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Safeguards for HYDROmorphone–Results of a Targeted Demonstration Project

All opioid medications require attention to ensure patient safety. HYDROmorphone, a potent opioid, is the most common medication associated with harmful medication incidents voluntarily reported to ISMP Canada. From January 2000 to September 2013, ISMP Canada received 233 incidents involving HYDROmorphone with an outcome of harm or death via AnalyzeERR®* and individual practitioner reports. Over the past 5 years, 256 incidents, also with an outcome of harm or death, were reported to the National System for Incident Reporting (NSIR).†[1-2]

ISMP Canada has reviewed these incident reports, conducted in-depth investigation and analysis, and developed recommendations and strategies to mitigate harm.[3-5] Numerous agencies across Canada, including Health Canada, provincial ministries of health, Accreditation Canada, and provincial and territorial offices of the chief coroner or medical examiner, have recognized the need for additional safeguards with HYDROmorphone and have supported initiatives such as removal of high-concentration HYDROmorphone from patient care areas, use of TALLman lettering, and implementation of independent double checks. Despite dissemination of information about these and other harm-reduction strategies, medication incidents involving HYDROmorphone continue to occur. Review of medication incident associated deaths involving HYDROmorphone and other opioids investigated by coroners and medical examiners[6] identified 3 specific risk factors for patient harm: continued presence of high-dose HYDROmorphone in patient care areas leading to ten-fold overdoses, excessive starting doses of HYDROmorphone, and inconsistent monitoring of patients receiving opioids. This bulletin will describe the results of a targeted demonstration project designed to address these risk factors.

Project Description

ISMP Canada reviewed the global patient safety literature for recommendations related to enhancing the safe use of HYDROmorphone, including recommendations previously published by ISMP Canada.[3-5] Recommendations were sorted according to a hierarchy of effectiveness[7] and the area of the medication-use system targeted. A team of medication safety experts reviewed the recommendations and used them to develop a set of 5 actions (see Table 1) that would focus on the target concerns and that had not previously been recommended by ISMP Canada. The actions selected had to be suitable for implementation within a 3 month time period.

* AnalyzeERR®, available from ISMP Canada, is a web-based medication incident and near miss reporting system for healthcare facilities.
† The NSIR (provided by the Canadian Institute for Health Information) is a component of the Canadian Medication Incident Reporting and Prevention System (CMIRPS) Program. More information about the NSIR is available from: http://www.cmirps-scdpim.ca/?p=12 (NSIR data extraction period from Nov 13, 2008 to Sept 30, 2013)

Table 1: HYDROmorphone Demonstration Project—Recommended Actions and Rationale (listed according to a hierarchy of effectiveness[7])

Action #	Action to improve system safety	Rationale
1	Preparation by pharmacy of doses less than 1 mg in prefilled syringes	To prepare in advance, doses that are commonly used in practice, reducing the risk of inadvertent overdose
2	Availability of a standard-volume chart for usual doses withdrawn from a 2 mg/mL vial or ampoule	To reduce the risk of dose miscalculation in the preparation of doses
3	Creation of an electronic alert in CPOE screens, pharmacy information systems, and ADC screens for initial doses greater than 1 mg IV/IM/SC/PO	To minimize the risk of an initial dose that is too high and to ensure assessment of opioid tolerance and comorbidities that might necessitate a dose reduction
4	Performance of a weekly audit to remove high-dose HYDROmorphone (i.e., parenteral dose greater than 2 mg) from patient care areas	To prevent inadvertent administration of 10-fold overdoses by limiting availability of 10 mg/mL concentration
5	Distribution of an opioid information sheet to patients and families	To assist patients and families in becoming part of the monitoring process, thus supporting the ability of healthcare staff to recognize and respond to overdoses

CPOE = computerized prescriber order entry; ADC = automated dispensing cabinet

A small number of hospitals were recruited to participate in a demonstration project to test implementation of these 5 recommended actions, with each hospital being asked to commit to undertaking at least one of the actions between January and March 2013.

