International Journal of Clinical Pharmacology & Toxicology (IJCPT)
ISSN: 2167-910X

Defining And Improving Data Quality In Pharmacovigilance: A Step Towards Generating Robust Evidence

Editorial

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Pharmacovigilance is an essential component of pharmaceutical safety [1]. This science can be defined as all activities relating to detecting, assessing, understanding and preventing adverse effects or any other medicine-related problem [2].

When addressing drug surveillance issues, adverse reactions are undoubtedly the most significant source of concern with medicines. According to Guideline on Good Pharmacovigilance Practices, an adverse drug reaction (ADR) can be defined as "a response to a medicinal product which is noxious and unintended" [2]. In contrast to an adverse event, an ADR is characterised by the causal relationship between a medicinal product and an occurrence is suspected [2]. However, despite the definitional differences between an ADR and an adverse event, for regulatory reporting purposes, if an event is spontaneously reported, even if the relationship is unknown or unstated by the primary source (healthcare professional or consumer), an adverse reaction exists. Among the different methodologies used in pharmacovigilance, spontaneous reports (SR) remain the basis of the entire system [3]. In SR systems, case reports of suspected ADR are submitted to pharmacovigilance systems by patients or healthcare professionals, such as physicians, pharmacists and nurses, either directly or via the drug's manufacturer. For most pharmacovigilance systems, the information requested from consumers is similar, while that required from manufacturers is more detailed and mandatory with specific timelines for reporting[4]. Under-reporting is only one limitation of SR systems. The success or failure of SR systems depends on patients reporting events to healthcare professionals, who recognise that the event may be an ADR and complete and submit the report; or, instead, patients report directly to the system.

Another limitation of the SR system is the quality of the reports received [5]. Quality data could be defined as data that correctly represents reality. While this definition is acceptable for defining data quality, the "absolute" perception of quality may vary depending on the data context. For example, in interpreting a case report in routine pharmacovigilance, it is certainly not relevant to have an exact value with grams of the patient's weight. It would be desirable, but it does not translate absolutely the actual data quality. Thus, the data quality must also be assessed from the perspective of a more outstanding balance, taking into account costs, potential risks in its collection and other constraints of everyday practice. As such, we can assume a definition of quality data as those that can respond to the objectives for which they are being used. Even so, the quality data in pharmacovigilance are not only those that correctly represent the reality of the patient's clinical case but those that allow the generation of quality information and ultimately allow informed decision-making within the regulatory framework.

In pharmacovigilance, the medical data is collected, transmitted, and coded using medical dictionaries for regulatory activities. This tool is complex and requires specific training to avoid variability in coding processes; data interpretation in reports can cause problems. Therefore, some recommendations for data quality assurance can be applied concerning the investigator (certification, reinforcing professionalism in research, improving accessibility in pharmacovigilance reporting); the origin, transcription, and validation of the critical data; the data processing; and reporting/publication processes [6].

The essential information on a suspected ADR is case identification and source of the report, age and gender of the patient, the

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Received: May 03, 2022
Accepted: May 04, 2022
Published: May 05, 2022

Citation: Renato Ferreira-da-Silva, Mario Forrester Quesada. Defining And Improving Data Quality In Pharmacovigilance: A Step Towards Generating Robust Evidence. *Int J Clin Pharmacol Toxicol.* 2022;S1:02:001e:1-3.

indication for the treatment suspected to have caused the event, the name of the drug (including brand name), the dose, treatment dates, a description of the reaction (including onset date), all concomitant drugs (including doses and treatment dates) and the eventual outcome. In addition, it is preferable to have details of the patient's relevant medical history, the response for stopping the drug (dechallenge), and, if done, the response for restarting the drug (rechallenge) [4]. Even given the inherent limitations of SR, the usefulness of this data source can be improved with good data quality management. While underreporting cannot be remedied in this way, the negative impact of incomplete reporting, which is another serious problem in pharmacovigilance, can be reduced. A study recently published in Portugal concluded that the evidence in the low level of criteria documentation needed to make a reasoned causality imputation of SR of ADR, and the high proportion of serious ADR reported through incomplete SR increase the higher probability of a serious ADR being reported incompletely compared to a non-serious ADR [7]. Other previous studies [5, 8-10] agree with the results of this study, despite opposing the literature regarding the association between the robustness of an SR and the seriousness of ADR [8].

