

Incentives to Increase Pharmacovigilance Practices from an Educational and Ethical Point of View



Müberra Devrim Güner*¹ and Perihan Elif Ekmekci²

¹Department of Medical Pharmacology, TOBB Economy and Technology University, Turkey

²Department of History of Medicine and Ethics, TOBB Economy and Technology University, Turkey

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***Corresponding author:** Müberra Devrim Güner, TOBB Economy and Technology University, Medical Faculty Department of Medical Pharmacology. Söğütözü Cad. No: 43 06560, Ankara, Turkey, E-mail: devrimguner@etu.edu.tr

Abstract

An adverse drug reaction (ADR) is a burden both to healthcare system and has economic, medical and ethical dimensions. ADR reporting is a responsibility of all healthcare professionals and is essential for the effectiveness of Pharmacovigilance system. ADR reporting in Turkey is still below the average of similar income countries. The main reason for low reporting rates can be lack/insufficiency of reporting culture and limited awareness about the importance of reporting. This can be improved by incorporating pharmacovigilance practices and ADR reporting procedures education and training to both undergraduate and continuous education of healthcare professionals.

Keywords: Pharmacovigilance; Medical education; Adverse drug reaction reporting

Abbreviations: ADR: Adverse Drug Reaction; WHO: World Health Organization; TÜFAM: Turkish Pharmacovigilance Center; TADMER: Turkish Drug Adverse Event Monitoring and Evaluation Center

Introduction

The World Health Organization (WHO) defined adverse drug reaction (ADR) as “a response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function” in 1972. Pharmacovigilance was defined as “the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other drug-related problem” in 2002 by WHO. WHO initiated a program for international drug monitoring which is based in Uppsala since 1978 Turkey became the 27th member of the program in 1987.

In Turkey, pharmacovigilance activities were institutionalized by the establishment of “Turkish Drug Adverse Event Monitoring and Evaluation Center” (TADMER) in 1985. However, a regulation on the Monitoring and Assessment of the Safety of Medicinal Products for Human Use was published 20 years later in 2005 by Turkish Republic Ministry of Health, and was updated as “Regulation on safety of drugs” in 2014 [1]. Pharmacovigilance practices were reevaluated by this regulation and activities carried by “Turkish Pharmacovigilance Center” (TÜFAM) such as data collection, risk evaluation, trainings, and inspections were increased. Since 2005, hospitals have

been required to assign a healthcare professional to function as a “contact point” for pharmacovigilance activities within the hospital. “Good Pharmacovigilance Practices” guidelines were also published in 2014 [2].

These efforts are all in line with the current activities in European Union (EU) and the United States of America (USA), but as proven by scarce literature on this issue, ADR reporting rates are still below the expected numbers Turkey[3-6]. ADR reporting is a responsibility of all healthcare professionals and is essential for the effectiveness of pharmacovigilance system [1]. According to a current study reporting rates gradually increased since 2005 [3], however still below the average of similar income countries: the ADR reporting rate of Turkey is 2 reports/million inhabitants/year [7]. Most of the ADR reports from Turkey were reported by physicians (59.8%), followed by pharmacists (9.1%) and other healthcare professionals (28.7%) [3].

ADR is an important public health problem. According to a meta-analysis of 39 USA studies, the overall incidence of serious ADRs is 6.7% and fatal ADRs is 0.32% making ADRs 4th -6th leading cause of death [8]. Hospital admission rate is 5.1% and increases with age up to 9.8% (>75 years) and 40% of these admissions are considered to be avoidable [9]. According to a

current meta-analysis, the median prevalence of ADR is 6.3% and median proportion of preventable ADRs accounts to 71.7% [10]. ADRs also bring an important economic burden to the health system, causing an average cost of 260\$ per patient and total estimated cost per year 588 million \$ for Germany [11]. Hospitalizations due to ADR cost about 1840-3000€/hospital admission for France [12]. Drug-related morbidities cost about 30 – 130 billion \$/year in USA [13].

ADR reporting also carries a very important ethical dimension besides the health and economic burden. Considering the main ethical principles of medicine, underreporting of ADR is problematic in terms of two principles: beneficence and respect for autonomy. The concept of benefit includes avoiding any potential risk of harm as well [14]. Reluctance in reporting ADR inarguably augments health risks for other patients who are subject to the same treatment. It also avoids the accumulation of scientific knowledge regarding effects the drug, which would lead to the dominance of false data in literature and misuse of resources. This would breach the prima facie duty of the physicians' to respect the autonomy of their patients as well since the information they provide during informed consent would lack some information essential to their patients' health. Therefore, it is plausible to say that the principle of benefit and respect to autonomy require the physicians to take active action to report ADR.

Physicians' responsibility in reporting ADR is justifiably broadened by utilitarian ethical theory, which suggests that an action that produces maximum utility for a maximum number of people is ethically right and therefore should be done [15]. This approach enhances the responsibility of the physician to provide benefit not only for her particular patient but for all patients suffering from the same health problem and have the potential to use the same drug, as well as contributing to the accumulation of scientific data. Moreover underreporting ADRs may lead significant negative economic and public health consequences by diverting health expenditures to futile or even harmful treatments.

