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Risk Perception and Reasons for Noncompliance in Pharmacovigilance

A Qualitative Study Conducted in Canada

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Abstract

Background: The postmarketing safety evaluation of drugs relies on the spontaneous reporting of adverse reactions to authorities. Under-reporting is a known issue, with only 3% of all adverse reactions that occur actually being reported. Therefore, the postmarketing safety evaluation of medications is compromised.
Objective: This investigation aimed to identify determining factors that influence reporting as well as corrective actions. We specifically wanted to define the perceptions physicians and pharmacists have of pharmacovigilance, of the local and national reporting systems, of their role and that of other players in reporting adverse reactions, and of its consequences in their clinical practice.
Methods: Three focus groups with pharmacists and 16 semi-structured interviews with physicians from four different clinical services were conducted.
Results: Four major obstacles to reporting adverse reactions were identified: (i) pharmacovigilance is seen as an unrealistic ideal; (ii) the reporting authority is perceived as a virtual and remote entity; (iii) healthcare professionals do not feel concerned by the risks associated with the medications used in their practice; and (iv) healthcare professionals are uncertain about the scope of their role in reporting adverse effects.
Conclusion: In order to promote reporting and a greater awareness of the system, a redefinition of its expectations and targeted feedback seem to be essential. Increased reporting can also be achieved by the presence of an onsite professional dedicated to reporting and educating others. Several definite measures are proposed in order to achieve this goal.

Background

In the last decade, the pharmaceutical industry has favoured postmarketing studies of new drugs at the expense of pre-marketing studies.[1] Monitoring the safety profile of drugs for long-term therapy or in specific populations now comes under the umbrella of pharmacovigilance studies. In spite of adverse drug reaction (ADR) monitoring systems and evidence-based medicine

practices, only 3% of the ADRs detected by healthcare professionals are actually reported, which suggests significant under-reporting.[2-4]

A meta-analysis of 39 prospective studies by Lazarou et al.[5] reported a 12.0–18.1% incidence of ADRs in hospitalized patients. From a paediatric standpoint, a systematic review showed an overall ≈9.5% incidence of ADRs in inpatients, with an overall 2.1–6.2% rate of secondary hospitalizations following serious ADRs, 39% of which were potentially fatal or life-threatening.[6] Given such significant rates, under-reporting is an issue that should be addressed.

Because of the limited market it represents, difficulties in recruiting children and very strict research regulations, very few clinical trials focus on the paediatric population.[7] In fact, 36–67% of children admitted to hospital receive medications for indications or in doses that are not approved.[8-14] Almost 33–50% of the ADRs in paediatric hospitals occur with the administration of medications for off-label use.[8] Therefore, the need for ADR reporting is even greater for children, due to an obvious lack of data.

The factors that influence ADR reporting and the behaviour of the healthcare professionals and authorities involved have interested a number of authors. According to a mail survey conducted by Belton,[15] the main reasons for under-reporting include the impression that an ADR is already well known (78.5% of the respondents), forgetting to report (44.3%), unwillingness to report on suspicions alone (23.4%), a lack of time (20.2%), prioritizing other clinical activities (12.8%), uncertainty regarding the reporting process (9.1%) and the unavailability of forms (9.1%).[15] Certain data suggest that specialist physicians report more ADRs than general practitioners do, and it seems that more physicians report ADRs in teaching hospitals.[16] More hospital physicians than general practitioners state that a lack of time prevents them from reporting ADRs, and fewer general practitioners know how to report ADRs to authorities.[17]

The most frequently cited factors discouraging ADR reporting include the lack of available forms, the unavailability of contact information of reporting agencies in the workplace, ambiguities related to the reporting process, forgetting to report, a preference for other clinical activities, a feeling that reporting isolated cases cannot have much of an impact on medical knowledge, as well as a lack of time.[18,19] Uncertainty as to the ADRs that should be reported and the aims of the reporting systems has also been described.[15,20-22] Even so, it seems that spontaneous reporting systems are not seen as unnecessary.[17,20,21,23-26] Yet, even with these factors in mind, most of the solutions proposed to date have not turned out to be conclusive or have led to only a temporary improvement at best (lasting a year or so with educational interventions).[27-31]