At the outset of the project, representatives of the participating hospitals were asked to complete a structured assessment of safety strategies for HYDROmorphone already in place at their respective sites. The assessment consisted of 20 items in 6 categories: prescribing, order verification and dispensing, administration, monitoring, management of overdose, and education of patient and family. The assessment included the 5 actions described in Table 1, as well as other safety strategies applicable to HYDROmorphone and other opioids. ISMP Canada's Medication Safety Self Assessment format and secure web-based platform were used for the assessment, which allowed individual hospitals to rate themselves on a set of criteria and then review their own results and also compare themselves to the whole group.

During the project, support was provided to participating hospitals by means of 3 conference calls facilitated by the ISMP Canada project team. At the end of the project, participants were asked to complete a project evaluation survey to assess their progress and to describe any barriers encountered.

Findings

Of the 10 hospitals that initially expressed interest in the project, 6 completed the HYDROmorphone assessment and 5 completed the project evaluation survey. One hospital participated in the conference calls but did not complete any of the other project activities. It is not known whether the other 3 hospitals implemented any of the recommended actions. The implementation results and comments from participants are summarized in Table 2.

Table 2: Implementation Results Summary

	Recommended action to improve system safety	Number of hospitals	Selected comments from participants
1	Preparation by pharmacy of doses less than 1 mg in prefilled syringes	In place before project (n = 1) Considered but not implemented (n = 4)	- Barriers reported: workload; requirement to standardize doses; lack of perceived benefit of 0.5 mg vs. 2 mg doses; potential for errors if multiple doses are available in ADCs.
2	Availability of a standard-volume chart for usual doses withdrawn from a 2 mg/mL vial or ampoule	In place before project (n = 1) Implemented in some areas (n = 4)	- On the units where it was piloted, nurses were extremely positive! Now planning to roll out throughout the hospital. - A chart and basic HYDROmorphone facts were included in a one-pager that prints on the back of the narcotic sheets. No official feedback but positive comments.
3	Creation of an electronic alert in CPOE screens, pharmacy information systems, and ADC screens for initial doses greater than 1 mg IV/IM/SC/PO		
3a	Prescribers receive an electronic alert about limiting initial doses of HYDROmorphone to 1 mg or less IV/IM/SC/PO	Considered but not implemented (n = 1) NA: hospital does not have CPOE (n = 4)	- Current computer system is not set up to alert specific doses, so there was concern about alert fatigue if all HYDROmorphone doses resulted in alerts. Also, a number of order sets include doses of 1 mg or more, so it wouldn't be appropriate for that dose to result in an alert.
3b	Pharmacy information systems provide an electronic alert about limiting initial doses of HYDROmorphone to 1 mg or less IV/IM/SC/PO	Considered but not implemented (n = 5)	- Because of the number of warnings already in place, there is no plan to implement this strategy. - With our pharmacy system, the alert would have had to be attached to every entry for HYDROmorphone. For this reason we did not add an alert to our pharmacy system due to the potential for alert fatigue.
3c	ADCs provide an electronic alert about limiting initial doses of HYDROmorphone to 1 mg or less IV/IM/SC/PO	Implemented throughout hospital (n = 2) Implementation planned (n = 1) NA: hospital does not have ADCs (n = 2)	- ADCs provide an electronic alert about limiting initial doses of HYDROmorphone to 1 mg IV/IM/SC/PO or less. - We felt having the dose/volume information on the ADC as well as posting the chart in the medication room was beneficial to the nursing staff. Feedback was positive.
4	Performance of a weekly audit to remove high-dose HYDROmorphone (i.e., parenteral dose greater than 2 mg) from patient care areas	In place before project (n = 1) Considered but not implemented (n = 1) Implemented throughout hospital (n = 2) Implementation planned (n = 1)	- The nursing units were audited once weekly…. after discussion with the technicians, it was felt that a daily audit would be easier to remember. - This was thought to be common practice…but with closer investigation it was clear improvements were necessary. - This is a valuable and simple intervention. It is now implemented. - We do not dispense HYDROmorphone in dosage forms greater than 2 mg to the floors.
5	Distribution of an opioid information sheet to patients and families (suggest piloting for 2 months on a surgical unit or preoperative clinic)	In place before project (n = 1) Implemented in some areas (n = 1) Implementation planned (n = 3)	- The handout is being distributed in the pre-admission clinic and evaluated on our inpatient surgical unit. Some patients have questioned the meaning of "opioid naïve" and others found it very thorough and helpful. - All materials provided to patients must first be approved by the hospital communication department. [time factor]

ADC = automated dispensing cabinet, CADD = continuous ambulatory delivery device [cartridges],
CPOE = computerized prescriber order entry, NA = not applicable.

