PATIENT REPORTING OF ADVERSE DRUG EVENTS – A NARRATIVE REVIEW

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ABSTRACT

PURPOSE: The aim of this review is to examine the role and experience with direct patient adverse drug reactions reports in the spontaneous reporting systems.

MATERIAL AND METHODS: A computerized literature search or relevant English publications regarding the role and characteristics of direct patient reporting from 1996 to 2012 was completed in January 2013. The latest update in the search was performed from September to October 2013.

RESULTS: The results show that direct patient reports could contribute to the pharmacovigilance system qualitatively as well as quantitatively. There are a lot of factors that influence patient participation such as personal characteristics, disease perception, and previous experience. Critical issue in the process is considered to be the noise effect on the signal generation.

CONCLUSION: Inclusion of patients as a source of information will help to change the perspective of pharmacovigilance. The factors that affect the decision of the patient's report of an adverse drug reaction and possible external influences that would shape their opinion and could affect the quality of reports are not well studied.

Keywords: *pharmacovigilance, adverse drug reaction reporting systems, review, pharmacy, patients*

INTRODUCTION

Nowadays there are three main sources of information for the adverse drug reactions (ADR) reporting systems (9). The first one which is considered to be the most reliable is the health professionals (20). In Bulgaria, their obligation to report is regulated by law (8). In some countries, the only medical professionals who may report are physicians while in others pharmacists and nurses are also included in the pharmacovigilance system. Since many dietary supplements and Over-the-counter (OTC) medicines are of herbal origin, pharmacists are a very important source of information because they are the most accessible health professional from the perspective of the patient (15).

The second source of information is data obtained from the literature: medical journals, publications describing clinical cases, meta-analyses. It is the obligation of the Marketing authorization holder to routinely review the published literature for clinical cases associated with their products (8).

The third main source of information is patients. Although subjectively, they can describe and report reactions experienced due to their drug thera-

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Received: February 27, 2014
Accepted: April 3, 2014

py (17). Patients may report the occurrence of ADRs directly to the pharmacovigilance centers or to medical specialists and the reports can be done orally, electronically or in hard copy by mail. In EU, direct patient reporting of ADRs has been introduced with Directive 2010/84 since July 2012. There are some member states that have had introduced patient reporting earlier (17).

METHODS

A computerized literature search of relevant articles written in English regarding patients reporting of adverse drug events published from 1996 to 2012 was completed in January 2013. An updated search of the literature was performed from September to October 2013.

References of interest were identified through searches of Medline, Scopus and Google Scholar. Combinations of search terms were "adverse drug reactions", "patients reporting" and "adverse reactions reporting system". The search terms were used alone or in combination. Review articles were scanned to find also additional eligible studies. The reference lists of all original articles and systematic reviews were hand-searched for other relevant articles. Duplicates were removed. Studies discussing the following issues were included: patients' role in the adverse reactions reporting systems, comparison between patients' and health professionals' reports, patients' contribution to the adverse drug reactions reporting systems. Eventually 34 articles were selected for this review.

Patients' role in the spontaneous reporting systems

Blekinsopp et al. (2007) published a systematic review of practices related to direct patients' reporting of suspected ADRs (5). The review included seven studies, although none of them directly examined patients' spontaneous reporting. The results show, however, that where comparison is possible, the messages from patients and medical professionals are of similar quality.

Reporting of ADRs by patients has the potential to raise awareness about the potential harm of taking drugs. Under reporting of ADRs by patients we understand the adapted definition of van Grootheest "... drug users (parents and carers) who report suspected ADRs to the spontaneous reporting system" (31). Reporting of ADRs by patients has been first introduced in several countries, including the USA, Canada, Australia, New Zealand, Denmark, Sweden and the Netherlands. Later, patient reporting of ADRs has also been introduced in the United Kingdom (5,25,21,18,1).

Comparative study of suspected ADR reports by patients and health professionals

In 2011, a research team from the UK published a comparative study of ADR reports from patients and health professionals (2). The purpose of this study was to assess the potential of patients as a source of spontaneous reports, to assess the characteristics of patients' messages and their real contribution to the generation of signals. The results show that patients reported ADRs for different groups of drugs than health professionals thus generating new signals and describing suspected adverse reactions in sufficient detail to provide useful information on a possible causal relationship and impact of ADRs on the everyday life of the patient.

According to the authors of the study, timely and quality reporting of adverse drug reactions by patients can be fostered in several steps:

- Increasing public awareness;
- Availability of guidelines for patient reporting;
- Providing information to patients on medicinal products under supervision by regulators;
- Change in the way of reporting;
- Feedback on the effects of patient reports.

Direct spontaneous reporting of ADRs by patients supports the collection of new data on drug safety. In countries where it is already possible it is observed that patient reports are more detailed and more accurate than those of health professionals. Unlike reports of physicians and pharmacists, patients often describe how ADRs affect their lives. Spontaneous patient reporting has some other advantaged also:

- More active involvement of patients in their treatment;
- Increased adherence to drug therapy;
- Better communication with health professionals;

- Assessment of impact of the severity of ADRs on the everyday life of the patient, which is generally omitted in physician's reports.

For these reasons, reporting by patients needs to be implemented in national pharmacovigilance systems. The data obtained will allow the assessment of the severity and outcome of ADRs, which according to Benichou and Solal-Celigny are leading indicators of the clinical features of the cases (4).

Potential contributions of patient reports

The contribution of patient reports can be considered in two aspects – qualitative and quantitative (23).