While the large amount of available quantitative data provides a global picture of the situation, the circular pattern of the factors identified so far is evident and a complementary qualitative approach seems necessary to understand the dynamics of reporting in a real clinical setting. In addition, our search has not revealed any studies conducted in a paediatric setting, and only a very limited number of studies have evaluated the specific role of pharmacists in ADR reporting systems[30,32-35] even though, in Canada, pharmacists play the most significant role. Moreover, the failure or limited impact of most of the possible solutions that have been studied to date suggests the necessity of assessing healthcare professionals' perceptions. Therefore, the main goal of this study is to explore the dynamics involved when physicians and pharmacists report ADRs to a mother-child tertiary-care university health centre (UHC) in order to identify the factors that influence reporting, as well as any approaches that may improve the ADR reporting system. The specific objectives of the study were to identify physicians' and pharmacists' perceptions of the principles and definitions of pharmacovigilance, of their local and national reporting systems, of their role as well as that of other players, and of the clinical consequences of reporting ADRs.

Methods

Setting

The study was conducted at the Centre Hospitalier Universitaire Ste-Justine, a mother-child

tertiary-care UHC in Canada. Based on local data, ADRs are reported in at least 1% of the annual admissions, and approximately 0.3% of the admissions may be caused by an ADR.[36] By comparing these local data with data from the medical literature, there seems to be an under-reporting of ADRs.

The pharmacovigilance authority in Canada is the Canadian Adverse Drug Reaction Monitoring Program (CADRMP), a voluntary ADR reporting system for healthcare professionals similar to that of the US FDA. Physicians and pharmacists who suspect that a patient has experienced an ADR are asked to report the ADR to a regional centre, which then conveys the information to the national centre if the ADR is considered serious. ADRs may be submitted using either a paper form faxed to the CADRMP's toll-free number or an online form. ADR reporting guidelines published on Health Canada's website[37] indicate that any presumed ADR, especially if unexpected, serious or related to a product that has been put on the market within the last 5 years is pertinent. Finally, certainty as to the relationship between the ADR and the health product is not required when reporting ADRs to the CADRMP.

ADR reports are logged by Health Canada in a computer database and analysed in order to detect any possible signals regarding the safety of health products. The public can access a database to consult data on previous reports and see the ADRs that have been reported for a specific product. In terms of feedback, Health Canada sends out the Canadian Adverse Reaction Newsletter (CARN) to healthcare professionals every 3 months in order to inform them of any new alerts that the CADRMP has identified. Health Canada sends clinicians a notice to confirm that their form has been received, but there is no such thing as an ADR helpline to offer healthcare professionals real-time advice.

Design

We used a qualitative approach derived from grounded theory[38-41] due to the exploratory character of the study and in order to generate new hypotheses. We collected our data by means of semi-structured interviews and focus groups, which were the most flexible tools available. The semi-structured interviews were built around open-ended questions organized according to themes. Details of the semi-structured interviews for both pharmacists and physicians can be found in appendix 1 (see Supplemental Digital Content 1, http://links.adisonline.com/PBZ/A7). Respondents were encouraged to express their own views in an open manner with minimal intervention from the interviewer.[38,39] Semi-structured interviews were used for individual meetings with physicians, while focus groups were used for discussions with pharmacists. The protocol was approved by the Internal Review Board.

A qualitative estimate was used to get around the limitations of quantitative methods. Faced with an abundance of quantitative data describing under-reporting, the only way to further our understanding was an in-depth qualitative analysis of the dynamics at play in the reporting of ADRs.

For the semi-structured interviews with physicians, respondents had to be practicing oncology, neonatology, obstetrics-gynaecology or general paediatrics at the UHC from September 2006 to the end of March 2007. Pharmacists who participated in the focus groups had to be practicing in specialized or general services at the UHC from September to the end of November 2006. Medical and pharmacy residents, medical students, as well as the physicians and pharmacists who participated in pre-testing the interview were excluded.

We opted for a contrast sampling strategy, which focused on the use of strategic variables aimed at providing the widest viewpoints possible within the study population. The strategic variables used in building the sample were based on the main factors of influence identified in the literature. For physicians, field of practice (general vs specialized), clinical specialty (oncology, neonatology, obstetrics-gynaecology and paediatrics) and sex (male vs female) were selected, all of which were identified as having an impact on the willingness to report.[40] For pharmacists, a single strategic variable was used – i.e. the clinical practice sector (paediatrics, gastroenterology/hepatology/transplantation, pneumology, intensive

care, HIV, oncology, obstetrics-gynaecology, neonatology) – due to the exploratory character of the study and the focus group approach.