The scarce reporting rates can be attributed to the lack/insufficiency of reporting culture and limited awareness about the importance of reporting. According to several surveys although healthcare professionals have knowledge of pharmacovigilance and ADRs, the reporting rates are around 10-15% [16]. The awareness and knowledge, although not sufficient, is highest among medical doctors, and decreases significantly for other healthcare professionals [4,6,17,18]. Moreover, the healthcare professionals other than medical doctors think that suspecting an ADR, detecting and reporting it is only a responsibility for medical doctors [6,17,18]. Competent and confident health professionals can be accomplished by increasing the knowledge of pharmacovigilance and prioritizing medical safety and ethics at each step of daily medical practice. The necessary incentives to obtain the goals are to develop a more comprehensive pharmacovigilance syllabus underlining the ethical aspects of

individual patients' and public's health and wellbeing, medical professionals 'competency, pharmaceutical companies and regulatory authorities' roles and responsibilities. Moreover, this education must also not be limited to graduate schools but must be expanded to continuous professional education.

The numbers of Turkish medical schools are 81 as of 2017. In order to harmonize and increase the quality, standardization of the medical education is required. Council of Higher Education published "National Core Education Program" in 2002 and updated in 2014 [19]. Medical schools are required to set their curricula in coherence with the core program. According to the updated program of 2014, pharmacovigilance related competencies of a medical student graduate can be listed as:

- a) To plan, apply and monitor a rational medical treatment
- b) To comply with principles of treatment of special populations (pediatric, geriatric, pregnant, lactating and patients with hepatic and renal diseases)

To calculate drug doses accurately

Moreover "adverse effects of drugs and drug interactions" is listed in "symptoms and clinical conditions". The subject of "drug side effects" is classified as a multisystem problem and the skill objectives defined as follows in National Core Education Program [19]:

- i. To diagnose and treat
- ii. To define and treat the emergency condition
- iii. To refer to a specialist in case of need
- iv. To monitor and control for long term under primary health care conditions
- v. To apply the prevention methods

The activity of ADR and other related pharmacovigilance practices are not mentioned in the "record keeping, reporting and communication" part of the basic medical practices defined by National Core Education Program [19]. We suggest that next update must include a comprehensive handling of ADR and pharmacovigilance practices, as "reporting an ADR" is defined as "responsibility of healthcare professional" by above mentioned national pharmacovigilance regulations.

Beckmann et al. defined elements of pharmacovigilance training and stated that comprehensive pharmacovigilance syllabus can be achieved only by multidisciplinary collaboration and involvement of all stakeholders in order to achieve a custom-made curriculum covering the needs of each party. With this background, these experts created a comprehensive, detailed and balanced curriculum of pharmacovigilance [20]. Moreover, the guideline on good pharmacovigilance practices, which is a set of measures drawn up to facilitate the performance of pharmacovigilance in the EU can also be consulted while preparing a comprehensive and continuing education for pharmacovigilance [21] (Table 1).

Table 1: Basic elements of pharmacovigilance education and training.

Basic elements of pharmacovigilance education and training
What is and Why do we Need Pharmacovigilance?
Subject and scope of pharmacovigilance
History of pharmacovigilance: important ADRs and methodological and organizational developments
ADRs and public health
Fundamental Clinical Aspects of ADRs
Types and mechanisms of ADRs
Pharmacogenetic causes of inter-individual variability in the susceptibility to ADRs
Non-genetic risk factors for ADRs and complex interactions
Clinical management of ADRs
Product specific considerations
Vaccines pharmacovigilance
Biological medicinal products
Important ADRs and 'Risk Driving' ADRs of Important Medicines
ADRs at organ classes where 'Type B' reactions are important and the most involved drugs
ADRs at organ classes where 'Type A' reactions are most important and the most involved drugs
'Risk drivers' of important drugs for common illness and chronic diseases, biologicals, herbals
'Individual Case Safety Reports' (ICSRs)
Concerns about ADRs: medical, ethical and regulatory background and reasons for reporting
Contents, structure, and validity of reports and reporting procedures
Pharmacovigilance in Clinical Trials
Characteristics of pharmacovigilance in clinical trials
Guidance and regulatory framework
Medication Errors
Medication error (ME): definition, impact, detection
ME reports: description and assessment
Preventive measures
Spontaneous ICSR Reporting Systems (SRS)
Definition, settings, potential, and limitations of SRS
Computerized ICSR: introduction and practical application of national SRS
Data transmission and entry
Benefit-Risk Assessment
'Benefit-risk': definitions, methodological approaches; disease as criterion of benefit
Drug-related risks (ADRs): analyzing, weighting and combining their components
Balancing benefit/chance vs. harm/risk and comparing different treatment options

We believe that elements of this curriculum can be incorporated into the education of healthcare professionals both in undergraduate and continuing professional training, with a tailor-made approach. Profound knowledge of subjects such as rational drug use, prescription skills, drug use in special populations such as geriatric, pediatric and pregnant and lactating women are also essential to minimize the risk of ADRs and other prescription and medication errors. We also believe that both pharmacovigilance and these subjects should be covered in theoretical and practical courses and should be

integrated to medical education program spirally, and the learning objectives and the outcomes should be defined adequately. This will not only increase the quality of diagnostic, prescription and treatment skills of future healthcare professionals but also will increase the knowledge, ability, and skills sufficient to perform pharmacovigilance activities properly.

Conclusion

In conclusion, realization of the centrality of pharmacovigilance to public health and its ethical importance

by the regulatory authority, educators and pharmaceutical industry is the first step to improve the quality and quantity of pharmacovigilance activities and prevention of ADRs. Adding a comprehensive pharmacovigilance curriculum both to graduate and professional continuing education of all healthcare professionals, measuring of pharmacovigilance performance by governments and policymakers consistently and comprehensively on individual and institutional basis will also contribute to the idealization of pharmacovigilance activities. Raising not only professional but public awareness of the need and importance of pharmacovigilance through campaigns, seminars, workshops and, the creation of online and/or other means of user-friendly reporting mechanisms are also important elements of improvement.

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