

Adverse Event Reporting for Herbal Medicines: A Result of Market Forces

Déclaration des effets indésirables associés aux médicaments à base de plantes médicinales : le résultat des forces du marché



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Abstract

Herbal products are readily available over the counter in health food stores and are often perceived to be without risk. The current Canadian adverse event reporting system suffers from severe underreporting, resulting in a scarcity of safety data on herbal products. Twelve health food store personnel in the Greater Toronto Area were interviewed about their responses to herbal product-related adverse reactions. They generally fostered customer loyalty by offering generous return policies, which included collecting contact information to be sent to the manufacturers with the returned product. Thus, despite the public's lack of knowledge about the formal reporting system, adverse reaction information was directed to manufacturers whenever it resulted in a product return. The relationship between health food stores, industry and Health Canada provides a new opportunity to facilitate adverse event reporting. Additional information could be collected during the return process, and educational initiatives could be implemented to augment current post-market surveillance procedures for herbal products.

Résumé

Les magasins de produits naturels offrent sans ordonnance des produits à base de plantes médicinales qui, souvent, donnent l'impression de ne comporter aucun risque. Au Canada, le système actuel de déclaration des effets indésirables présente un très faible taux de déclaration, ce qui se traduit par une insuffisance de données sur la sécurité des produits à base de plantes médicinales. Les employés de 12 magasins de produits naturels du Grand Toronto ont été interrogés sur leur réponse aux cas d'effets indésirables associés aux médicaments à base de plantes médicinales. En général, ils encouragent la fidélisation de la clientèle en proposant de généreuses politiques de retour, qui comprennent la collecte des coordonnées, lesquelles sont transmises aux manufacturiers avec le produit retourné. Ainsi, en dépit du manque de connaissance sur le système officiel de déclaration, l'information sur les effets indésirables est trans-

mise aux manufacturiers quand un produit est retourné. La relation entre les magasins de produits naturels, l'industrie et Santé Canada offre de nouvelles occasions pour faciliter la déclaration des effets indésirables. Des renseignements supplémentaires pourraient être récoltés au cours du processus de retour d'un produit, et des activités d'éducation pourraient être mises en place pour accroître la surveillance post-commercialisation des produits à base de plantes médicinales.



THE EXTENSIVE USE OF NATURAL HEALTH PRODUCTS (NHPs), SUCH AS vitamins and herbal medicines, is partially explained by a widespread belief that such products are “natural” and thus safe. Increasingly, it has become clear that NHPs, especially herbal medicines, can have adverse effects, including drug interactions (McNeill 1999; Pittler and Ernst 2003). However, relatively little is known about the adverse effects associated with herbal medicines.

Adverse drug reactions (ADRs) are defined as unintended consequences suspected to be related to the use of medicinal products, including herbal medicines (WHO 1995). Spontaneous reporting systems, such as the Canada Vigilance Program (previously named the Canadian ADR Monitoring Program), are used by many countries as a way of monitoring suspected ADRs. Voluntary reports of serious or unexpected ADRs and those associated with recently marketed products are particularly encouraged (Fletcher 1991). In Canada, physicians, pharmacists, other healthcare providers and consumers can submit reports for assessment to identify product safety concerns that require action, such as changes to product labelling or dosing, or removal from the market.

Although NHPs are widely used, few adverse reactions are reported to pharmacovigilance systems (Green et al. 2001; Barnes 2003; Health Canada 2007). It is well established that underreporting of suspected ADRs is an important limitation of spontaneous reporting systems (Rogers et al. 1988; Fletcher 1991; Mann and Andrews 2002). Low ADR reporting rates associated with prescription medicines are recognized as an international problem. It is generally accepted that less than 10% of adverse drug reactions are reported (Rogers et al. 1988; Moride et al. 1997; Alvarez-Requejo et al. 1998). Underreporting is likely to be greater for herbal medicines and other NHPs than for pharmaceutical drugs for several reasons. For example, healthcare professionals are often unaware of patients' NHP use (Barnes et al. 1998; Winslow and Shapiro 2002; Barnes 2003; NHPD 2005; Wheaton et al. 2005), how to identify adverse reactions associated with NHPs and what to report (Herdiero et al. 2004; Charrois et al. 2007). In Canada, NHPs have been categorized as medicinal products and regulated by Health Canada only since January 2004 (NHPD 2003). It is unclear whether the lack of ADR reports for NHPs suggests that they are truly

rare, or reflects a history of inadequate effort (in Canada and internationally) to encourage, collect and assess such reports.

