ADVERSE EVENTS RELATED TO MEDICATIONS IDENTIFIED BY A CANADIAN POISON CENTRE

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ABSTRACT

Background
Poison centres are an underutilized source of information on adverse events related to medications, including therapeutic errors and adverse drug reactions.

Objective
To demonstrate the feasibility of using a poison centres' electronic data to identify and describe adverse events related to medications.

Methods
This one-year, retrospective cross-sectional pilot study was conducted at one Canadian Poison Centre. All records from the IWK Regional Poison Centre database in Nova Scotia between November 1, 2007 and October 31, 2008 for unintentional exposures were abstracted for a descriptive data analysis.

Results
An issue related to use of a medication was the main reason for 1,525 (32.5%) of 4,697 eligible calls. Of the 1,525 calls, 970 (63.6%) were coded as 'unintentional-general.' There were 470 (30.8%) calls for unintentional therapeutic errors and 61 (4.0%) for adverse drug reactions. The majority of calls involving medications were judged to have resulted in minimal or no toxic effect (78.4%). However, 3.3% of calls involving adverse drug reactions resulted in admission to a critical care unit (*n*=2). Approximately 1% of calls involving unintentional therapeutic errors resulted in admission to hospital (*n*=6).

Conclusions
Calls to poison centres provide a potentially valuable source of information on adverse events related to medications that are likely not reported elsewhere. Establishment of a mechanism to routinely share information from *all* Canadian poison centres with relevant national drug safety programs (e.g., MedEffect™ Canada) will provide a supplementary source of information and contribute to building capacity for detection of sentinel events and pharmacosurveillance.

Key Words (MeSH): *Poison control centers; drug toxicity; medication errors; adverse drug reaction reporting systems*

Medications are one of the most common therapeutic interventions administered in our healthcare system today. Their widespread use has resulted in adverse events or unintended harm to some patients from mechanisms such as adverse drug reactions or medication errors. International patient safety studies have identified that such harm is an important and common problem, estimated to cost the Canadian and US healthcare system billions of dollars annually.[1-4]

Prevention of adverse events related to medications can have a significant impact on healthcare costs.[1,5,6] An important element of an effective prevention strategy is information about the magnitude and nature of adverse events related to medications that result in harm to patients. The need for information has resulted in substantial investments in the establishment of voluntary reporting systems such as MedEffect Canada™ for reporting adverse drug reactions.[7] However, one of the major limitations of voluntary reporting systems is significant under-reporting. For instance, it is estimated that approximately 5% of adverse drug reactions in children are reported to Health Canada.[8] Concerns related to under-reporting have led to exploration of alternate sources of information.

Poison centres have been identified as a potentially valuable source of information on adverse drug reactions and unintentional therapeutic errors.[9-14] The information gathered by poison centres differs from other reporting sources. Centres typically operate every day of the year on a 24-hour basis and calls can be made from the public and/or healthcare professionals. Poison centres are staffed by trained nurses or pharmacists with expertise in toxicology, history-taking, and risk assessment.[9,10,15] Use of electronic data collection systems increases the capability for a systematic approach to identifying sentinel events.[11,15] For instance, in a study of five US poison centres, Spiller et al. identified a ten-fold increase in the number of reports of adverse drug reactions related to lisdexamfetamine compared with the previously reported mean rate for other amphetamines. Spiller et al. also reported that only half of the adverse drug reactions identified by the poison centres were reported to the FDA Medwatch program.[16]

In Canada, poison centre services operate in all of the provinces and territories; although, in some cases the resource is shared by more than one province.[17] The data collection systems in the country are not standardized; however, most systems collect detailed information about the nature of the toxic ingestion. In the case of a medication-related exposure, the data are classified into different etiologies (e.g., adverse drug reaction, excessive dose, therapeutic error etc.). The purpose of the current study is to demonstrate the feasibility of using electronic data from one Canadian poison centre to identify and describe adverse events related to medications. The use of existing data is a relatively inexpensive approach that will help efforts to more completely identify the true burden of the problem, those at greatest risk and to develop targeted prevention strategies.

METHODS

The study was conducted using data from the Izaak Walton Killam Regional Poison Centre (IWK RPC). The centre provides a 24-hour telephone service that operates 365 days a year for the population of Nova Scotia and Prince Edward Island (approximately one million).[18] Staff from the centre collect data on pharmaceutical and non-pharmaceutical exposures that are intentional or unintentional in nature. The information is entered into an electronic database. The centre provides services to the public as well as healthcare providers caring for both adult and paediatric patients. The study was approved by the IWK Health Centre Research Ethics Board.

