South African General Practitioner. 2022;3(2):52-54
https://doi.org/10.36303/SAGP.2022.3.2.0118

S Afr Gen Pract
ISSN 2706-9613 EISSN 2706-9621

REVIEW

Adverse drug reactions: To report, or not to report?

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Spontaneous reporting of suspected adverse drug reactions (ADRs) is a passive surveillance method that forms the cornerstone of the collection of medicine safety data post-marketing for all medicines and devices. Pharmacovigilance is a science that involves detection, assessment, understanding and prevention of ADRs, and it is a shared responsibility of pharmaceutical applicants, regulatory authorities, clinical institutions, public health programmes, academic researchers, healthcare workers, the media and the public. Clinicians can significantly contribute to medicine and device safety monitoring. They, however, need to be adequately informed, educated and trained on the principles of pharmacovigilance and how to report suspected ADRs. Clinicians should be active reporters of suspected ADRs and spontaneous reporting must be part of daily clinical practice to provide high-quality medical care to their patients at all levels.

Keywords: adverse drug reactions, pharmacovigilance, spontaneous reporting, post-marketing surveillance, Med Safety App

Introduction

One advantage of the COVID-19 pandemic was that it highlighted the crucial importance of pharmacovigilance and the actual reporting of adverse drug reactions (ADRs). There was a significant increase in the awareness of medicine safety due to the extensive media coverage on all the different communication platforms that brought medicine safety to the attention of the public.[1] This heightened attention and awareness on medicine safety shone a spotlight on the role that medicine regulatory authorities, the pharmaceutical industry, healthcare workers and the public play in the global and local pharmacovigilance field. The World Health Organization (WHO) defined pharmacovigilance as the "science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem".[2] Whereas an adverse drug reaction (ADR) is a response to a medicine in humans that is "noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, therapy of disease or for modification of physiological function".[2,3]

The importance of pharmacovigilance

The ultimate goals of pharmacovigilance are: to ensure the safe use of medicines and devices, to improve public health safety, to contribute to rational medicine use by preventing harm, to reduce medicine-related morbidity and mortality, to contribute to the assessment and monitoring of benefit, harm, risk and effectiveness of medicines and devices by ensuring early detection and effective communication of any medicine-related problems.[4,5]

Spontaneous reporting of suspected ADRs is a passive surveillance method and the key mechanism to collect medicine safety data that is fed into the provincial and national reporting database.[6] All of the activities associated with pharmacovigilance should be a shared responsibility by all the key stakeholders: pharmaceutical applicants, regulatory authorities, clinical institutions, public health programmes, academic researchers, healthcare workers, the media and the public.[7] Spontaneous reporting during post-marketing surveillance is crucial for all medicines and devices to ensure that they remain safe, effective and of good quality throughout the entire lifecycle of the product. The role healthcare professionals play to strengthen medicine safety, monitoring and reporting in the post-marketing phase is crucial to identify and contribute to signals of rare (1 in 1 000) and very rare (1 in 10 000) ADRs which are often not detected in the respective clinical trial phases.[8]

There are many confounding factors that affect the reporting of ADRs. Some of the biggest challenges in pharmacovigilance globally and also in South Africa is underreporting of suspected ADRs.[6,9-12] The burden (cost, mortality and morbidity) of ADRs on health systems in general is also an important obstacle, especially in the South African context.[13-15]

Pharmacovigilance in clinical practice

Clinicians are in a good position to contribute to the safety monitoring of medicines and devices. They must be informed, educated and trained about the principles of pharmacovigilance and how to exchange and communicate information that links their clinical experience with medicine safety to contribute to the improvement of patient care at all levels. Clinicians should be active reporters of suspected ADRs and spontaneous reporting must be part of daily clinical practice to provide high-quality medical care. Practising clinicians are in an ideal situation to make clinical judgement calls on the reporting of their patients' suspected adverse reactions. This will enhance and expand the medical science and ultimately contribute to inspire the doctor-

