Commentary

ARE WE READY TO MANAGE NATURAL HEALTH PRODUCTS IN HOSPITAL PRACTICE?

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Under the *Natural Health Products Regulations* that came into effect in Canada in January 2004, natural health products (NHPs) are defined as vitamins and minerals, herbal remedies, homeopathic medicines, traditional medicines, probiotics and others. Healthcare professionals and patients can identify licensed NHPs by the eight-digit Natural Product Number (NPN) or Homeopathic Medicine Number (DIN-HM) on the product label. The number indicates the issuance of a product license and the product's assessment by Health Canada as being safe, effective and of high quality under its recommended conditions of use.[1] By September 2009, more than 15,000 NHPs were licensed in the Health Canada Database.

A random telephone survey conducted among more than 2,000 Canadian adults in 2005 revealed that 71% had already used an NHP and that 38% of these had done so on a daily basis.[2] Various studies have documented that patients seen in the emergency room or admitted to the hospital used NHPs at home.[3-5]

Accreditation Canada has identified two required organizational practices (ROPs) on medication reconciliation (i.e., reconcile the patient's/client's medications upon admission to the organization and with the involvement of the patient/client; reconcile medications with the patient/client at referral or transfer; and communicate the patient's/client's medications to the next provider of service on referral or transfer to another setting, service, service provider or level of care within or outside the organization).[6] Despite the fact these ROPs have been in place since 2007, very few hospitals systematically collect full data on NHPs used at home during the medication reconciliation process. Even when the information is collected, it is not necessarily entered into the patient's computerized medical record if the NHP is not prescribed and used during hospitalization. Detecting NHP-drug interactions is, therefore, difficult on a large scale, given the large number of potential NHP-drug interactions and the lack of data entry. The increasing use of NHPs, combined with over-the-counter and prescription medicines, suggests that NHP-drug interactions and NHP adverse effects may be of significant public health consequence even though we recognize a very low rate of declaration of such events.[7-12]

Therefore, are we ready to manage natural health products in Canadian hospital practice? We are not quite sure. Different barriers and factors should be pointed out. Physicians, nurses and pharmacists have limited exposure to NHPs in their academic curriculum and suffer from a lack of exposure to these products in hospital practice. Moreover, there are a limited number of reliable sources of information on NHPs. Available evidence includes mainly adverse event database entries, spontaneous case reports, in vivo and in vitro drug metabolism studies as well as in vivo drug interaction studies in healthy subjects and patients. However, very few controlled studies that assess the clinical significance of NHP efficacy or NPN-drug interactions have been published. A systematic review of American and Canadian pharmacists' attitudes, knowledge and professional practice behavior as they relate to dietary supplements showed that pharmacists do not perceive their knowledge of dietary

supplements to be adequate. Pharmacists also recognize they do not routinely document, monitor or inquire about their patients' use of these products.[13]

In a Canadian mother-child teaching hospital (CHU Sainte-Justine), the hospital formulary includes 2,120 products. Fewer than 100 products are considered NHPs under the 2004 revised definition of which 90% are vitamins previously classified as drugs under the *Food and Drug Act*. In-house audits revealed limited documentation of NHP use in the emergency room or upon admission even though the use of a medication reconciliation form had been implemented throughout the hospital since 2007.[14,15]

In order to improve the management of NHP data information at the hospital, we compared two NHP databases (Natural Standards® [NSD][16] and Natural Medicines Comprehensive Database® [NMCD9][17]) for the purpose of possibly integrating them into the institution's pharmacy information system. Both databases offer a significant amount of information, but also show many differences (e.g., data presentation, type of quality score/scale used for data available, risk rating of drug-NHP interactions, and ability to interface with the in-house pharmacy information system).[18] We developed a web report in asp.net accessible through the pharmacy intranet to allow the display of a list of patients from the pharmacy information system (GesphaRx®, CGSI TI, QC) for pharmacists on wards with the NSD. The list can be printed by pharmacy users in real time per patient care unit including a list of active drug prescriptions and natural health products with a potential drug-NHP interaction. A total of 53,895 interaction pairs and 1,512 generic drug names were imported from the NSD in 2008.

