Informatics applied to pharmacovigilance: Future perspectives

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ABSTRACT

Spontaneous adverse drugs reaction (ADRs) reporting represents a precious resource for control and information about the drug's safety and pharmacovigilance. The current reporting system is mainly based on handwritten forms and later manually loaded into a national electronic database by few local pharmacovigilance centers. This reporting system is complicated for both reporters and pharmacovigilance centers which often avoid reporting ADRs for several reasons such as the lack of data on the report. The reporting system might be implemented by improving online platform for ADRs upload; this could allow inspecting all ADRs loaded. Currently, the database is only accessible by the Italian Medicine Agency (AIFA) and local pharmacovigilance centers; neither reporters nor other healthcare professionals can access the database. Finally, it would be right to implement pharmacovigilance centers with specific professional figures qualified in the pharmacovigilance to support both citizens and reporters on various aspects of ADRs reporting.

Key words: ADRs, AIFA, database, drugs, Italy

INTRODUCTION

Spontaneous ADRs reporting represents a precious resource for control and information about the drug's safety, since it allows the detection of potential warning signals related to the use of all drugs available in a country.[1,2] Pharmacovigilance involves the entire community physicians, healthcare professionals, pharmacists; reporting can be made not only by healthcare personnel but also by the patients.[3,4]

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Reporting instruments

Waiting for the implementation of the directive 2010/84/CE and subsequent acts, a spontaneous report of ADRs can be made in two different ways.[3] Specifically, healthcare personnel and/or citizens will be able to fill in:

A) Offline, by printable reporting form of the suspected adverse reaction (established by the Ministerial Decree 12/12/2003), which can be downloaded from AIFA website or all health websites and pages of pharmaceutical services; there are two different versions of the form depending on the reporter qualification: healthcare personnel[5] or citizen.[6] Once completed it should be sent, by mail or fax, to the nearest pharmacovigilance center or directly to AIFA;

B) Online, an electronic reporting form of suspected adverse reaction on AIFA website; this form is realized for healthcare personnel[7] or patients reporting.[8] After filling out online, the

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form can be saved on a Personal Computer (PC) or printed, and then it has to be signed and sent by email again to the nearest pharmacovigilance center or directly to AIFA. No electronic signature nor email certificate is allowed at the moment.

Critics to the current Italian pharmacovigilance system

Compilation and transmission of ADRs

Despite new advances, the current reporting system remains complicated and poorly operational. As mentioned above the reporting form exists in two different models, depending on whether the reporter is a healthcare professional or a patient.

In the first case, the compilation requires technical and medical expertise, while in the second case the form is composed of very simple questions. The splitting of the reporting is certainly a good way to involve consumers in pharmacovigilance activities; however, the spontaneous reporting system is further improvable.

There are many causes for under-reporting by physicians or pharmacists, the lack of time; the amount of information that the form requires.[1] More often, crucial information is not available (i.e., patient does not remember the concomitant medications or the exact brand for generic drugs) and it results in incomplete or invalid reports. Perhaps, it would be enough to simplify the form pattern to increase the number of reports. However, most of the information required to fill the form appear to be essential in order to obtain reliable signals. Another important problem is that the ADR form is not really online; in fact, it cannot be compiled and transmitted simultaneously, but the generated form files are created with word processing software, which requires software to be installed on your own PC.

It is not necessary to have the Microsoft version; however, some open-source software might not always be 100% compatible with that used by AIFA to compile the form. Another problem is that it is not enough to fill the online form to report ADRs, but the form has to be saved on a computer, signed and then sent by fax, e-mail or mail. In this way, the reporting is more difficult for the reporter who will spend more time to complete it.[3] Finally, the module form ends with a field named "*signature*", to which instructions do not make any reference, name and surname are already included in the module so that it is just one signature missing. This means that the reporter is forced to print the form, sign it manually and send it by fax or mail, and the only way to use the convenient tool of the email is represented by the digital signature or scanning of the form that can be subsequently attached to the electronic mail message. Clearly such a mechanism appears uncomfortable and discouraging.

Once the form finally comes to the collection center, it must be loaded onto a database by manually inserting all required information into the national database. This can cause significant delays in data entry, not to mention the countless possibilities of errors in the interpretation and transcription of handwritten data.

Sharing or access to reports by health professionals and citizens.

The national database has a main limitation because it is only accessible to few selected authorities (e.g. AIFA). This raises few major questions: is it only good for AIFA? Why would it be deleterious or not useful for healthcare professional access to database?

Certainly, we need to pay attention to the dissemination of this information to ordinary citizens, since there is the risk of self-interpretation or self-medication, based on a small amount of information. Therefore, the information should be properly presented.

