ADVERSE DRUG REACTIONS: A CASE REPORT

Domina Petric*
*University Hospital Center Split, Soltanska 1, Croatia

ABSTRACT Introduction: Adverse drug reactions are a challenge in modern healthcare. With the increasing complexity of therapeutics, an ageing population and rising multimorbidity, it is worth emphasizing the importance of pharmacovigilance and rationale pharmacotherapy. **Case report:** A case report of an elderly female suffering from iatrogenic bicytopenia, which is likely associated with the chronic use of rosuvastatin and valsartan, is presented in this article. **Conclusion:** Understanding adverse drug reactions is very important for everyday clinical practice. Good pharmacological databases are a very important tool in the clinical assessment, management and surveillance of ADRs, and therefore, the availability of such databases is crucial for the implementation of pharmacovigilance in everyday clinical practice, as well as high quality national and international ADRs reporting systems.

KEYWORDS pharmacovigilance, bicytopenia, pharmacotherapy, adverse drug reactions

Introduction

Adverse drug reactions (ADRs) are a challenge in modern healthcare because of the increasing complexity of therapeutics, an ageing population and rising multimorbidity [1]. ADR can be defined as a harmful or unpleasant reaction resulting from an intervention related to the use of a medicinal product: adverse effects usually predict hazard from future administration and warrant prevention, or specific treatment, or alteration of the dosage regimen, or withdrawal of the product [2]. The term adverse effect (adverse reaction) is preferable to other terms such as toxic or side effects. A toxic effect can be defined as an effect that occurs as an exaggeration of the desired therapeutic effect and which is not common at normal doses. A toxic effect is always dose-related, whilst an unwanted side effect occurs via some other mechanism and may be dose-related or not. The terms adverse reaction and adverse effect are interchangeable, except that an adverse effect is seen from the point of view of the drug, whereas an adverse reaction is seen from the point of view of the patient. An adverse effect is an adverse outcome that can be attributed to some action of a drug. An adverse event is an adverse outcome that occurs while a patient is taking a drug but is not or not necessarily attributable to it [3]. Pharmacovigilance is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse events or any other drug-related problem [4].

DOI: 10.5455/IJMRCR.AdverseDrugReactions-case-report
First Received: January 3, 2022
Accepted: January 24, 2022
Associate Editor: Ivan Inkov (BG);
[1]Corresponding address: University Hospital Center Split, Soltanska 1, Croatia
ORCID: 0000-0001-5609-1675 E-mail: domina.petric@gmail.com

Case report

An elderly female patient is suffering from bicytopenia (thrombocytopenia, leukopenia). She was examined in detail by a haematologist and immunologist, and all hematologic and immunologic causes of bicytopenia were excluded. She has been taking rosuvastatin for the last 5 years because of dyslipidemia, bisoprolol for the last 10 years and valsartan for the last 3 years because of arterial hypertension. She says her platelet count started to drop after rosuvastatin was introduced into therapy and that her leukocyte count has been low for the last five months. Her laboratory test results show severe thrombocytopenia, mild leukopenia and moderate neutropenia. Thrombocytopenia has been reported during postmarketing use of rosuvastatin [5]. A case report of a 65-year-old woman with dyslipidemia that had been taking rosuvastatin (dose not specified) for 1 year when her platelet count dropped to 31 x 10(3)/microL was published. Her physical exam and other laboratory tests at the time were within normal limits, including Hb, WBC and erythrocyte sedimentation rate. Her past medical history included only vitiligo and appendectomy; she took no other medications. A platelet count performed the year before had been within normal limits. Thrombocytopenia was confirmed via peripheral blood smear; no abnormalities were detected via chest radiograph, abdominal

ultrasound, or bone marrow biopsy.

After other potential causes were ruled out, rosuvastatin was discontinued. Her platelet count increased to 55 x 10(3)/microL within one week and to 150 x 10(3)/microL within 6 months of discontinuing rosuvastatin [6]. Neutropenia was reported as a side effect of valsartan during adult clinical trials (1.9%), and thrombocytopenia has been reported during postmarketing surveillance for valsartan [5]. Based on these findings, bicytopenia is probably caused by rosuvastatin and valsartan. Therefore, these drugs must be discontinued. No hematologic adverse effects were reported for atorvastatin and fluvastatin so far. Therefore, one of these two statins can be prescribed to this patient. Hematologic adverse effects were reported for almost all angiotensin receptor blockers as well as for all ACE (angiotensin-converting enzyme) inhibitors, except for azilsartan medoxomil (so far). Hematologic adverse effects were also reported for amlodipine and nifedipine, whilst for lacidipine and lercanidipine, no such adverse effects were reported so far [5]. For the treatment of arterial hypertension, this patient can be prescribed azilsartan medoxomil, lacidipine or lercanidipine. A follow-up examination after one and six months is advised for this patient because platelet and leukocyte count is expected to improve during the maximum of six month period, with a note that a partial improvement should become evident during the first month after the discontinuation of suspected drugs. Probable side effects were reported to the national adverse drug reactions database (HALMED).