Assessment of Existing HYDROmorphone Safety Strategies

Responses from the hospitals suggested opportunities for improvement in each category of assessment. The average response was less than 50% of achievable score for each category, with the lowest overall scores in the area of education of patient and family about HYDROmorphone (less than 30% of achievable score).

Implementation of Recommended Actions

All of the 5 hospitals that completed the project evaluation survey reported that they had implemented at least one of the recommended actions. The activities most frequently undertaken were provision of a standard-volume chart for withdrawal of doses of HYDROmorphone from a 2 mg/mL vial (Action 2) and implementation of weekly audits of narcotic stock for removal of high-dose HYDROmorphone from patient care areas (Action 4). One hospital pharmacy was preparing prefilled syringes of HYDROmorphone (Action 1) at the outset of the project because of a supply problem, but workload issues prevented this institution from continuing the practice. None of the hospitals tested alerts about maximum initial doses in order entry systems (pharmacy or prescriber) (Action 3). One hospital added an alert about initial maximum doses of HYDROmorphone to its automated dispensing cabinets; the alert included a reminder to start HYDROmorphone at the lowest dose if a dose range was ordered. One hospital implemented the patient information sheet (Action 5), and 3 hospitals reported their intention to adapt the sheet for internal use; the fifth hospital was already using a similar information sheet so did not participate in this activity.

Discussion

Not surprisingly, the activities undertaken over the course of this demonstration project were those that could be implemented easily and quickly and that were within the direct control of the pharmacy department (i.e., standard HYDROmorphone volume charts and routine audits of narcotic stock). There was a high level of interest in the patient information sheet. The recommendation to prepare prefilled syringes by the pharmacy was expected to be difficult to implement because of the associated workload, but this measure did generate discussion among the participating hospitals about dose standardization. ISMP Canada and the Office of the Chief Coroner for Ontario[8] have advocated for lower dose formats and it is hoped that manufacturers will soon step forward in this area. Concerns about "alert fatigue" influenced hospitals' decisions not to test "blanket" electronic alerts about maximum recommended initial doses of HYDROmorphone. Alternative approaches, such as including this information in order sets, may be more successful.

Completion of the HYDROmorphone assessment provided participating hospitals with a baseline for improvement efforts, and respondents indicated that participation in the project would help them to focus on specific areas requiring enhancement. The results from this small group of hospitals are not widely generalizable, but the findings will support further initiatives and educational efforts.

Conclusion

Hospitals participating in this project had a unique opportunity to test targeted safeguards with support from ISMP Canada and a peer group. All of the participating hospitals indicated that it was a valuable undertaking and that their participation would affect practice in their facilities. This project has highlighted some approaches that organizations may not have previously considered to enhance the safe use of HYDROmorphone and other opioids and reduce opportunities for patient harm.

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Opioid Resources for Practitioners and Consumers

1. **Information for Patients and Families about Opioid Pain Medicines** (customizable PDF)**:**
   www.ismp-canada.org/download/HYDROmorphone/ISMPCanada_OpioidInformationForPatientsAndFamilies.pdf
2. **Consumers Can Help Prevent Harm from Opioid Use** (videos)**:**
   English (with and without subtitles): www.safemedicationuse.ca/tools_resources/tips.html
   French (with and without subtitles): www.medicamentssecuritaires.ca
3. **HYDROmorphone Safety Self-Assessment program:**
   Contact ISMP Canada at mssa@ismp-canada.org

Look-Alike / Sound-Alike ALERT:
trastuzumab emtansine (Kadcyla) and trastuzumab (Herceptin)

Health Canada recently approved Kadcyla (generic name: trastuzumab emtansine), as a single agent, for the treatment of patients with HER2-positive, metastatic breast cancer who have received both prior treatment with Herceptin (generic name: trastuzumab) and a taxane (e.g., docetaxel, paclitaxel), either separately or in combination.[1]

Herceptin is the brand name for trastuzumab (an anti-HER2 antibody), whereas Kadcyla is a HER2-targeted antibody drug conjugate, combining trastuzumab and a cytotoxic agent (derivative of emtansine).[1] As both Herceptin and Kadcyla share an identical component in their respective generic names (trastuzumab), and both have indications for HER2+ metastatic breast cancer,[1,2] there is a strong potential for medication error between the two compounds. Mix-ups of these 2 products can lead to serious patient harm.