All records from the IWK RPC database between November 1, 2007 and October 31, 2008 for unintentional exposures were abstracted for a descriptive data analysis. Potentially eligible calls included all unintentional exposures to any product. Electronic records for all unintentional exposures were reviewed to ascertain pharmaceutical exposures. Descriptive statistics were performed using STATA statistical software (STATA Corp., College Station TX, Version 9). Calls from out-of-province, calls involving intentional exposures and any calls involving animals exposed to poison were excluded from the analysis.

Call information at the RPC is captured using an electronic patient management tool called Visual Dotlab© (VDL) which utilizes data elements from the Toxic Exposure Surveillance System (TESS)©, a uniform data set developed by the American Association of Poison Control Centers.[15] In TESS©, ***therapeutic errors*** are defined as "an unintentional deviation from a proper therapeutic regimen that results in the wrong dose, incorrect route of administration, administration to the wrong person, or administration of the wrong substance." The instructions for data entry in the TESS© manual

state that drug interactions resulting from unintentional administration of drugs/foods which are known to interact should also be included in this category.[12] The category of ***adverse reaction*** is used to monitor a variety of products. Events should be coded as an adverse reaction if the event occurred "with normal, prescribed, labeled or recommended use of the product, as opposed to overdose, misuse, or abuse."[14] It includes any events that result in an "unwanted effect caused by an allergic, hypersensitive, or idiosyncratic response to the active ingredients, inactive ingredients or excipients."[14] Only non-pharmaceutical products are coded as unintentional – misuse (e.g., mixing cleaning products containing bleach and ammonia).[19] Events coded as 'unintentional – general' included events not otherwise defined as therapeutic error, adverse drug reaction or unknown. During a call and subsequent follow-ups, information is gathered about the patient, the substance or exposure, toxic effects, therapy and outcome. For purposes of the study, adverse events related to medications included calls to the RPC that were coded as adverse drug reactions, therapeutic errors and any other pharmaceutical exposures (e.g., accidental ingestion by a child) in which there was no documented intent for self-harm.

RESULTS

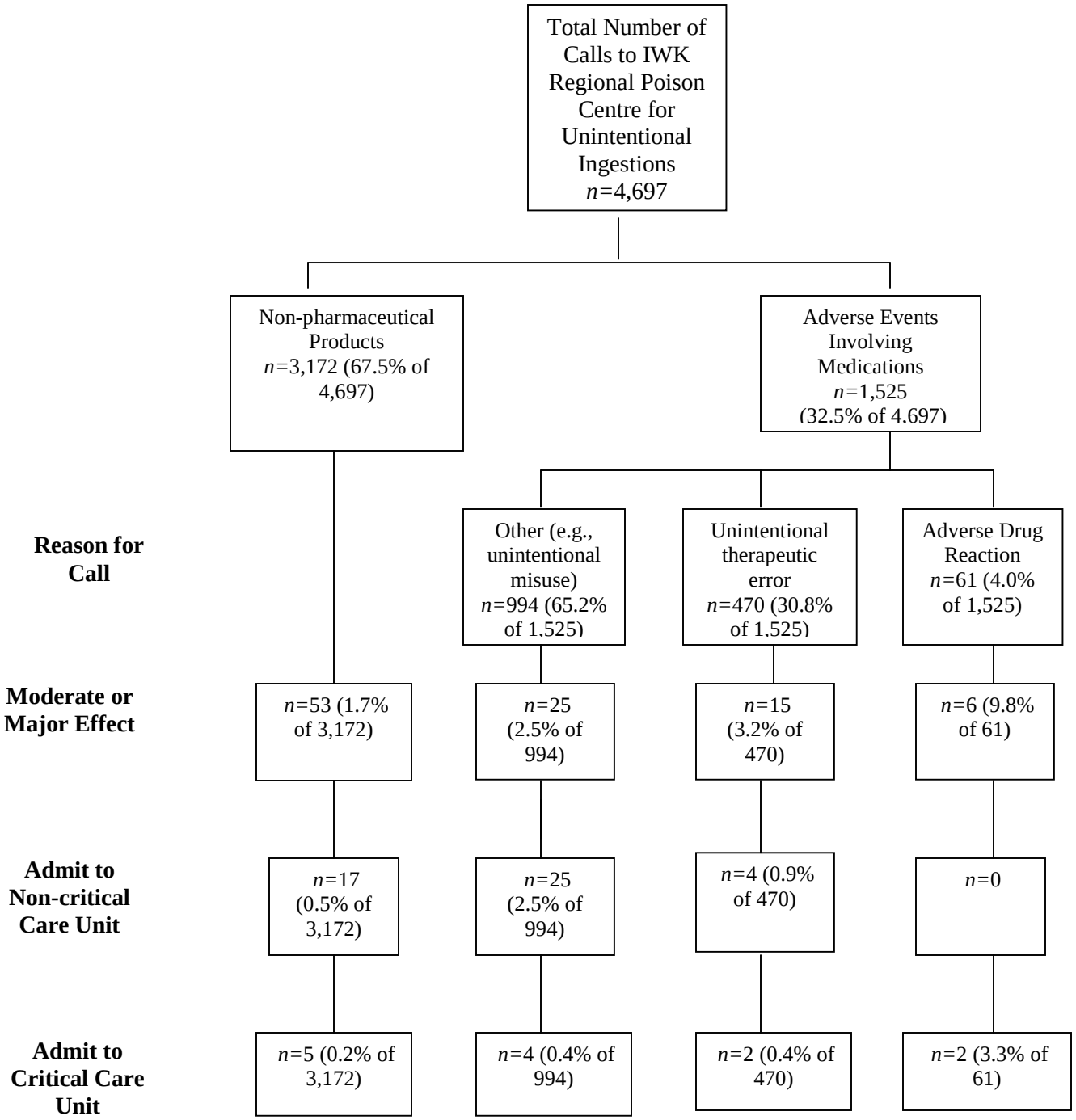
Of the 8,557 calls made to the RPC during the one-year study period, 45% (*n*=3,860) were excluded on the basis of geographical location and intent. The majority of unintentional exposures were non-pharmaceutical in nature (3,172 of 4,697 [67.5%]). Figure 1 is a flow chart of the study population and Table 1 describes their characteristics.