However, it would be useful for health professionals to have access to these data to be informed about unknown or infrequent adverse reactions and to evaluate several treatments already tested by other colleagues.

Health professionals, before prescribing drugs, may verify if an ADR or a drug-drug interaction has already been reported by others and determine the specific risk.

Furthermore, we should not ignore the risk that the operator may, at that point, be tempted to find a solution to the problem further ignoring the need to carry on with the signaling, since "it already exists, it is not necessary to compile the ADR form". In any case, this kind of problem cannot be overcome by preventing the access to certain information, but rather raising the awareness of those involved with extensive information; the latter should explain the fundamental importance of signaling, for the purposes of research, feedback and the comparison of ADRs in order to continuously improve the appropriateness of prescribing and patients' health.

Interaction between the citizen or a reporter and specialist

Another issue, often brought out by healthcare professionals, is the lack of an immediate contact between the person wanting to report a suspected ADR and a specialist in pharmacovigilance who could play the role of advisor or ADR consultant. Telephone or e-mail could help the compiler as he can clarify his doubts with a pharmacovigilance specialist leading to compilation of reports with extreme precision. Also he could give the feedback to one who reported the ADR. Unfortunately, this professional figure is not currently available in the national system.

Compilation and reporting of ADRs form

Based on the experience at the Calabria's Pharmacovigilance Center,[1,2] we suggest that the form should be exclusively compiled online and immediately storable. Then, it should be automatically sent to the pharmacovigilance manager. The original signature could be easily replaced with a mechanized processing code identifier for each health care or for citizens it could be enough to use the tax code, perhaps enhanced by a further identifier element obtained during the registration on the website. This will avoid the necessity to print the form to sign and then to send it to the center. Moreover, the online compilation allows to set required fields that avoid loading forms with inappropriate or missing data. The online form can be created with sections of different colors to facilitate the compilation.

The paper version might be maintained and transformed into the so-called "pigeon hole" form that can be completed manually of which each box is filled in with capital letters; this method allows the adoption of a modern system of digital scanning and recognition that allows the transformation of the paper form into a digital form, and then it could be used for "database". Also, in this case the use of colored fields will facilitate the proper completion by the user (e.g. mandatory fields colored in red). In this case, the form submission will be done through traditional current channels (mail, fax, email).

Sharing and access to the reports

The use of digital forms allows the immediate data transfer, after appropriate assessments, into a database. Then, the data could be easily made available to the world; it could be enough to connect it to a website.

We have already discussed the possible problems of free diffusion of these data and the negative impact that could have on health professionals and the citizens. Therefore, it should be limited to a specific group of customers such as scientific researchers; it would limit access to the system only to allow the researchers for setting various search criteria.

Instead, common customers such as citizens or healthcare professionals (not for researchers) may only have access to the statistical data collected from the database. For example, the user may specify the drug's name, active principle, or ADR, and get a presentation of cumulative statistics that allow to get directions and findings without requiring any identifications. There are several internet sites that already provide this type of information, are easily accessible and very powerful; the vast majority of these sites are only in English language, it would be appropriate to have multi-lingual replication or national web-site since not all the people understand English language.

These websites, which however could be replicated in Italian or in any other language, allow the user to enter just drug's name (or its active ingredient) or adverse event produced, and immediately provides the information such as age, sex, therapy, drugs associated.[9]

In case of a single drug also other additional information are available such as list of side effects, the number of events, the percentage, the degree of dangerousness.[10]

Interaction between the citizen/reporter and pharmacovigilance specialist

The direct experience of the Calabria's Pharmacovigilance Center allows us to guarantee the training of specialized figures, quickly reachable by phone or email by users (citizens or healthcare professionals). The specialist helps the customer to complete the form of suspected ADR, preventing mistakes or omissions, paying attention to possible emergencies. The specialist answers the questions to colleagues and healthcare professionals, being able to access all the information in the database; he can provide important advice in case of ADR during the event. The creation of an email address and a free telephone number, and the appointment of an adequate number of specialized figures would result in a short time logarithmic increase of ADR reports, a greater and more conscious involvement of the healthcare professionals in the fundamental problem of ADR and consequently, an improvement of their competences in this field of improving patients' quality of life and safety.

CONCLUSIONS

The actual situation of pharmacovigilance in Italy and other countries seems to have several problems mainly related to the complexity of reporting and little knowledge about the relevance and importance of the signals. The regional centers of active pharmacovigilance seems to play an important role in supporting the signaling as confirmed by the difference between the regions where the pharmacovigilance center is supported and funded than in regions without funded activities.[1,2]

The use of electronic support will be the future, as it has happened in many fields and it will help to provide better health care professional prescribing patterns and therapies to enhance patient's safety.

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