Herbal medicines and other NHPs are available over the counter in Canada at community pharmacies, grocery outlets and health food stores, as well as from the Internet. The Canadian regulatory status of NHPs (i.e., non-prescription, non-pharmacy only) has provided an opportunity for health food stores to respond to public demand, and they now offer a wide selection of such products. There are approximately 2,700 health food stores (typically, retail outlets where at least 50% of stock comprises NHPs, health foods or both) across Canada, mostly in the provinces of Ontario, Quebec and British Columbia (CHFA 2005). These stores may be independently operated or belong to a retail chain with multiple outlets city- or nationwide. There are no legal requirements regarding educational background or training for staff; each store has different employment requirements, ranging from online courses or in-store training/mentoring to no training/experience requirements (Glisson et al. 2003; Mills et al. 2003).

Although health food stores are an important source of NHPs, their staff do not have a defined role in monitoring the safety of the medicinal products they sell (Healey et al. 2002). Rather, their business is providing health-related products, meeting customer demands and providing adequate customer service to remain viable in a competitive marketplace. In contrast, conventional healthcare professionals (e.g., doctors, pharmacists) are bound by professional and ethical standards to report serious or unexpected instances of suspected ADRs. In reality, however, many health professionals do not report, despite expectations to do so (Inman 1985; Alvarez-Requejo et al. 1998; Hazell and Shakir 2006).

One way in which health food stores remain competitive is by offering generous return policies for dissatisfied consumers to reduce the purchase risk of finding a good product match or a product of acceptable quality. Money-back guarantees can signal sellers' confidence in the quality of their products (McWilliams and Gerstner 2006). The economic rationale for return policies is that of warranty. Return policies insure customers against products about which they are uncertain, making risk-averse customers willing to pay for the product (Che 1996). With NHPs, uncertainty about product benefits and the wide range of product options may raise doubts for the consumer. This uncertainty, along with strong competition from other stores selling similar goods, provides a rationale for these return policies.

Against this background, this study examined the views of health food stores' staff on herbal product safety issues. The work forms part of a larger study also involving pharmacists and consumers who have experienced adverse reactions from NHPs. This paper explores how business incentives influence collection and reporting of adverse effect information in health food stores and how return policies may be related to store personnel's ability to respond to Health Canada's attempts to collect ADR information

associated with herbal products. Herbal products were specifically selected based on the increased risks associated with these products, compared with other NHPs.

Methods

Ethics approval was obtained at the University of Toronto. In-depth, semi-structured interviews were conducted with 12 health food store personnel by a single interviewer (RW) with extensive training in qualitative research methods. A purposive sample was chosen to include participants from independent and chain health food stores, from city and suburban areas as well as from different age and gender groups, and with varying retail experience. Participants from health food stores located in the Greater Toronto Area, identified from telephone directories, Internet listings and by word of mouth, were approached in person. Interviews were conducted until theoretical saturation of the key emerging themes was obtained (Creswell 1998). Interviews were audio-recorded, and field notes were handwritten during and immediately following the interviews. Interviews and field notes were transcribed and coded using content analysis techniques by two independent coders; disagreement was resolved through in-depth discussion. NVIVO 7 software was used to organize the data (Richards and Richards 2002). Data analysis and coding took place throughout data collection. The interview guide was updated and modified after the coding sessions to ensure more elaborate data collection in key emerging themes.

Results

The results of this study show that health food store personnel were unaware of the reporting system for ADRs. They also perceived and identified ADRs differently than does the medical community. When the ADR resulted in consumer dissatisfaction, however, the product was returned to the manufacturer, including a report of some type. Table 1 summarizes participants' demographic characteristics.

Generally, health food store personnel did not know that suspected herbal-related ADRs could be reported to Health Canada, whom to contact to report ADRs or which types of reactions should be reported.