TABLE 1 Characteristics of calls for unintentional exposures to the IWK Regional Poison Centre from November 2007-October 2008

Characteristic	**No. (%) of patients[§]** ***n* = 4,697**
Sex	
Male	2,562 (54.7% of 4,683[†])
Female	2,121 (45.3)
Age in years, median (IQR[¶])	9.0 (2.0-20.0)
Reason for Call	
Unintentional – general	3,996 (85.1)
Unintentional therapeutic error	504 (10.7)
Unintentional misuse*	114 (2.4)
Adverse drug reaction	65 (1.4)
Unintentional unknown	18 (0.4)
Acuity	
Acute	4,470 (95.2)
Acute-on-chronic	177 (3.8)
Chronic	44 (0.9)
Unknown	6 (0.1)

[§]Unless otherwise specified; [¶]Interquartile range;[†]Number with information recorded; [Ω]Regional Poison Centre; *Applies to non-pharmaceutical exposures only

FIG. 1 Flow diagram of study population



In 1,525 (32.5%) of 4,697 eligible calls, an issue related to use of a medication was the main reason for the call. Of the calls involving medications, the median age of the exposed individual was five years, and slightly more occurred in males (51.1% *vs*. 48.9%). A total of 970 (63.6%) calls involving medications were coded as 'unintentional-general.' There were 470 (30.8%) calls for unintentional therapeutic errors and 61 (4.0%) for adverse drug reactions. There were 24 (1.6%) calls coded as 'unintentional-unknown.' The majority of calls involving medications were judged to have resulted in minimal or no toxic effect (78.4%). However, 3.3% of calls involving adverse drug reactions resulted in admission to a critical care unit (*n*=2). Approximately 1% of calls involving unintentional therapeutic errors resulted in admission to hospital (*n*=6).

Calls involving unintentional therapeutic errors were evenly distributed between males and females, although the median age was greater for females (37.0 *vs*. 16.0 years). The medications most often implicated in therapeutic errors were analgesics and anti-pyretics (116 of 470 [24.7%]), antibiotics (37 [7.9%]), anti-depressants (25 [5.3%]) and sedatives hypnotics (15 [3.2%]). The medications identified in the most serious therapeutic errors (i.e., admission to a critical care unit) were phenytoin and flupenthixol.

Calls involving adverse drug reactions were more common in females (57.4% *vs*. 42.6%) and the median age was greater for females (30.0 *vs*. 14.5 years). The medications most often implicated in adverse drug reactions were analgesics and anti-pyretics (16 of 61 [26.2%]) and antibiotics (14 [23.0%]). The medications identified in the most serious adverse drug reactions were diazepam and pentobarbital. Of note, there were five calls related to vaccines of which three identified specific vaccines: MMR, menjugate and pneumococcal vaccine polysaccharide. Two were classified as therapeutic errors and one as an adverse drug reaction.