Since notions of risk and professional responsibility are more easily dealt with individually and surveys of large groups of physicians had already been conducted, we adopted a semi-structured interview approach to meet physicians. We considered that the diversity of viewpoints and perceptions generated by the contrast variables would allow us to reach empirical saturation of the studied concepts (the point at which additional data repeatedly confirm the interpretation already formed) with 16 interviews, two for each final branch of the contrast tree (table I).[41] Two members of the research team conducted these interviews at the UHC from December 2006 to March 2007, a longer period than that required by the focus groups, given the heavier workload involved in completing 16 interviews compared with three focus groups. The interviews lasted 25–90 minutes each.

Since pharmacovigilance is more of a collective issue for pharmacists, with whom the approach turned out to be more exploratory in nature, small focus groups seemed the best way to discuss their role and generate new ideas. Consequently, we organized three focus groups made up of five to eight pharmacists each. A total of 20 pharmacists participated in the study – about 60% of the pharmacy staff at the UHC (table II). The focus group meetings lasted about 1 hour each and were conducted during the month of October 2006. Two researchers led the focus groups, ensuring a conducive climate throughout.

The interviews and focus groups had two phases. The first semi-structured phase explored the definitions of the principles of pharmacovigilance (risk, uncertainty and causality, seriousness, report), the perception of the place of pharmacovigilance (perceived efficacy, perception of the authorities, roles) and the clinical impact of pharmacovigilance (accountability, confidentiality, change in practice, ambivalence/confidence in the system) on the participants. The second phase consisted of filling out a short data sheet that made it possible to gather sociodemographic data from the participants in order to better understand their views. The discussions were recorded using a digital recorder, then transcribed, separated by themes and entered into a Microsoft® Access® database used to the same effect as standard dedicated coding software (NU*DIST, for example).

Table I. Physicians' characteristics

Participant number	Field of practice	Clinical specialty	Sex
MD 21	Specialized	Oncology	Male
MD 22	Specialized	Neonatology	Male
MD 23	Specialized	Oncology	Male
MD 24	Specialized	Neonatology	Male
MD 25	General	Paediatrics	Male
MD 26	Specialized	Oncology	Female
MD 27	General	Gynaecology/obstetrics	Female
MD 28	General	Gynaecology/obstetrics	Male
MD 29	Specialized	Oncology	Female
MD 30	General	Gynaecology/obstetrics	Female
MD 31	General	Paediatrics	Female
MD 32	General	Gynaecology/obstetrics	Male
MD 33	General	Paediatrics	Female
MD 34	General	Paediatrics	Male
MD 35	Specialized	Neonatology	Female
MD 36	Specialized	Neonatology	Female

MD = Physician.

Results

Ishikawa Diagram of Adverse Drug Reaction Reporting

Since an Ishikawa ('fishbone') diagram depicts a series of events (causes) leading to a final effect, it is the best way to relate the information we obtained, while trying to ascertain the factors that can influence ADR reporting (figure 1).

The central arrow illustrates the action of reporting an ADR. Each of the 'fishbones' represents one of the four major barriers to reporting that were identified. The themes that explain important paradoxes and possible obstacles to the reporting process surround these 'fishbones'. The paradoxes in the upper portion of the diagram concern the reporting systems and the concepts of pharmacovigilance, whereas

Table II. Pharmacists' characteristics

Focus group number	Participant number	Clinical practice sector
1	PHM 1	Oncology
	PHM 2	Neonatology
	PHM 3	Paediatrics
	PHM 4	Gynaecology/obstetrics
	PHM 5	Gastroenterology
	PHM 6	Intensive care
	PHM 7	HIV
2	PHM 8	Gynaecology/obstetrics
	PHM 9	Intensive care
	PHM 10	Pneumology
	PHM 11	HIV
	PHM 12	Oncology
	PHM 13	Oncology
	PHM 14	Oncology
	PHM 15	Oncology
3	PHM 16	Paediatrics
	PHM 17	Paediatrics
	PHM 18	Gynaecology/obstetrics
	PHM 19	Pneumology
	PHM 20	Neonatology

PHM = Pharmacist.

those in the bottom portion relate to the personal involvement of healthcare professionals.