Discussion

In order to better understand the art of pharmacovigilance, it is important to discuss the classification of ADRs and the clinical assessment of ADR probability. Type A reactions (dose-related, augmented reactions) are dose-dependent and predictable on the basis of the pharmacology of the drug [1,3]. These reactions are common, related to a drug's pharmacological action, predictable, associated with a low mortality rate, and are managed by reducing or withholding drug dose [3]. Type B reactions (bizarre reactions) are idiosyncratic and not predictable based on pharmacology [1,3]. These reactions are uncommon, not related to a pharmacological action of the drug, unpredictable, associated with a high mortality rate, and are managed by withholding the drug dose or even avoiding the drug in the future [3]. Type C reactions (dose-related and time-related) are chronic, uncommon and related to the cumulative dose. These reactions are managed by reducing or withholding drug doses. Type D reactions (time-related) are delayed, uncommon, usually dose-related, occur or become apparent sometime after the use of the drug, and are often intractable. Type E reactions (withdrawal, end of use) are uncommon, occur soon after the withdrawal of the drug, and are managed by reintroducing and withdrawing the drug slowly. Type F reactions (unexpected failure of therapy) are common, dose-related, often caused by drug interactions, and are managed by increasing drug dosage [3].

Causality assessment of suspected ADRs can be classified as certain (plausible time relation to drug administration, the event is definitive pharmacologically or phenomenologically), probable/likely (reasonable time relation to administration of the drug, the event is unlikely to be attributed to concurrent disease or other drugs or chemicals), possible (reasonable time relation to administration of the drug, the event could also be explained by concurrent disease or other drugs or chemicals), unlikely (temporal relation to administration of the drug, causal relation improbable; other drugs, chemicals or underlying disease provide plausible explanations), conditional/unclassified (the event is reported as an adverse reaction, but more data are essential for a proper assessment or the additional data are being examined) and unassessable/unclassifiable (a report suggesting an adverse reaction that cannot be judged, because information is insufficient or contradictory and cannot be supplemented or verified). The time relation between the use of the drug and the occurrence of the reaction must be assessed. Pattern recognition is also very important because the pattern of the adverse effect may fit the known pharmacology or allergy pattern of one of the suspected medicines or of chemically related or pharmacologically related compounds. Additional investigations (laboratory tests, allergy tests, pathohistological investigations) can aid diagnosis, establish baselines for organ function, and provide a means for monitoring the suspected adverse event [3].

The case of bicytopenia presented here is probably caused by chronic use of valsartan and rosuvastatin. It might be classified as a type C reaction (chronic, uncommon, related to the cumulative dose).

Conclusion

Understanding adverse drug reactions is very important for everyday clinical practice. Clinical assessment, management and surveillance of ADRs require pharmacological skills, which are important for every physician dealing with pharmacotherapy. Good pharmacological databases are a very important tool in the clinical assessment, management and surveillance of ADRs. Therefore, the availability of such databases is crucial for implementing pharmacovigilance in everyday clinical practice. High-quality ADRs reporting systems are another important foundation pillar of pharmacovigilance. Physicians must be encouraged to report every reasonable suspicion of an adverse drug reaction. Collaboration of physicians with scientists working in national and international health agencies must be promoted and improved according to the principles of transparency in medicine and science. Patients must also be educated and encouraged to report possible ADRs themselves to establish good communication between patients and health agencies scientists/physicians.

Funding

This work did not receive any grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest

There are no conflicts of interest to declare by any of the authors of this study.

References

1. Coleman JJ, Pontefract SK. Adverse drug reactions. Clin Med (Lond). 2016 Oct;16(5):481-485.

2. Aronson JK, Ferner RE. Clarification of terminology in drug safety. Drug Saf. 2005;28:851-70.

3. Edwards IR, Aronson JK. Adverse drug reactions: definitions, diagnosis, and management. Lancet.2000;356(9237):1255-9.

4. World Health Organization. The importance of pharmacovigilance. Geneva: Wolrd Health Organization, 2002.

5. Micromedex® (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com/ (cited: 01/01/2022).

6. Vrettos I, Papageorgiou S, Economopoulou C, Pappa V, Tsirigotis P, Tountas N, et al. Rosuvastatin-induced thrombocytopenia. South Med J. 2010;103(7):676-8