To ensure data quality, guidelines and procedures are approaching these issues for clinical trials, as well as pharmacoepidemiology and pharmacovigilance studies. Still, they fail to address a critical and essential point: the validation of the quality of source data and information to guarantee the validity and accuracy of the medical information [11].

The efficiency of SR of ADR is evaluated by its performance in identifying potential risk signals early enough to allow regulatory interventions. The quality of the transmitted information in ADR, the timeliness of feedback from healthcare professionals, and real-time pharmacological and medical analysis can help national and international pharmacovigilance authorities to identify relevant safety signals promptly [12, 13]. Therefore, these events can be evaluated according to their seriousness and report source.

Over the last decades, complementary pharmacoepidemiology methods have been introduced [1], allowing for hypothesis-testing and incidence estimates. Prescription-event monitoring systems and longitudinal healthcare information databases (registries) can be used for signal detection and follow-up, albeit in a defined, relatively small population. In order to move from passive to active pharmacovigilance, existing databases should be integrated. With the use of electronic hospital information systems, large amounts of health information can be gathered to monitor drug safety, consequently becoming great allies for active pharmacovigilance. Moreover, hospital ADR quick reporting systems can be connected to national databases to increase the interoperability in reporting frameworks which could partially solve the problem of underreporting, undue delays and miscommunication [14].

Other efforts in active pharmacovigilance include creating new ways to obtain information to add to the range of drug safety available from hospital records. Multi-triggered models and text-recognition methods are the main methods to achieve the latter; however, this requires human judgment to decide if an ADR occurred or not. Text mining is also emerging as a potentially helpful tool to process free texts in hospitals and can be very promising for active pharmacovigilance [15]. Moreover, using quantitative data from laboratory test results, ADR reporting is also on the future panorama [14].

The management of data quality in pharmacovigilance faces several challenges due to the limitations previously mentioned in this article. Increasing data volumes and increasing data complexity is currently forcing the drug safety systems to look for solutions to reduce case processing costs while remaining compliant with continually changing regulations worldwide and, at the same time, maintaining or even improving the quality of information generated. As such, and like the development of data and computational science, artificial intelligence in ADR processing is perhaps the most significant challenge today. Adverse event processing is one of the most obvious targets for automating pharmacovigilance processes as this has been a repetitive task routinely performed by all regulatory systems and pharmaceutical companies. One of the other significant challenges is regulatory requirements for reporting. With the evolution of digital systems to support ADR reporting and management of security signals, legislation on data policy must be in line with this new reality, considering the protection of personal data and the guarantee harmonising the quality of data submitted on different platforms.

It seems pharmacovigilance is taking primary directions toward the future in expanding sentinel hospital alliances, exploring new partnerships, and constructing more flexible and efficient coordinating centres. However, some major limitations for active pharmacovigilance systems are the range of ADR that can be reported in a particular system since only those of interest for the pharmacovigilance studies are taken into consideration in the system[14].

Pharmacovigilance knowledge is built by accumulating individual case safety reports and their subsequent analysis and data obtained from active pharmacovigilance strategies with methodological robustness.Access to up-to-date and accurate information is crucial - without it, the process is slowed down or halted.

Funding: This manuscript was supported by the PhD scholarship 2020.10231.BD (DOCTORATES 4 COVID-19), funded by Portuguese national funds and Community funds from the European Social Fund (ESF) through FCT - Fundação para a Ciência e a Tecnologia (Portugal).