Reporting System

The Unattainable Ideal Paradox

The statements gathered led us to a first major paradox. Although healthcare professionals believe that pharmacovigilance is of the utmost importance very few actively participate in it. While healthcare professionals consider that pharmacovigilance can translate into tangible results, all claim that the expectations of the existing system lack definition. As one physician says: ''It'd be good to have a relationship with them [Health Canada]. To know what they are asking for and what they propose and especially what they expect of us. As I was saying, I haven't got a clue.'' (MD [physician] 24). Healthcare professionals face a stumbling block even before they start to think about reporting an ADR, since they do not know what type of adverse effect warrants reporting. This is particularly relevant in mother-child healthcare; given the scarce data available on the paediatric use of medications, sharing data on therapeutic agents and their potential risks is essential. Yet, while reporting should be encouraged in paediatric practice, the concept is never really applied.

The mutual expectations that Health Canada and clinicians have of pharmacovigilance also differ. On the one hand, healthcare professionals want to get something out of the pharmacovigilance data available without actively participating in the process. On the other hand, Health Canada uses the reported data to identify safety signals without providing direct feedback on the information sent.[42] In other words, it appears that each player needs the information the other has, but does not want to give anything back in return.

It is an interesting fact that, owing to a lack of knowledge about the system in place, healthcare professionals say they are reluctant to actively participate in it, although they remain convinced that pharmacovigilance is well founded.

The Remoteness Paradox

A second paradox lies in the absence of interaction between healthcare professionals and Health Canada. The healthcare professionals and the reporting system appear as two remote entities. There is a noticeable chasm between the two authorities, who seem to work separately rather than together.

The fact that healthcare professionals are obviously ambivalent about Health Canada's CADRMP explains part of the paradox. Indeed, it seems that the perceptions Health Canada and clinicians have of the aims of the pharmacovigilance system are diametrically opposed. While Health Canada's program is part of a public health approach aimed at protecting the population as a whole, clinicians expect a pharmacovigilance system to be able to help them in managing the patients they meet in their individual practice.[42]

As far as pharmacists are concerned, the notion of distance also has a significant impact on the perception of the system in place. The pharmacists indeed view a local reporting system very

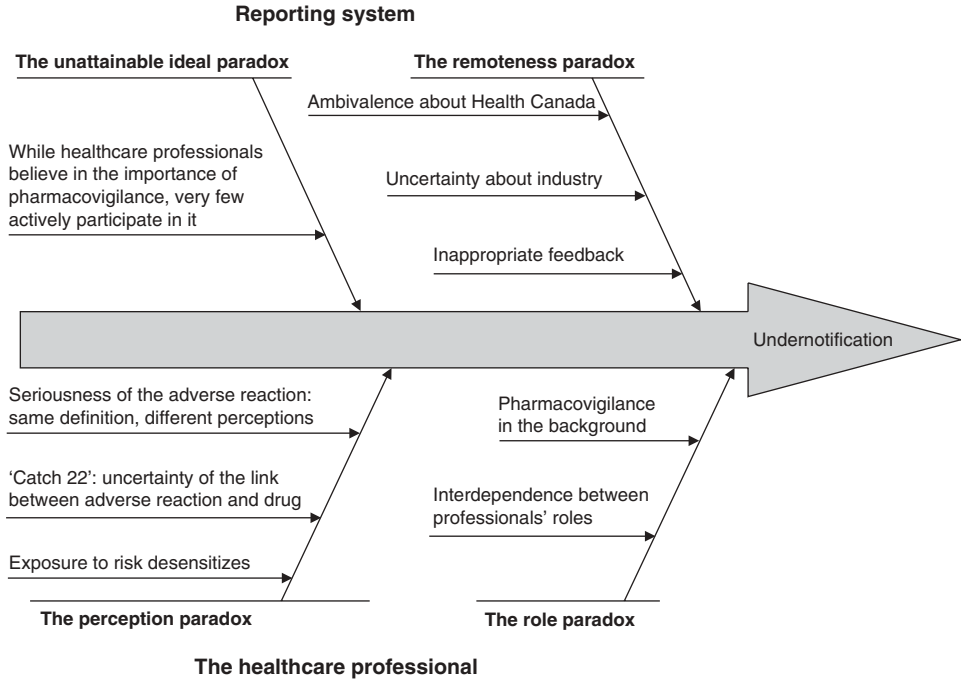

Fig. 1. Ishikawa diagram. The central arrow illustrates the action of reporting an ADR. Each of the 'fishbones' represents one of the four major barriers to reporting that were identified.