We then randomly selected five pediatric patient files in psychiatry, general pediatrics, infectious diseases, oncology and intensive care. None of the selected files had any active documented NHP prescriptions. A total of 21 different generic drug names were identified for active orders. Based on active orders, we calculated the number of potential NHP-drug interactions identified per drug, which varied from 12 to 129 in the NSD and from 1 to 96 in the NMCD. We found a total of 1,451 potential NHP-drug interactions in the NMCD and 1,276 in the NSD. Only 205 were common to both databases.

There was no significant difference between the overall average number of pairs per drug between the two databases.[19] Our pilot study revealed a high and variable number of pairs of NHP-drug interactions per drug between the NSD and the NMCD and a limited overlap of such pairs.

Finally, we extracted the data of active drug orders from the pharmacy information system on May 1, 2009, based on a census of 274 patients and 2,272 active drug orders. Our pharmacy information system uses an online version of Lexi-Interact® and included at that time a total of 14,696 pairs of the most relevant drug-drug interactions (e.g., Category X – Avoid combination and Category D – Modify Regimen).

The online database also included three other categories (e.g., Category C – Monitor therapy, Category B – No action needed, and Category A – No interaction) not interfaced locally.[20] On that day, the pharmacy information system flagged 49 potential drug-drug interactions for 21 patients. We previously published a description of that data integration in our system.[21] Having only active drug orders on patient file and none for NHPs, we calculated a total of 98,971 potential NHP-drug interactions using the same census for the same day with the NSD. A total of 120 out of 300 NHP monographs accounted for 80% of the potential NHP-drug interactions. A similar simulation with drug-drug interactions was not feasible, as we had interfaced only the more relevant drug-drug interactions from Lexi-Interact®. While these two numbers cannot be compared head to head (i.e., 49 potential selected drug-drug interactions and 98,971 potential all NHP-drug interactions), this one-day data extraction illustrates the significant amount of data information available for NHPs. Is this NHP information ready for use by clinicians?

Medical and pharmaceutical societies have strengthened the importance of documenting the use of NHPs.[20-24] The American Society of Health-System Pharmacists (ASHP) has urged pharmacists and other healthcare practitioners to become more aware of dietary supplement use in their everyday practice and has encouraged pharmacists to increase their efforts to prevent dietary supplement-drug interactions. ASHP has also pointed out that the training of pharmacists and other healthcare practitioners should include relevant content on the taxonomy, formulation,

pharmacology and pharmacokinetics of dietary supplements. Such training should also be part of pharmacy university curricula.[25-26]

Our experience suggests it is feasible to integrate an NHP database into pharmacy practice. While NHPs will probably remain largely undeclared in the near future, our pharmacists can now print a list of potential NHP-drug interactions to be taken into account in medical rounds or patient counseling activities.

The list can also help to investigate idiosyncratic or unexplained clinical effects in some patients. However, the full potential of this integration relies on the documentation of NHPs used by patients at home through the medication reconciliation process and with an online detection of potential NHP-drug interactions added to pharmacy information systems with the active participation of physicians, nurses, pharmacists and students in training. Aside from the use of a list of potential NHP-drug interactions, the Pharmacology and Therapeutics (P&T) Committee should adopt a policy on NHP evaluation and documentation. A list of targeted NHPs with significant known drug interactions (e.g., St. John's wort, red yeast, cassia, bloodroot, etc.) could be adopted locally and published to improve the medication reconciliation process. While the P&T Committee should not lower its standards for the scientific evaluation of products to be listed on the local hospital formulary, P&T members should identify a set of criteria to target NHPs.

While drug-drug interaction checkers have a long history in the literature, NHP-drug interaction checkers do not. By being exposed to NHP literature and tools at school and in clinical practice, clinicians will influence NHP database providers to improve their products and become more useful clinically; for instance, through the addition of risk rating scores to NHP-drug interactions. Therefore, NHP database providers must improve their products for them to become more meaningful to clinicians.

Our pilot studies did not address the relative likelihood or severity of NHP-drug interactions, nor can they provide the proportion of interactions perceived as clinically relevant. With sufficient exposure to NHP databases in clinical settings and with clinical experience, our group of pharmacists will eventually be able to identify clinically relevant NHP-drug interactions. Further studies are required to evaluate the usefulness of integrating NHP databases into our pharmacy practice. Finally, while a good dose of skepticism surrounds NHPs in clinical practice, we believe clinicians can no longer ignore their use by patients in the continuum of care.

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