DISCUSSION

A third of the calls to one Canadian poison centre for unintentional exposures involved medications. Of those, there were 470 calls for unintentional therapeutic errors and 61 for adverse drug reactions. Although the majority of calls involving medications were judged to have resulted in minimal or no toxic effect, 3.3% of calls involving adverse drug reactions resulted in admission to a critical care unit. Poison centres offer an accessible, well-established community resource for individuals and/or healthcare professionals to report adverse events related to medications. Poison centres are staffed by specialists in poison information with access to physicians for consultation as needed.[9-11,15] They routinely take detailed and timely histories, provide immediate treatment advice, and follow callers to determine disposition.[9-11,13] These attributes, particularly the information on patient outcomes, make poison centre data a potentially valuable and underutilized source of information on adverse events related to medications that could complement existing reporting systems.

There is growing recognition of this potential value as demonstrated by several large-scale studies of adverse drug reactions[12,14] and therapeutic errors involving medications[9,12] reported to US poison centres. Approximately 10% of all calls to US poison centres for human exposure cases are related to medication errors, the majority of which take place outside of the hospital setting. Over a five year period this accounted for more than one million cases in the National Poison Data System.[9] In the current study, approximately 30% of all calls involving medications were classified as unintentional therapeutic errors, underscoring the potential burden of the problem. Although most hospitals have reporting systems, there are few mechanisms to collect data on medication errors that occur and/or are managed outside of the hospital setting. Poison centres are one such resource.

The burden of harm from adverse drug reactions is also significant. They are estimated to occur in 11% of hospitalized patients and result in millions of outpatient visits annually.[11] Given the valuable information collected by poison centres, it has been recommended that there should be greater integration between their data and federal initiatives such as the FDA Medwatch program for reporting adverse drug reactions.[10-13] Yet, the rates of reporting remain low. There are a number of factors contributing to the low rates of direct reporting including the lack of time and resources to complete the documentation required by the

FDA, difficulty in determining causality for an event and the belief that many adverse drug reactions are already known and thus, not worth reporting.[11] The issue of under-reporting is not restricted to the United States. A systematic review involving 37 studies from 12 different countries estimated that the median rate of under-reporting of adverse drug reactions was 94%.[20] It is estimated that less than 10% of adverse drug reactions are reported to Health Canada by healthcare professionals.[21] MedEffect™ Canada and the Canadian Medication Incident Reporting and Prevention System (CMIRPS) are two national reporting schemes for adverse events involving medications.[7,22] The extent to which Canadian poison centres send direct reports to these programs is not known; it was beyond the scope of the study to survey provincial poison centres with respect to their reporting policies. No reports were sent directly from the IWK Regional Poison Centre to any of the national reporting schemes during the study period, even for most serious adverse drug reactions that resulted in admission to a critical care unit. There may have been reports sent by healthcare professionals who initially contacted the poison centre, although this is not routinely documented by the centre.

Monitoring medication use "has been widely advocated as necessary and feasible to optimize care at both the individual patient level (patient safety) and the public policy level (post-marketing surveillance and cost-effectiveness)."[23] In the US, real-time toxicovigilance using the TESS© database was started in 2003 to identify exposures with potential public health and safety concerns.[15] By pooling data collected in different states, national trends in reporting toxic effects for a medication can be identified in real-time, which can ensure a more rapid response to a public health threat.[15] This may be particularly valuable for post-marketing surveillance for new products or those used off-label.[11,14,21] Pooled data may also improve detection of rare events.[14,15]

National poison centre data have been used in the US to improve product safety through mechanisms such as the development of child-resistant packaging and classification of medications (i.e., prescription versus over-the-counter).[18] Adoption of a similar approach in Canada has not been fully explored. While there may be advantages to direct reporting of adverse drug reactions identified through poison centres, their data have some limitations. Calls to poison centres are voluntary in nature and there is no direct contact with callers or those exposed to the toxic substance.[14,15] There may also be reporting biases (e.g., more serious adverse drug reactions reported to poison centres).[14]

If a simplified mechanism existed to facilitate direct reporting of adverse drug reactions to Health Canada from all of the poison centres in the country, it is likely that the number of reports would increase substantially from current levels. Even though many lay people may not be aware of Health Canada's initiatives for reporting adverse drug reactions, poison centres are a familiar resource that is easy to access. Moreover, unlike some federal reporting schemes, centres typically conduct follow-up phone calls to collect much needed data on outcomes and have expert staff to assist in the interpretation of the information and its potential significance.[11] Given the US experience of low direct reporting rates from poison centres to federal agencies, careful consideration will need to be given to coordinating and streamlining processes for reporting events identified in Canadian poison centres to the relevant national system(s). Establishment of a mechanism or processes to routinely share information from *all* Canadian poison centres with national drug safety programs will provide a supplementary source of information and contribute to building capacity for detection of sentinel events and ongoing pharmacosurveillance.

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