favourably. Health Canada's ways of proceeding and handling information appear for all intents and purposes abstract to them. Described as a veritable 'black box' by the participants, the system is seen as a remote authority that issues alerts to healthcare professionals on an unknown basis. As one pharmacist said: "I'm under the impression that you send it into a big box and then it gets lost" (PHM [pharmacist] 1). Another pharmacist said: "Well, it's actually that, that's what doesn't encourage us, because we […] have absolutely no idea what they do with it […] we find it difficult to see whether our intervention is going to have an impact […] you say you're going to report, is it going to make any difference?" (PHM 2).

While professionals seem uncertain about the proceedings of Health Canada, the watchword seems to be 'uncertainty' in terms of the industry as a whole. The CADRMP, as part of a process that evaluates drug safety, is seen as being linked to the pharmaceutical industry. Many physicians think that the industry does not invest enough into research for the mother-child clientele. It is widely held that pharmaceutical companies have mainly financial motivations and they take only calculated risks. As one physician said: "Because the pharmaceutical industry is driven by profit, they want to make money all the time" (MD 34). This perception varies according to clinical specialty. Neonatologists think that the industry does not have any interest in the neonatal population, whereas healthcare professionals in oncology who take an active part in research view the industry's involvement favourably and think real breakthroughs are possible in their field.

For all these reasons, many healthcare professionals are less than confident about such reporting systems. As one physician said: "I am very suspicious of these reporting systems […] I am very … doubtful and that is why … I don't really feel like putting a lot of energy into something when I am convinced there's no point in doing so" (MD 23). While they consider that

experts devoted to pharmacovigilance are undoubtedly more capable of determining the possibility of an association between an ADR and a drug, those who participate in the reporting system are no less convinced that someone outside the clinical setting must have a hard time establishing a clear relationship.

As for what is expected of the expert system, the extent of the feedback leads to many interesting areas of discussion. While Health Canada uses the pharmacovigilance data to issue large-scale alerts, healthcare professionals would prefer an effective pharmacovigilance system to help them confirm the plausibility of the drug-ADR associations they detect in real time.[42] It is, therefore, the link between the ADR and the drug that needs to be confirmed and feedback is required.

In fact, professionals would like the feedback to be put into context, with an indication of the number of similar cases detected with the same agent, so as to be able to keep this information in mind and remain vigilant. Also, the physicians interviewed in our study would like to receive feedback geared to their individual practice, since they are not interested in information that does not concern their patients. As one physician said: ''99% of the time, it's about drugs we don't even use.'' (MD 36). Another added: ''Often it's about things we don't use in paediatrics, so I quickly read them just to have an idea of what it's about, but if it's about drugs I don't use every day, it goes into the recycling bin'' (MD 31). In this regard, healthcare professionals consider that an easily searchable database that includes locally detected ADRs would be a possible solution to the problem of under-reporting.

The type of feedback received from Health Canada is often limited to advisories the healthcare professionals are very critical about. Essentially, they consider the positions taken by Health Canada to be disconnected from reality, and even more so in a mother-child setting. As a matter of fact, healthcare professionals consider Health Canada's advisories somewhat moralizing. They believe these advisories suggest, in their opinion, a utopian practice that barely reflects reality, since children actually receive the targeted treatments, not by choice, but because there are simply no alternatives. Contributing to a system they believe disapproves of the use made of medications in a mother-child setting and then being taught a lesson and finding themselves in an uncomfortable position, hardly encourages healthcare professionals to report ADRs. As one pharmacist put it ''Once they give us a notice, sometimes we're stuck […] they make like a little summary of recommendations about what happened: 'We must remind you that this drug is not indicated for those under 18 years of age and you should not use it,' but you know we've got 25–50 patients on it so you say: what do I do? It's like I'm going against what they're telling me.'' (PHM 16). Since it is the only type of feedback they feel they receive from Health Canada, it is obvious that few healthcare professionals are confident in the system. The participants have an abstract vision of the system and, in their eyes, Health Canada has an abstract vision of the clinical reality professionals face and of the consequences of the advisories it issues.

