglycemia if metformin was consumed without a proper meal, though she has not experienced any hypoglycemia symptoms.

The pharmacist educated her that metformin alone is rarely associated with hypoglycemia¹². Furthermore, taking metformin as prescribed, reduces cardiovascular-related mortality rates and increases survival¹³. The pharmacist also explained that metformin is taken with food mainly to reduce gastrointestinal side effects such as diarrhea and abdominal pain¹⁴.

This case highlights the importance of patient education on appropriate medication use in improving adherence. The accessibility of community pharmacists also allows patients to clarify their doubts with regards to their medications or conditions. Community pharmacists are also well equipped to suggest measures to improve adherence such as the use of pillboxes if the patients have difficulty handling multiple medications.

DISCUSSION

This case series provided a few examples of the different types of DRPs detected in Octo-Pills review via a collaborative effort between the community and hospital pharmacists. In addition to the usual pharmacological counseling, community pharmacists also provided non-pharmacological advice to better manage patients' conditions.

Nonetheless, we recognized that the case series reported was not comprehensive as the community pharmacists did not have full access to the patients' medical records, which includes the full laboratory tests and clinical notes from the doctor.

CONCLUSION

Pharmacists are important healthcare ambassadors to ensure safe medication use and promote a healthy lifestyle. With increasing healthcare costs in Singapore, a collaborative effort between hospital and community pharmacists is crucial to prevent drug-related adverse events or hospital admissions among the older community dwellers.

Table 1. Drug-related problems categories

Drug therapy category	Cause of drug-related problem
Unnecessary drug therapy	<ul style="list-style-type: none"> • Duplicate therapy: multiple drug products are being used for a condition that requires only single drug therapy. • No medical indication at this time: there is no valid medical indication requiring drug therapy at this time. • Nondrug therapy more appropriate: the medical indication is more appropriately treated with nondrug therapy. • Addiction/recreational drug use: drug abuse, alcohol use, or smoking is causing the problem. • Treating an avoidable adverse reaction: drug therapy is being taken to treat an avoidable adverse drug reaction associated with another medication.
Needs additional therapy	<ul style="list-style-type: none"> • Preventive therapy: preventive drug therapy is required to reduce the risk of developing a new condition. • Untreated condition: a medical condition requires the initiation of drug therapy. • Synergistic therapy: a medical condition requires additional pharmacotherapy to attain synergistic or additive effects.
Ineffective drug	<ul style="list-style-type: none"> • More effective drug available: the drug is not the most effective for the medical condition and a different drug is needed. • Condition refractory to the drug: the medical condition is refractory to the drug product and a different drug is needed. • Dosage form inappropriate: the dosage form of the drug product is inappropriate. • Contraindication present: the drug product is contraindicated in this patient. • Drug not indicated for the condition: the drug product is not an effective product for the indication being treated.
Dosage too low	<ul style="list-style-type: none"> • Ineffective dose: the dose is too low to produce the desired response. • Needs additional monitoring: clinical or laboratory parameters are

	<p>required to determine if the dosage is too low for the patient.</p> <ul style="list-style-type: none"> • Frequency inappropriate: the dosage interval is too infrequent to produce the desired response. • Incorrect administration: the drug product was not administered by the appropriate route or method. • Drug interaction: a drug interaction reduces the amount of active drug available resulting in a lack of effectiveness in this patient. • Incorrect storage: the drug product was stored incorrectly and lost potency. • Duration inappropriate: the duration of the drug therapy is too short to produce the desired response.
Adverse drug reaction	<ul style="list-style-type: none"> • Undesirable effect: the drug product causes an undesirable reaction that is not dose-related. • Unsafe drug for the patient: a safer drug product is required due to patient risk factors. • Drug interaction: a drug interaction causes an undesirable reaction that is not dose-related. • Incorrect administration: the drug product was administered by the incorrect route or method resulting in an adverse reaction. • Allergic reaction: the drug product caused an allergic reaction. • Dosage increase/decrease too fast: the drug dosage was administered or escalated too rapidly resulting in an adverse reaction.
Dosage too high	<ul style="list-style-type: none"> • Dose too high: the dose of the drug is too high for the patient, resulting in toxicity. • Needs additional monitoring: clinical or laboratory parameters are required to determine if the dosage is too high for the patient. • Frequency too short: the dosing frequency is too short for the patient. • Duration too long: the duration of drug therapy is too long for this patient. • Drug interaction: a drug interaction increases the amount of active drug available resulting in toxicity in this patient.
Adherence	<ul style="list-style-type: none"> • Does not understand instructions: the patient does not understand

	<p>how to properly take or use the drug product and dosage regimen.</p> <ul style="list-style-type: none">• Cannot afford drug product: the patient cannot afford the drug therapy recommended or prescribed.• Patient prefers not to take: the patient prefers not to take the drug therapy as instructed.• Patient forgets to take: the patient does not remember to take sufficient doses of the medication.• Drug product not available: sufficient supply of the drug product is not available to the patient.• Cannot swallow/administer drug: the patient is not able to swallow or administer the drug therapy as intended.
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Note. Reprinted [adapted] from *Pharmaceutical Care Practice* (p.150-150), by Cipolle et al, 2007, New York: McGraw-Hill Companies.

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Conflict of interest

There is no conflict of interest to declare.

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