Table I: Summary of reporting channels for ADR/AEFI in South Africa

Reporting channels	Methods	Access details or links
Manual	Adverse Drug Reactions & Quality Reporting form https://www.sahpra.org.za/wp-content/uploads/2021/04/6.04_ARF1_v5.3_April2021-addition_of_Med_Safety_App.pdf	Email to adr@sahpra.org.za
Online	e-Reporting link to VigiFlow® Accessible from SAHPRA website	Complete and submit online https://primaryreporting.who-umc.org/ZA
Med Safety App (Preferred channel)	Download from Google Play (Android devices) or App store (iOs devices) All AEFIs should also be reported via the Med Safety App	https://medsafety.sahpra.org.za/
EML Clinical Guide mobile App	Download from Google Play (Android devices) or App store (iOs devices) EML Clinical Guide: Install "How to report ADRs using the mobile"	On successful completion, a copy of the report will be sent to the reporter and adr@sahpra.org.za

ADR – adverse drug reaction, AEFI – adverse event following immunisation, EML – essential medicine list

patient partnership and trust among patients in the quality of the medical care they receive.[2]

What to report

Clinicians have limited time to report suspected ADRs, especially in busy practices; the perceived paperwork, time and effort involved can be discouraging and their focus is primarily on the immediate clinical needs of the patient. It takes experience and sound clinical judgement to probe and ask the right questions to ascertain causal relationship of a suspected ADR.[16]

The South African Health Products Regulatory Agency (SAHPRA) provides a few pointers on their website that could be helpful to decide what to report or not. When in doubt, report all ADRs resulting from prescription and over-the-counter (OTC) medicines, devices or adverse events following immunisation (AEFI).[5]

It is important to report:

- All serious ADRs that resulted in death, disability or impairment, hospitalisation, prolonged hospitalisation, congenital anomalies, teratogenicity or life-threatening situations.
- Undocumented, unexpected or unusual ADRs/AEFI not clearly stated in the package insert.
- ADRs/AEFI occurring in children under the age of 18.
- ADRs/AEFI in the elderly.
- Therapeutic failure, especially in the treatment of life-threatening diseases, vaccines or contraceptives.
- Serious or clinically relevant interactions.
- ADRs/AEFI resulting from medication errors.
- ADRs/AEFI resulting from suspected overdose.
- Any product quality (stability, contamination, defective, poor packaging and labelling) related problem – Record the batch/lot number and expiry date.
- ADRs or poisoning following the use of complementary, traditional or herbal remedies.
- ADRs in newly marketed medicines or devices (< 5 years post-marketing).

When to report

SAHPRA encourages all healthcare workers and providers to report suspected ADRs/AEFI even if there is doubt whether the event constitutes an ADR or not. Providing evidence of causality is not a requirement and it is best practice to submit a report on a suspected ADR/AEFI even if some facts or information may still be unavailable or missing at the time of submission. It is, however, very important to note when completing these forms, that the following minimum requirements should be listed on the form (manually or online):[5]

- Identifiable patient and demographics.
- Identifiable reporter and facility.
- Suspected medicine(s) detail.
- Suspected reaction(s) detail.

How to report

The traditional manual reporting process originally involved facsimile transmission (fax) of suspected ADR reports. It was cumbersome, tedious and a process with little satisfaction and feedback. Despite having access to more evolved technology where suspected ADR forms can be scanned and emailed, this complex, varied and convoluted manner of reporting created an uncertainty resulting in the belief that reports are not captured nationally and that it may be considered a waste of valuable time in a busy clinical practice.[17]

In South Africa today, we have several methods by which a suspected ADR can be reported by healthcare professionals and the public. Table I summarises the various methods that can be used to report a suspected ADR in South Africa. The preferred option is to download the Med Safety App.[5]

Conclusion

The majority of ADRs are preventable most of the time. Suspected ADRs resulting in death, disability, hospitalisation, teratogenicity or life-threatening situations are of serious concern and important to report, rather than not.

To report or not to report a suspected ADR "does not constitute an admission that the reporter or any other healthcare professional contributed to the ADR" or that the medicine product or device contributed to the event. The information that is finally reported

to SAHPRA and captured on the VigiBase® system remains strictly confidential and all identifiable information of the reporter and/or patient is removed.[5]

The important take-home message for healthcare professionals is to report any suspected ADR even when in doubt. That single individual case report that gets submitted becomes part of the bigger national database of all the reported medicine safety information. As a collective, they are collated, analysed and evaluated to detect early warning signals so that possible medicine safety issues can be flagged, further investigated, suitable corrective action plans can be implemented and the appropriate health communications issued.

Conflict of interest

The authors declare no conflict of interest.

Funding source

None.

Ethical approval

Short review article for continuing professional development purpose. No ethics approval sought as this does not contain any studies with human or animal subjects.

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