Healthcare Professionals

The Perception Paradox

For healthcare professionals, a third paradox hinders reporting. While all healthcare professionals detect ADRs in their practice, very few deem them pertinent enough for reporting. This paradox can be explained by a multitude of factors that influence the perception of an ADR. Medical uncertainty, shown in the establishment of a causal link, and risk perception, determined by experience in using a medication, play roles in the perception of a phenomenon (in this case an ADR).

An important facet of this problem lies in each individual's perception of the risk they face. In fact, we noted that healthcare professionals from different clinical settings have diametrically opposed views. While physicians and pharmacists from the critical care and oncology services face ADRs on a daily basis and feel managing them is inherent to their practice, healthcare professionals from the neonatology and obstetrics-gynaecology services avoid at all costs exposing

their patients to any sort of drug risk. Moreover, it is their perceptions of the possible outcomes that differ and it is easy to establish a parallel with the opposite ends of life's spectrum. Whereas critical care and oncology patients are faced with the risk of imminent death, which calls for action even when it leads to an ADR, potential complications in newborns have life-long repercussions. In neonatology, risk assumes a temporal perspective and its consequences may be significant. In oncology, taking risks may prolong life, and ADRs can only occur if the patient is alive.

It is only when the consequences attributed to treatment are deemed serious and represent concrete complications that risk becomes tangible according to healthcare professionals. In this regard, the statements obtained relating to practice in a paediatric setting are revealing. Since they constantly manage the risks involved in off-label use and given the lack of data on drug utilization, mother-child healthcare professionals are not much troubled by the way their therapeutic arsenal is used on a daily basis. Using drugs in unapproved indications or without documented evidence of their safety and efficacy everyday, one becomes used to taking risks that cannot be measured. As one pharmacist said: ''We're under the impression that it's a drug we use a lot, but basically, you look at the real data we have on it and often we don't have so much after all! I think that … working in paediatrics gives us a sense of security. We feel that we can use anything'' (PHM 1).

The degree of ADR exposure also leads to a serious paradox. When there are no ADRs, the vigilance exercised by healthcare professionals diminishes. On the other hand, when continually exposed to ADRs, professionals become inured to them. Thus, certain clinical services and certain practices lead to risk desensitization. When inurement to risk is well established, vigilance toward unknown or more serious ADRs decreases and they are less likely to be reported. ADR occurrence becomes commonplace and the reporting alarm is no longer raised.

The problem of certainty and causality is an integral part of the perception paradox. On the one hand, it is obvious that the clinical management of ADRs requires a minimal evaluation of the plausibility of the association between a drug and the ADR detected. While Health Canada asks that any ADR that occurs be reported, whether the causality link is certain or not, it is impossible for clinicians not to verify the plausibility of the ADR before reporting it and they are sceptical about Health Canada's claim.[42] As one physician said: ''If the person who reports it is not sure himself, he's not going to report it'' (MD 24). We noted that participants are reticent to report ADRs they deem uncertain, since they believe they will only create noise. Some sort of confirmation of the plausibility of the association and its pertinence is needed. Furthermore, some simply see it as being impossible in terms of carrying it out in practice: ''When it gets to Health Canada, they won't be able to ferret out any interesting nuggets of truth from all the muck we're going to send them, so the sifting has to be done right from the start, because otherwise it's not going to result in anything, it's going to cost millions for nothing and then all the energy put into it … no way'' (MD 23).

To verify the causality link, healthcare professionals use cases that have previously been reported in the scientific literature. All of this creates an interesting paradox. When it is impossible to confirm causality with similar cases, healthcare professionals do not report ADRs. However, causality can only be established with certainty when reactions are well known, and then they feel the ADRs are not worth reporting.

