Unintentional medication incidents when using combination drug products

By Allen Chiu and Certina Ho

While the intrinsic nature of healthcare is to do good, the opposite may unintentionally occur. For example, something as simple as combining two pills as one in order to provide convenience and improve adherence in patients can still have the potential to cause patient harm. The following medication incident was anonymously reported to the Institute for Safe Medication Practices Canada (ISMP Canada):

*"Patient was admitted to emergency with confusion and hypotension. It was later found out that the patient took both metformin 1000 mg twice daily and a combination metformin/sitagliptin 1000/50 mg tablet twice daily. Several weeks ago, it was suggested that the patient switched to a combination pill [metformin/sitagliptin 1000/50 mg], but the old medication [metformin 1000 mg] was not discontinued."**

*Note: The maximum dose of metformin is 2550 mg per day. In this case, the patient has taken a total of metformin 4000 mg per day due to duplicate therapy.

Combination drugs or fixed-dose combinations, for the purpose of this article, refer to a medication that contains more than one active ingredient. They are also sometimes referred to as "combo pills" or "polypills". Using combination drug products can potentially reduce pill burden and may increase patient adherence, leading to better patient outcomes. This strategy may also reduce the financial cost to the patient. Fixed-dose combinations are most commonly seen in anti-hypertensives and anti-hyperglycemics, but they can also be found in other therapeutic categories, such as, glaucoma eye drops and anti-retrovirals, etc. A 2015 report of prescription data by the Canadian Healthcare Network showed that combination medications were the top two most commonly prescribed within the therapeutic class of cardiovascular drugs. Table 1 provides some examples of these combination drug products.

However, as seen in the above medication incident, using combination drugs can also inadvertently cause patient harm. This may not be an isolated case. A 2018 study on Irish prescription claims reported that therapeutic duplication errors were more likely in anti-hypertensive fixed-dose combinations compared to their individual components. While the above incident involved a different class of medications (i.e. anti-hyperglycemics), it was a therapeutic duplication error of metformin. While more research may be warranted on this topic, Table 2 offers some suggestions that may potentially decrease the risk of these incidents. In conclusion, while switching patients from single to combination drugs can have many benefits, healthcare practitioners should be aware of the potential risks associated as well. H

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Combination Drug Product	Individual Active Ingredients	Therapeutic Class
Janumet® / Janumet® XR	sitagliptin and metformin	Anti-hyperglycemic
Caduet® (generics available)	amlodipine and atorvastatin	Anti-hypertensive and antihyperlipidemic
Atacand Plus® (generics available)	candesartan and hydrochlorothiazide	Anti-hypertensive
Altace HCT®	ramipril and hydrochlorothiazide	Anti-hypertensive
Vimovo®	naproxen and esomeprazole	Analgesic and gastroprotection
Truvada®	emtricitabine and tenofovir	Anti-retroviral

Table 1. Examples of Combination Drugs or Fixed-Dose Combinations (Note: This is not a comprehensive list.)

Suggestions	Comments
Technology e.g. Computerized Clinical Decision Support (CCDS)	Differentiate between duplicate drug therapy alerts versus duplicate therapeutic class alerts from the CCDS. Discontinue inactive medications on patient profile to avoid unnecessary duplicate therapy alerts from the CCDS.
Communication and Patient Education	Counsel patients on new medications when switching to combination drugs or fixed-dose combinations. Ensure patients understand that the new fixed-dose combination replaces which of their old medications. Ask patients to bring back old medications (i.e. inactive medications on their profile) to the pharmacy for disposal to prevent any confusion.
Medication Review	Conduct medication reviews with patients periodically or during changes of their medication therapy. This may help patients better understand their medication regimen and update patient profiles at the same time to prevent unnecessary alerts from the CCDS.

Table 2. Suggestions to Prevent Therapeutic Duplication Errors Associated with Combination Drugs or Fixed-Dose Combinations

ICU national research network:
First of its kind in Canada

By Steven Gallagher

A Niagara Health physician is leading the launch of a national network to support the growth of research in Intensive Care Units at community hospitals in Canada.

The Canadian Community ICU Research Network, which held its inaugural meeting on Nov. 11 in Toronto, is the brainchild of Dr. Jennifer Tsang, Niagara Health's Research Lead and Intensivist.

Dr. Tsang worked closely with Dr. Alexandra Binnie, an Intensivist at William Osler Health System, to see her idea come to fruition.

"The goal of the network, a first of its kind in Canada, is to develop strategies for building and sustaining research programs in community hospitals," says Dr. Tsang, who also credited Niagara Health Intensivist Dr. Erick Duan for his collaboration in developing the network. "Research has a profound impact on the health and wellbeing of the people who live in our communities. Health research provides important information about disease trends and risk factors, outcomes of treatment and patterns of care, to name a few."

Members of the Intensive Care Unit at Niagara Health who conduct research.

More than 65 per cent of Canadian patients receive care in community hospitals, but, historically, most medical research has been conducted in academic hospitals in larger centres.

"If you're only studying patients in the academic centres, the results are not applicable to everyone," says Dr. Tsang.

Representatives from about 20 hospitals, universities and research organizations from four provinces – Ontario, Quebec, Alberta and Manitoba – attended the inaugural meeting, which was sponsored by Niagara Health and Niagara Health Foundation. The meeting focused on describing the current research landscape in community ICUs, discussing strategies to build research capacity in community ICUs and defining the structure and scope of the research network.

Niagara Health, a regional healthcare provider with multiple sites, has been a leader when it comes to research in a community hospital setting, working closely with its academic partners.

Niagara Health established a dedicated Research Office in 2015 to strengthen its research and academic partnerships and set out to conduct research that would inform care, inspire innovation and create environments of collaborative learning.

Research and clinical trials are taking place in several Niagara Health departments/divisions, including the Intensive Care Unit, Oncology, Urology, Cardiology and Emergency Medicine.

Dr. Tsang and Paige Gehrke, a Registered Nurse in the ICU at Niagara Health's St. Catharines Site, recently had their work published in the prestigious Canadian Medical Association Journal (September 3, 2019 issue), examining the impact of research activity in community health settings.

They were part of a team of clinicians who suggest that increased involvement in research could offer more capacity for national research, expedite knowledge translation, increase staff engagement, opportunities for continuing education and enhanced clinician career satisfaction, among many other benefits. H

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