Pharmacovigilance Informatics

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INTRODUCTION TO PHARMACOVIGILANCE INFORMATICS

All medicines have adverse effects, most of them unknown until the drug commercialization. As so, it is crucial to keep strategies to monitor the drug safety. Pharmacovigilance is the activity of drug surveillance, after its launch in the market, with the main goal of public health protection, ensuring that the drug benefit outweighs its risks. Worldwide, pharmacovigilance systems are mostly based on spontaneous Adverse Drug Reactions (ADR) reports made by healthcare professionals and consumers. Spontaneous ADR reporting has been described as an essential method to detect drug safety signals; however, underreporting is a major issue undermining the effectiveness of spontaneous reports. Several studies suggest that less than 10% of detected ADR are effectively reported to medicines regulatory authorities [e.g. Food and Drug Administration (FDA), European Medicines Agency (EMA), etc] (Hazell & Shakir, 2006; McGettigan, Golden, Conroy, Arthur, & Feely, 1997).

Tools used in pharmacovigilance are continually evolving and, worldwide, Information Systems (IS) to promote ADR reporting or to detect ADR occurred in healthcare institutions have been tested and used, such as software that allow voluntary and automated detection of ADR, tools that analyse clinical databases or Web sites that actively inform healthcare professionals (Molokhia, Tanna, & Bell, 2009).

In addition to the signal detection, ICT can also be used to encourage and facilitate reporting of suspected ADR, such as the creation of on-line reporting forms, development of tools to collect safety data from electronic health records (EHR), among others.

In this chapter, it will be described some tools to automatically detect ADR, or encourage ADR spontaneous report.

BACKGROUND ON PHARMACOVIGILANCE

Adverse Drug Reactions (ADR) defined as a response to a medicinal product which is noxious and unintended (WHO) are a well-recognized public health problem worldwide, and a major cause of death

DOI: 10.4018/978-1-4666-9978-6.ch025

and hospitalization in developed countries(Lazarou, Pomeranz, & Corey, 1998). It is estimated that about 6,5% of the hospitalizations are related to ADR(Pirmohamed et al., 2004). Besides, in the USA, about 100.000 people die each year due to ADR(Lazarou et al., 1998), and in Europe this annual mortality rate increases to 197.000(European Medicines Agency, 2014). ADR can be expressed in many ways and with different degrees of seriousness. An anaphylactic shock caused by penicillin is an example of a serious ADR (a serious ADR is any untoward medical occurrence that at any dose: results in death, requires inpatient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability/incapacity or is life-threatening(WHO). Another type of ADR, not always recognized as such, is the drug ineffectiveness, for example, a vaccination failure. This can be (or not) related with a product quality issue and should be reported when detected in order to allow the regulatory authorities to take appropriate decisions.

Rare and long term ADR are difficult to detect during the drug development stage. Only when the drug begins to be used by a large population after marketing authorization it is possible to detect new ADR not previously identified during clinical trials. In reality, it is known that the safety of a new drug cannot be established until it has been on the market for several years(Lasser et al., 2002). Exceptionally, in a pandemic scenario, drug launch is urgent and, in this particular case, can be justifiable that drug safety profile is not well established. In this scenarios, it is even more important that all the detected ADR are reported (serious or not, expected or not). It is, therefore, essential to keep drugs under close surveillance, after its commercialization, through a pharmacovigilance system, to continuously evaluate their safety profile. In most of the European countries, pharmacovigilance system is based on spontaneous ADR reports, which is passive method, made by healthcare professionals and, since July 2012, also by consumers (Ministério da Saúde, 2006). These reports can be made using paper, telephone, e-mail or through an on-line form and consist of a description of an Adverse Event (AE) apparently caused by a medicine.

To reverse the problem of underreporting of ADR, which is felt in most developed countries, several strategies have been tested(M. T. Herdeiro et al., 2012; McGettigan et al., 1997; Ribeiro-Vaz, Santos, da Costa-Pereira, & Cruz-Correia, 2012). Particularly, some studies were developed focused on educational interventions to raise awareness on the importance of ADR reporting(Figueiras A., Herdeiro T, Polonia J, & JJ, 2006; M. T. Herdeiro, Polonia, Gestal-Otero, & Figueiras, 2008; Ribeiro-Vaz, Herdeiro, Polonia, & Figueiras, 2011) and showed to be very effective increasing the quantity and relevance of spontaneous ADR reports (among health professionals). However, these studies involved a large financial and personal outlay and the authors concluded that the effect was lost after a few months(McGettigan et al., 1997; Nazario, Feliu, & Rivera, 1994).

In a recent American study, the authors developed a signal-detection strategy that combines the Adverse Event Reporting System (AERS) of the regulatory Authority (FDA) and EHR, by requiring signaling in both sources, with promising results(Harpaz et al., 2013). Another study used the unstructured clinical notes included in EHR to detect ADR through a computerized system. The authors concluded that data mining can be used for hypothesis generation and for rapid analysis of suspected AE risk(LePendu et al., 2013).

With a similar aim, a recent study used a physician's network, created through a mailing list, to send regular emails to doctors, with humorous component attached with informative component, recalling the importance of reporting their suspected ADR(Goldstein, Berlin, Saliba, Elias, & Berkovitch, 2013). The results showed that this type of intervention has impact on the number of ADR reports made by these professionals (the study did not assess the relevance of reported ADR). In France, it is being done a work that tries to facilitate the act to ADR report, habitually considered a tedious process by health