In terms of the seriousness of the ADRs, healthcare professionals seem to agree on a theoretical definition of a serious ADR that is not unlike Health Canada's own definition. This having been said, the perception of healthcare professionals of the seriousness of the ADRs detected in their practice diverges significantly. Besides having a different conception of risk, healthcare professionals in critical care services clearly seem less concerned by more serious ADRs than are healthcare professionals in services where ADRs occur less frequently. In both cases, it seems that an element of surprise comes into play in the perception of ADRs as serious or

not. An unexpected reaction, a reaction professionals are not used to facing, is an ADR they see as pertinent for reporting. In addition, healthcare professionals in certain clinical services do not feel concerned by Health Canada's definition of serious ADRs, even though some of the reactions they detect do meet this definition. A better definition of what ADRs should be reported, one that is a balance between Health Canada's and the healthcare professionals' definitions, would probably not go amiss.

The Role Paradox

A final important paradox relates to the roles healthcare professionals play in the reporting process: an inextricable interdependence curtails healthcare professionals from acting out and reporting ADRs, since they do not believe they are by themselves adequately equipped and they feel they require the intervention of others. On the one hand, diagnostic considerations are the responsibility of physicians, who are capable of characterizing ADRs and ruling out any possible differential diagnoses. On the other hand, pharmacists are best qualified when it comes to identifying the potential implications of given medications in ADR events and explaining the phenomena. As a result, ADRs always turn out to be differential diagnoses made by physicians who rely on the pharmacists' knowledge to identify causal agents, whereas pharmacists identify medications involved, but require the opinion of physicians to resolve diagnostic issues. Pharmacists, therefore, seem to feel that the identification of ADRs should be left to physicians' expertise, particularly since they prescribe the drugs at issue and are often in the front line in hospital settings. Once again, this interdependence stresses that healthcare professionals want to have a clear causality link and that it is difficult to establish such a link.

Given these complementary roles, the issue has two distinct facets: defining what happens (physician's role) and explaining how a drug may be involved (pharmacist's role). Even when the causality link has been established, the problem remains unresolved. Since at least two professionals look into an ADR, who is responsible for reporting it? As one pharmacist said: "If it's not targeted by a team, the physician is going to count on the pharmacist doing it. The pharmacist is going to rely on the physician doing it… I mean if it's not targeted, we expect it to be done through some sort of wishful thinking" (PHM 12). The feeling of responsibility inevitably dissipates and finally vanishes. Everyone shifts the responsibility of reporting the ADR over to someone else. Each professional requires the contribution of another to decide with certainty and establish the causality link, which is why the ADR is never reported.

Confidentiality issues do not seem to be of concern to clinicians. On the one hand, healthcare professionals doubt that the little information they conveyed can really be prejudicial to the patient. So, although they question Health Canada's proceedings, the clinicians are confident in its ability as a regulatory authority to maintain confidentiality.

The reporting process is time consuming and this issue has been raised chiefly by pharmacists. Although they do not actively participate in the CADRMP, pharmacists are at least somewhat aware of what reporting involves and that most likely comes from training courses. More to the point, physicians seem to attribute many roles to pharmacists when ADRs occur. Pharmacists are supposed to be the centre of expertise on medications and therefore ADRs, recommend some sort of clinical behaviour to the physician and report the ADR. Once the ADR has been identified and managed, reporting it then seems like one duty too many.

Pharmacists do not easily see how they could manage to report all the ADRs they detect, and reporting in no way appears to be a priority in relation to their other clinical activities: "In a hectic day, let's say that the last thing you have time to do… you're going to manage the ADR on the floor, you're going to change your medication, you're going to adjust your dose… and come 5 o'clock, your day is over, the patient's OK […] you did everything you had to" (PHM 16). Furthermore, when the patients present complex pharmacotherapy along with a lengthy medical history and significant co-morbidities, the task

can quickly become overwhelming. Such considerations have the greatest impact in services like oncology. What Health Canada asks then seems unrealistic to pharmacists. Pharmacists feel even more so that the system is disconnected from reality and this in turn further discourages participation.

Discussion

First and foremost, we know that the difficulty in establishing a causality link with certainty, the reluctance to report previously known ADRs, the impression that a personal report cannot have an impact, the absence of familiarity with the ADR detected, poor knowledge of the objectives of the reporting system as well as a lack of time are all explanations brought forward to explain the issue of under-reporting.[15,20,21] Although surveys, questionnaires and a few rare qualitative studies make it possible to quantify the importance of the isolated factors, the way in which they are all linked together remains poorly understood. In this matter, our study sheds light on the issue and provides major advances in the understanding of the dynamics of ADR reporting. Furthermore, it illustrates the problem from a paediatric standpoint. Essentially, the paradoxes observed explain the circularity of the reporting process and the inevitable failure of the possible solutions studied thus far.[24,27-29,36] Beyond the considerations described in previous research, we have noted that more fundamental issues underlie the phenomenon.