Qualitative aspects

Consideration of direct patient reports is expected to improve qualitatively the periodic and final safety reports of medicines. Avoiding the filtering of initial reports by physicians and pharmacists will lead to the inclusion in the systems of ADRs reports previously considered minor. Further wise, health professionals are not and cannot be familiar in detail with all medicines on the market including their ADRs.

Quantitative aspects

Patient reports will increase the overall number of spontaneous reports which will improve the effectiveness of the system. The indicator "reporting rate" will also increase leading to improvement in the parameters of the spontaneous reporting systems and raising awareness on this issue.

It should be noted that there are significant barriers and constraints to the implementation in practice of direct patient reporting.

There are significant difficulties in incorporating patient reports into the existing ADR databases and/or construction of any new integrated system for post-marketing control and monitoring on various objective and subjective legal reasons. Such a system would require significant financial and personnel resources of the competent authorities and organizations dealing with issues of national level.

Critical issues in direct patient reporting

Spontaneous reporting of ADRs by health professionals is a useful method in pharmacovigilance and post-marketing surveillance of medicines (13). It has helped identify a number of issues in drug safety (24). There is a consensus among the scientific community that direct reporting of ADRs by patients will contribute to the development of pharmacovigilance (28,32,33). However, there are not enough studies on the full value of spontaneous reports from patients. Available comparisons show significant differences in serious adverse reactions, the identification of new ADRs and types of medicinal products and systems included in the reports. The interpretation of the differences and their practical application in signal generation remains to be seen. Only Avery et al. (2011) investigated the effect of patient reports on the generation of signals relative to those of health professionals (2). Perhaps future comparative studies will try to assess the impact of patients' spontaneous reports on the functioning of the spontaneous reporting systems. Critical evaluation and comparison of data and studies on spontaneous reporting of ADRs directly from patients should be encouraged. These reports should be sent to the Pharmacovigilance centers, special centers for patients/consumers or directly to the competent authorities (19).

Patients and their perceptions of ADRs

Efforts of health systems in recent years are specifically aimed at reducing the incidence of ADRs and improvement of dealing with them in ambulatory practice. There are numerous studies that examine the relationship between patients, their disease, their therapy and the incidence of ADRs. Higher age, number of comorbidities and number of accepted medicines are proven risk factors for ADRs (10,16,30). However, these studies examine risk factors for ADRs documented or confirmed by the patients' medical records or computer databases. The added value of direct patient-reported ADRs is that the reflected patients' experience with ADRs is more important to their health status than clinical assessment of ADRs (3). De Smedt, Shiyanbola and Farris argued that demographic and clinical variables such as age and comorbidities are not able to predict the risk of patient-reported ADRs (29,7). There are other factors such as perceptions of the disease and treatment, which may affect reporting of ADRs by patients (29). In 2011 De Smedt and coauthors published a study which evaluated the impact of perceptions of the disease and the treatment of patients suffering from heart failure, on the side effects reported by them (7). The results show that patients with ADRs have negative perceptions of their disease and

Scripta Scientifica Pharmaceutica, vol. 1, 2014, pp. 14-19

therapy than patients without ADRs. They perceive their disease as more volatile, with more impact on the daily lives and suffer more from emotional stress. Also they have more reserves to therapy and believe that they are taking too many drugs. The authors explain the results with the example that patients suffering from severe heart failure are more likely to experience more symptoms associated with the disease. According to Gandhi et al. (2003), this leads to intensive therapy and respectively to more drug-related problems (11,12). Another possible factor between the disease and possible ADRs is the lack of knowledge and inability of patients to distinguish between the symptoms of the disease and those that are drug-related (7). In addition, elderly patients often experience symptoms regarded as inevitable aspects of the aging process, rather than as a part of the disease or associated with drug therapy (22).

Patients with higher levels of negative beliefs about their illness and treatment are more vigilant for side effects and biased to the medicinal products they take (34). Concerns about their therapy can lead to the attribution of symptoms to the medicinal product and to be a sign of the level of tolerance for ADRs (26). Brown et al. (2006) discuss the perspective of patients for the occurrence of ADRs in ambulatory practice (6). After the interviews, the authors summarized the eight key elements that lead to the incidence of ADRs:

- Poor communication between doctor and patient;
- Patients do not follow the instructions given to them by doctors;
- Self-medication with herbs, OTC products and medicines without a prescription;
- Patients do not read the leaflets of medicinal products;
- Drug interactions;
- Individual patient's characteristics affect the patterns of prescribing and treatment outcomes;
- Poor communication between patient and pharmacist;
- Patients receiving inadequate medication.

Some of these elements could be affected by the fruitful contact between patients and pharmacists – adherence, possible drug interactions and more comprehensible medicines information (14,27).

CONCLUSION

Pharmacovigilance and spontaneous reporting systems have evolved significantly since their formal beginning in the 1970s. Today, the scope is broadened and includes not only drugs, but also medical devices, cosmetics, vaccines, products of herbal origin, even health and medicines information. The sources of information are also evolving – from the pages of scientific journals through the development of adverse drug reactions spontaneous reporting systems and conducting non-interventional post-marketing studies to computer databases. Inclusion of patients as a source of information will help change the perspective of pharmacovigilance. Published studies indicate that the information received by them is qualitatively and quantitatively different from that of medical professionals. The factors that affect the decision of the patient's report of an adverse drug reaction and possible external influences that would shape their opinion and could affect the quality of reports are not well studied.

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