Q: Are you familiar with the reporting system in Canada for side effects?
A: No. [interviewer explains] I didn't know about it at all. (#10)

Most participants described examples of "side effects" (a lay term for ADRs as defined by Health Canada) associated with NHPs that were reported by consumers. Store personnel considered predictable untoward responses, such as a niacin flush, or diarrhea from a "detoxification" product, as examples of possible ADRs about which

TABLE 1. Demographics of health food store personnel interviewed (n=12)

Interview	Gender	Position	Contact hours*	Years of experience	Training in natural health products	Type of store
1	F	Advisory staff	Part time	10 years	3 years formal training	Small chain
2	M	Manager	Full time	16 years	Self-study	Independent
3	F	Staff	Part time	3 years	3 weeks in-store training	Chain
4	M	Manager	Full time	5 years	6 months in-store training	Chain
5	M	Sales rep	Full time	11 months	Graduate student in healthcare	Chain
6	M	Advisory staff	Full time	9 years	2 years formal training	Independent
7	F	Owner	Full time	8 months	Self-study	Independent
8	F	Sales staff	Full time	7 months	6 weeks in-store training	Small chain
9	F	Sales staff	Part time	1 year	6 months formal training	Small chain
10	F	Owner	Full time	1.5 years	Self-study	Independent
11	F	Sales staff	Part time	3 years	Self-study	Small chain
12	F	Sales staff	Part time	2 years	3 years formal training	Independent

* Part time < 24 hours per week; full time ≥ 25 hours per week

they might inform consumers prior to purchase of the product. They reported that these “true” ADRs were rare. More common was a situation they described as NHPs that “did not agree” with or “did not suit” specific customers. This situation might manifest as an upset stomach or “uneasy feeling” after taking the product. Although these effects would be classified as ADRs by Health Canada, health food store personnel did not consider them cause for concern about the product per se. Rather, such incidents were conceptualized as a need to help the consumer find a better product “fit”:

I think I would take it back from them thinking that maybe it really didn't suit them and then I will ask them why, what happened to you? Why don't you feel that it suited you, or maybe I will tell them “why not try another one to see if it suits you.” In that way, I could guide them. (#8)

Health food store personnel described more serious symptoms, such as rashes, as the result of individual allergies, which they did not classify as ADRs. Often, store personnel would attribute “side effects” to inappropriate product use by consumers rather than ADRs (allergies, and effects associated with inappropriate use, are considered ADRs by Health Canada). Health food store personnel therefore perceived and

identified ADRs differently than the medical community. Participants stated that they commonly referred customers to their healthcare providers, or the product manufacturer, for more information if they suspected that a customer had a reaction.

Oh, I take it very seriously. I want to make sure that ... if it was really serious I would say "go and see your doctor," and if it was a side effect and I don't really know why [it happened] I would give them the phone number and the website to contact the company so that they can directly call them and double-check with them because they have to know that as well, and if they don't feel comfortable, I will call them myself with them there. (#10)

This example relates to another key theme that emerged from the data: the strong drive of health food store personnel to provide good customer service. Store personnel described the importance of developing and maintaining relationships with their customers, and this extended to provision of advice and information about NHPs. Health food store staff appear to encourage consumers to see them as a source of information about NHPs to help maintain customer loyalty.

You know, at the store level we have to be prudent to gain enough information about the dangers and risks of products to be able to guide the consumer, and they are, after all, looking at us for advice. (#2)

[Customers] want technical information, and they are looking to us as if we're naturopaths in a health food store, not sales associates in a health food store. (#12)

Another perceived component of providing good customer service was swift response to product dissatisfaction (possibly resulting from ADRs) by accepting returns. The return procedure included collection of customer contact information, subsequently submitted to the manufacturer in conjunction with the reason for the return in order to recoup retailer losses on the product. Health food store personnel had difficulty conceptualizing ADRs, and thus also had difficulty describing how they might respond if one occurred. They talked about how they would return products to the manufacturer and refund the cost if the customer were dissatisfied with the product for any reason:

Even if it is not a bad reaction ... you believe them and you refund it regardless, but just by their answers. You have to trust them; whether you believe it or not you have to return the product if they have a reaction, and then we just take their information and we contact the company and sometimes the com-

pany calls them back. [It happens about] once a week. (#9)

Thus, participants essentially reported ADRs to product manufacturers as a consequence of processing product returns. They described their continuing relationships with the manufacturers, in particular with staff answering questions about their products and the department that handles returns.

I know this company, because ... we buy many of their products. ... They give us very good information. Especially if they have enough time with you, they don't hurry you and they explain things and they also tell you things. You know, we are not doctors – they just advise [us], so they are very good. (#8)

Participants described how the return policy was used as a mechanism to generate customer loyalty and satisfaction by reducing the customer's perceived risk. The return policy was also used to evaluate a product's quality to help decide whether the store should continue to sell it.