Although their indications may be similar, the dosing and treatment schedules for these 2 products are quite different. Herceptin (trastuzumab) can be given as a loading dose of up to 8 mg/kg intravenously (IV), followed by a maintenance dose of 6 mg/kg IV every 3 weeks, or as a loading dose of 4 mg/kg IV, followed by a maintenance dose of 2 mg/kg IV weekly.[2] However, the recommended and maximum tolerated dose of Kadcyla (trastuzumab emtansine) is 3.6 mg/kg as an intravenous infusion administered every 3 weeks as a single agent.[1]

In the United States, the Food and Drug Administration (FDA) recognized the potential for medication error with these 2 medications and approved the use of the generic name ado-trastuzumab emtansine for Kadcyla to help distinguish it from trastuzumab.[3] As a result, Canadian practitioners who are using US-based drug information references or resources may see the name "ado-trastuzumab emtansine" where they might have expected to see "trastuzumab emtansine", and they may not find a monograph listing under "trastuzumab emtansine". Health Canada has published a recent alert advising health practitioners of the risk for mix-ups when using these 2 medications.[4]

Recommendations

Given the look-alike, sound-alike nature of these 2 medication names, the manufacturer has used different colours on the product packaging to help differentiate the 2 medications (Figures 1 and 2). In addition, facilities are encouraged to consider the following strategies to reduce the risk of harmful errors:

- Use both the brand and the generic name for these 2 medications throughout the medication-use process (e.g., medication order, medication label, medication administration record).
- Review computerized and automated processes to ensure that the complete generic name and the brand name are properly displayed to the end users (e.g., on drug selection screens).
- Create an automated alert for computerized prescriber and pharmacy order entry systems showing information such as the following:
  - "Trastuzumab and trastuzumab emtansine are **NOT** interchangeable – switching a patient from one drug to the other requires the close supervision of a specialist."

- Provide recommended dosing for the 2 medications at the point of order entry, to increase the chance a drug selection/dosing error can be recognized.
- Actively involve patients (and family members) in the medication-use process. Educate patients about the potential for this mix-up to occur.
- Employ strategies to differentiate the generic names of Kadcyla and Herceptin and implement safeguards in your practice to prevent mix-ups. For example:
  - Review pharmacy storage areas to determine if the 2 products are stored in close proximity in the refrigerator.
  - Place warning labels on the 2 products and/or in their storage areas.[5]
- Distribute this alert widely in your organization to enhance awareness of this potential hazard.

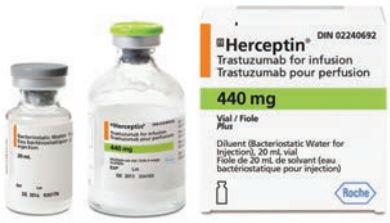

Figure 1: Canadian product labels and packaging for trastuzumab (Herceptin)

Figure 2: Labelling and packaging for trastuzamab emtansine (Kadcyla)

Manufacturer Note: Kadcyla labelling and packaging will be modified for the Canadian market (e.g., add Drug Identification Number).

Note: Confusion between these medications stems from the sharing of an identical component in their generic names; as such, healthcare professionals must ensure safety strategies are in place to avoid product mix-ups.

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International Medication Safety Network Releases Position Statement on Naming, Labelling and Packaging of Medicines

The International Medication Safety Network (IMSN) was formed in 2006 and includes representatives from more than 20 countries. The IMSN recently released a position statement with recommendations for a comprehensive global solution to the unsafe naming, labelling and packaging of medicines. It was recognized that the approach to this global challenge requires collaboration between regulators, pharmaceutical industry, healthcare providers and patient organizations. In Canada, such collaborations are occurring nationally to enhance patient safety.[1,2]

More details can be found in the press release available at:

http://www.intmedsafe.net/ArticleFiles/IMSN%202013%20Paris%20Press%20Release%20%283%29.pdf

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