Firstly, the theories of Giddens[43] on the consequences of modernity relate to this issue. The problem of under-reporting involves considerable ambivalence toward the established reporting system. The authority that the expert system claims to have is not fully recognized by healthcare professionals. Their mutual incomprehension is explained by the issue of remoteness, the gap that exists between healthcare professionals and the expert system. Healthcare professionals have no idea of how the data in the ADR reports they submit are handled. Healthcare professionals want relevant data for their practice – a confirmation that the relationship between the ADR and the medication is plausible or not. In contrast, the reporting system expects professionals to convey all the ADRs they detect. It offers them tools they consider difficult to use and adopts a public health approach without really knowing, in the eyes of clinicians, about current field practices. It seems both parties, isolated by their distance, know nothing about each other. These findings confirm the work by Vallano et al.[21] Since the way in which alerts are issued is unknown by the physicians interviewed, they find it difficult to judge the reliability of the pharmacovigilance system in place.

Secondly, the healthcare professionals' practice obviously reflects the perspective of a 'clinical mentality' as described by Freidson[44] – what is important is for clinicians to treat their own patients. The here and now is uppermost in their mind, and any population health perspective is relegated to the backstage. In contrast, the CADRMP expects healthcare professionals to participate on a voluntary basis and it uses the data it receives for the good of the greatest number. However, the CADRMP does not state that it is its duty to give an account to healthcare professionals or help them in their individual practice. The outcome is an obvious impasse.

We then note that the issue of under-reporting is in many ways akin to Beck's theories of risk society. The more healthcare professionals are led to manage risk on a day-to-day basis, the less they feel that an ADR is of concern.[45] In addition, healthcare professionals who have been desensitized to risk no longer see the ADRs they detect as pertinent for reporting, since managing such effects is an integral part of their practice. Cognitive rationality comes into play. If healthcare professionals use a drug, it is because they have a good reason to believe in its usefulness, and when it then leads to an ADR, their responsibility is to manage it and limit the consequences for the patient as best they can.

In a complementary way, the work by Freidson[44] on uncertainty in medical practice is completely to the point. Healthcare professionals must manage uncertainty on a day-to-day basis.[44] They continually face situations for which there is no clear or precise approach. From

this perspective, interdependence among healthcare professionals is a significant aspect of the phenomenon of under-reporting. As physicians and pharmacists shift responsibility back and forth, many ADRs they detect inevitably fall between the cracks and are never reported.

There still remains a lot to do when it comes to raising awareness and educating about the established reporting system; greater transparency in the internal operations of the system and better visibility are to be encouraged. Moreover, it is obvious that the system's expectations need to be redefined. A better targeted approach, especially in relation to ADRs, is recommended. To get around the problem of remoteness and uncertainty in terms of the expert system, it seems essential that a local reporting system be implemented. Such a system would provide contact with a familiar trained caregiver, who is known to healthcare professionals in the sector, greater transparency and feedback at the local level, thereby building up trust in its utility. These findings are in agreement with Biriell and Edwards[46], whose pilot study found that a positive relationship between the reporting authority and healthcare professionals is essential to encourage ADR reporting.[46] Finally, better targeted feedback is essential to the proper functioning of the system. To this end, an online database that can be queried in a user-friendly and effective way seems to us to be an excellent approach that should be adopted.

Of course, the qualitative estimate used does not allow the external generalization of these findings, since it deals with a specific clinical setting. This having been said, the phenomena observed provide an understanding of the issue of under-reporting and there is no reason to believe that the situation is actually any different in any other healthcare setting. Given the qualitative approach, the importance of each of the paradoxes observed cannot be quantified, and certain particularities specific to the paediatric setting call for distinctions in the interpretation of the findings.

Conclusions

In conclusion, the explanatory model we propose seems an excellent representation of the issue of under-reporting. Although the data collected relate to a paediatric UHC setting, there is good reason to believe that the Ishikawa diagram of the ADR reporting system reflects a wider perspective that extends beyond this context. It is essential that the observed paradoxes be addressed in order to implement effective interventions that encourage ADR reporting.

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