We have a very good return policy, and we actually encourage people to give us the feedback: if they're not satisfied, we want to hear about it, because we might not carry the line in the future if there are problems with it. It helps us, and it helps us not to lose the customer as well, where some people, if they bought something [and] they have no recourse to get any money back or refund, they might just stop shopping at this location, or other locations, for that matter. Whereas if they come back here, well, we could encourage them to exchange the product or try something else that may be more to their liking, and that way we could have a satisfied customer that continues to come back. (#4)

The costs of the returned product can be recouped by the store that accepts the return from the customer only if the product is returned to the manufacturer with customer contact information and a reason for the return:

We write up a credit request from the company and we fax the company the credit request. We phone them and we email them and we put the paperwork together, and leave the product to be picked up by the company at some point. It is just pretty much a form that asks for return address, name, phone number, that sort of thing. (#11)

Health food store personnel considered manufacturers responsible for providing good-quality products.

Sometimes batch numbers are also messed up. We have had [product] recalls before. I would go with the company first. For sure, it would be the company's responsibility. (#6)

Discussion

Although health food store staff were unaware of the Canada Vigilance Program for reporting suspected ADRs, they learn of consumers' experiences of suspected adverse reactions associated with NHPs and they return products to manufacturers in cases where customers may have experienced them. The arrangement between health food stores and manufacturers regarding product returns raises the question of whether this process could be harnessed to improve ADR reporting for NHPs.

Financial incentives have been used to encourage health professionals to complete ADR reports, but it is not clear whether this approach improves the number and quality of such reports (Inman 1985). For health food store personnel, providing information to the manufacturer along with the return is the result of a financial incentive – recouping losses on returned products. In order to receive financial remuneration for their product costs, they provide consumer contact information and reason for the return. It is possible that this process could be expanded to facilitate submission of more information to the manufacturer by retailers, which the manufacturer could then use for ADR reporting to Health Canada. Additional information (such as other medications/products taken at that time, length of exposure to the product, a description of the reaction) would need to be incorporated into the return reports to allow them to be used as ADR reports. The manufacturer would then send the information to Health Canada, as is currently required under Canadian NHP regulations, as expedited reports for serious ADRs or, for non-serious events, in an annual summary. Given the close relationships between health food stores and industry, reporting of ADR information by retail staff to manufacturers would seem relatively straightforward to implement.

However, reliance on product manufacturers to submit reports of suspected ADRs to Health Canada has limitations. A key issue for pharmacovigilance for herbal medicines and other NHPs concerns the accuracy and comprehensiveness of manufacturers' ADR reports to Health Canada as part of their legal obligations. Regulatory changes have been implemented to ensure quality, safety and efficacy of NHPs. Safety information is particularly important for appropriate regulation of these products (NHPD 2003; Citizen Petition 2008; Harvey et al. 2008). Where manufacturers or licensees receive information on serious ADRs (those that require hospitalization, are life-threatening or result in significant disability or death), the NHP regulations (which are still being phased in) require them to provide Health Canada with case reports within 15 calendar days after becoming aware of the reactions (NHPD 2003). Licensees are also

required to prepare annual summary reports containing an analysis of all ADRs occurring for their products within the previous year. Because of the inherent conflict of interest, questions remain over whether all relevant reports are included and whether the information presented complies with Health Canada's requirements.

Another important limitation to submission of information to manufacturers is confidentiality. Manufacturers require a customer name and contact information as a measure of authenticity of the return. Health Canada's ADR reporting form, however, requires anonymity to ensure confidentiality of health information.

If submission of suspected ADR reports by health food stores to Health Canada via product manufacturers is not an ideal mechanism, how else might the information obtained by health food store staff reach the pharmacovigilance system? There are three ways in which retail staff could be more actively involved in reporting suspected ADRs associated with NHPs. On learning of adverse reactions or "problems" with herbal medicines or other NHPs, health food store staff could:

1. *Advise the purchaser to contact his or her doctor or pharmacist.* Study data suggest that this is happening to some extent. While this approach would direct purchasers to conventional healthcare professionals (who are generally trained in identifying ADRs and have a formal role in reporting them), there are still several barriers to a report's reaching Health Canada. For example, consumers appear to be hesitant to disclose use of NHPs to physicians and other conventional healthcare providers, particularly if they experience adverse effects associated with these products. In addition, the healthcare provider must recognize the symptoms as a suspected ADR, as well as follow through to complete an ADR report which is submitted to the Canada Vigilance Program. However, underreporting from healthcare professionals is a problem owing to lack of time or knowledge, or uncertainty about ADRs and the ADR reporting system (Sweis and Wong 2000; Herdiero et al. 2004; Hazell and Shakir 2006).
2. *Advise the purchaser to report the event directly to the Canada Vigilance Program,* possibly with the assistance of the customer's conventional healthcare provider or health food store personnel.
3. *Store personnel report the event to the Canada Vigilance Program on the purchaser's behalf.*

Options 2 and 3 have their own limitations. Health Canada would categorize reports from either health food store personnel or consumers as public or "lay" reports. While these reports may serve to improve signal detection on certain products, they may not have the detail or quality of information required, such as laboratory test results and accurate records of concomitant medications (although these details can also be missing from health professionals' reports). Healthcare providers are encour-

aged to submit all reports of suspected ADRs – it is not necessary for them to attempt to confirm causality nor to undertake intensive investigations of the events. However, the quality and completeness of ADR reports are important factors in Health Canada's ability to undertake causality assessments. Although some argue that patient ADR reports may be less likely to represent true reactions than are physician reports, large-scale reporting from laypersons (such as retail personnel) might be valuable for detection of symptomatic reactions to new drugs (Mitchell et al. 1988). For example, signals might be identified earlier when patient reports are included in the data analysis (Jarernsiripornkul et al. 2003; Hammond et al. 2007). Patient reports may be particularly important when little is known about the product and its use with other products, as is the case with many NHPs (Woo 2007). In fact, some research shows that consumer reports may be of higher quality than physician reports, with more complete descriptions of the event (Medawar et al. 2002; Medawar and Herxheimer 2004).

Another challenge is that health food store staff would need training in Health Canada's ADR reporting procedures. Training for health food store personnel varies widely, and staff are often untrained in disease recognition or medical terminology, making it difficult for them to assess whether a given return was actually associated with an ADR. False positives could be generated if customers exaggerate symptoms to receive refunds on purchased products. Additionally, suspected ADRs will be identified only if consumers attempt to return the products. Even if a system were devised to train health food store personnel in ADR recognition and completion of ADR reports, there is currently no way to enforce standards in the unregulated retail industry. Furthermore, there is no incentive for health food store staff to report ADRs directly to Health Canada other than contributing to protection of public health; thus, willingness to participate may vary.

Limitations

This study has some limitations. First, it involved only a small number of interviews. Nevertheless, participants varied in their demographic characteristics, and saturation of key themes indicates that additional interviews were unlikely to raise completely new views. Participants reported very similar return policies and gave similar answers regarding their knowledge about the Canada Vigilance Program. The highly focused research questions for the study (regarding perceptions of herbal ADRs and how they are handled) may also have contributed to early saturation of key themes after a small number of interviews (Guest et al. 2006).

Although the intent of the research was to ask participants primarily about herbal medicines, they interpreted the term more broadly and discussed perceptions related to all NHPs, implying that they would behave similarly regardless of the type of NHP associated with an ADR.

Conclusions and Policy Implications

Consumers utilize health food store personnel for information about NHPs and to make complaints about the products they are using. Store personnel, through business and economic incentives, are motivated to process returns for dissatisfied consumers and, in so doing, transmit ADR information to industry. Through the existing process, with certain caveats, there may be an opportunity to improve ADR monitoring by enhancing the detail of information collected. Educating health food store personnel about the ADR reporting system to facilitate their direct reporting to Health Canada, or at minimum, informing customers of the option to report to Health Canada, should be investigated.

This study has important policy implications for ADR reporting and post-market surveillance of NHPs. Encouraging health food store personnel to report NHP-related ADRs might be an important step in populating the Canada Vigilance Program database with valuable information. Increasing awareness of the ADR monitoring system within the NHP sector is an essential part of improving safety monitoring. Important next steps will be to ensure, through improved communication, that health-care providers and consumers understand the true degree of risk. Additionally, it is important to investigate how health food retailers react to an invitation to participate actively in NHP pharmacovigilance, including the quantity, quality and completeness of their submitted ADR reports. Health Canada will need to assess how best to use this new source of information for protection of public health.

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