References

[1]. Härmark L, van Grootheest AC. Pharmacovigilance: methods, recent developments and future perspectives. Eur J Clin Pharmacol. 2008 Aug;64(8):743-52. PubMed PMID: 18523760.
[2]. Guideline on Good Pharmacovigilance Practices (GVP): Annex I - Definitions. In: Agency EM, Agencies HoM, editors. 2017.
[3]. van Manen RP, Fram D, DuMouchel W. Signal detection methodologies to support effective safety management. Expert Opin Drug Saf. 2007 Jul;6(4):451-64. PubMed PMID: 17688389.
[4]. Rawson NS. Drug Safety. FriesenPress; 2016 Nov 8.
[5]. Bandekar MS, Anwikar SR, Kshirsagar NA. Quality check of spontaneous adverse drug reaction reporting forms of different countries. Pharmacoepidemiol Drug Saf. 2010 Nov;19(11):1181-5. PubMed PMID: 20845409.
[6]. Alla F, Rosilio M, Funck-Brentano C, Rosenheim M, Weisslinger-Darmon N, et al. How can the quality of medical data in pharmacovigilance, pharmacoepidemiology and clinical studies be guaranteed? Therapie. 2013 Jul-Aug;68(4):209-23. PubMed PMID: 23981258.
[7]. Salvador MR, Monteiro C, Pereira L, Duarte AP. Quality of Spontaneous Reports of Adverse Drug Reactions Sent to a Regional Pharmacovigilance Unit. Int J Environ Res Public Health. 2022 Mar 22;19(7):3754. PubMed PMID: 35409436.
[8]. Durrieu G, Jacquot J, Mège M, Bondon-Guitton E, Rousseau V, Montastruc F, et al. Completeness of Spontaneous Adverse Drug Reaction Reports

Sent by General Practitioners to a Regional Pharmacovigilance Centre: A Descriptive Study. Drug Saf. 2016 Dec;39(12):1189-1195. PubMed PMID: 27688025.

[9]. Niu R, Xiang Y, Wu T, Zhang Z, Chen Y, Feng B. The quality of spontaneous adverse drug reaction reports from the pharmacovigilance centre in western China. Expert Opin Drug Saf. 2019 Jan;18(1):51-58. PubMed PMID: 30574811.

[10]. Plessis L, Gómez A, García N, Cereza G, Figueras A. Lack of essential information in spontaneous reports of adverse drug reactions in Catalonia-a restraint to the potentiality for signal detection. Eur J Clin Pharmacol. 2017 Jun;73(6):751-758. PubMed PMID: 28251276.

[11]. Costa-Santos C, Neves AL, Correia R, Santos P, Monteiro-Soares M, Freitas A, et al. COVID-19 surveillance data quality issues: a national consecutive case series. BMJ Open. 2021 Dec 6;11(12):e047623. PubMed PMID: 34872992.

[12]. Tuccori M, Giustarini G, Blandizzi C, Capogrosso-Sansone A, Rossi M, Gori G, et al. Quality of Adverse Drug Reaction (QADRA) reports: an algorithm to appraise the efficiency of spontaneous reporting systems in pharmacovigilance. J Public Health. 2013 Aug;21(4):365-72.

[13]. Grandvuillemin A, Drici MD, Jonville-Bera AP, Micallef J, Montastruc JL; French Pharmacovigilance Network. French Pharmacovigilance Public System and COVID-19 Pandemic. Drug Saf. 2021 Apr;44(4):405-408. PubMed PMID: 33372244.

[14]. Li X, Li H, Deng J, Zhu F, Liu Y, Chen W. Active pharmacovigilance in China: recent development and future perspectives. Eur J Clin Pharmacol. 2018 Jul;74(7):863-871. PubMed PMID: 29637279.

[15]. Harpaz R, Callahan A, Tamang S, Low Y, Odgers D, Finlayson S, et al. Text mining for adverse drug events: the promise, challenges, and state of the art. Drug Saf. 2014 Oct;37(10):777-90. PubMed PMID: 25151493.