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Derleme

Tıp Lisans Eğitiminde Eğitimsel İlerlemenin Farmakolojik Bakış Açısından Bir Yansıması

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ÖZ

Teknolojideki gelişmelere yeni bilginin hızlı birikiminin eşlik etmesi yüksek öğretim kurumlarını sağlık bakımı sağlayıcı sistemler için mezunlarını hazırlama şekillerini değiştirmeye zorlamaktadır. Yüksek öğretimdeki tıp eğitim uygulayıcıları mezun olacak tıp öğrencilerinin yaşam boyu akademik performanslarında ilerlemeler sağlayacak uygun ders programı revizyonlarını araştırmalıdır. Advers ilaç reaksiyonlarının ve tıbbi cihaz olaylarının çok ciddi sağlık sorunlarına yol açabileceği literatürde ortaya konmaktadır. Üniversitelerde tıp, eczacılık, diş hekimliği, hemşirelik ve ebelik öğrencilerine farmakovijilans eğitimi için bir uluslararası standart bulunmamaktadır. Bu derlemenin amacı yüksek öğretimde farmakoloji ders programında farmakovijilansın, ekofarmakovijilansın ve tıbbi cihaz olumsuz olaylarının önemine dair bir farkındalık yaratmak ve tıp akademisyenlerinin mezun olacak öğrencilerin advers ilaç reaksiyonlarını ve tıbbi cihaz olumsuz olaylarını ulusal yasalarla uyumlu bir şekilde vijilans sistemine uygun raporlamasını teşvik etmedeki ve uygun atık yönetiminin ve farmasötiklerin ve kişisel bakım ürünlerinin güvenli atılımının desteklenmesindeki rolünün altını çizmektir.

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Review

A Reflection of Educational Advancements In Undergraduate Medical Education From Pharmacological Perspective

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ABSTRACT

Advances in technology accompanied by the rapid accumulation of new knowledge force higher education institutions to change the way in which they prepare their graduates for healthcare delivery systems. Medical education administrators in higher education should seek the appropriate curricular revisions that will yield the improvements in the lifelong academic performance of undergraduate medicine students. Adverse drug reactions and medical device incidents may cause “serious health issues” as shown in literature. There is no international standard exists for teaching pharmacovigilance at universities for undergraduate medical, pharmacy, dentistry, nursing and midwifery students. The aim of this review is to raise the awareness of the importance of pharmacovigilance, ecopharmacovigilance and medical device incidents in pharmacology curriculum in higher education and to underline the role of medical academics in encouraging undergraduate students for appropriate reporting of adverse drug reactions and medical device incidents to vigilance systems in accordance with national regulations and also in promoting for proper waste management and safe disposal of pharmaceuticals and personal care products.



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Introduction

Transformation experienced in medical sciences and the increasing number of faculties of medicine has required determination of importance of the national undergraduate pharmacovigilance (PV) education for medicine students, in particular. The “World Health Organization” (WHO) defined an “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” (1). In addition, the WHO defined PV as “the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other drug-related problem”. The WHO defined the concept with specific aims that would broaden the term. One of the specific aims of PV defined by the WHO was “to improve patient care and safety in relation to the use of medicines and all medical and paramedical interventions”. Another example for the specific aims of PV defined by the WHO was “to promote understanding, education and clinical training in pharmacovigilance and its effective communication to health professionals and the public” (1, 2). Initiation of the “WHO Programme for International Drug Monitoring” had started with the thalidomide’s worldwide tragedy. The safety monitoring systems were set up to prevent this tragedy from ever happening again. In 1961, the drug was taken off the market in many countries. The WHO created a collaborative system for international drug monitoring in 1968 in order to collect individual reports of suspected ADRs (1,2). In 1978 establishment of the “WHO Collaborating Centre for International Drug Monitoring Uppsala Monitoring Centre” (UMC) accelerated providing technical support to countries so that they could form national PV centers (PVCs). “Individual case safety reports” (ICSRs) are submitted to the “WHO database” known as “Vigibase” by the national PVCs (1,3).

The history of PV began in 1985 by the foundation of the institution named “Turkish Adverse Drug Reaction Monitoring and Evaluation Center (TADMER) under the General Directorate of Pharmaceuticals and Pharmacy”. Turkey connected

to the network of the UMC as the 27th member in 1987 (4-6). In 2005, TADMER was reconstructed with a new name “Turkish Pharmacovigilance Center” (TUFAM). National PV program has been conducted by TUFAM since 2005. The term PV in the name was chosen to place particular emphasis on this topic. Adding PV to the name of the institution may be interpreted as the global integration of TUFAM to the network of national PVCs; the collaborative system created by the WHO. “The Regulation on the Monitoring and Assessment of the Safety of Medicinal Products for Human Use” came into force as the first PV regulation. In 2014, it was updated to the “Regulation on safety of drugs” by the Turkish Republic Ministry of Health “in the context of harmonization with EU directives”. In addition, the “Good Pharmacovigilance Practices Guidelines” were published (5-8). From 2005, hospitals with fifty or more beds have been required to assign a “pharmacovigilance contact person (PCP)” who is identified in the regulation as “a medical doctor, pharmacist, or, where these are not available, a dental practitioner” in the hospital (4,9).

“The General Directorate of Pharmaceuticals and Pharmacy” changed its name as “Turkish Medicines and Medical Devices Agency (TMMDA)” in 2012 (4,6). TMMDA is the sole responsible authority for developing and implementing regulatory, supervisory, and steering policies for medicines, medical devices and cosmetics. Three main “EU Directives 90/385/EEC, 93/42/EEC, 98/79/EEC” relating to medical devices are harmonized to Turkish Legislative Acts by the Agency (10). Inspections related to medical device vigilance system, are also conducted by the TMMDA. Health institutions and organizations have been required to assign a contact person responsible for medical device incidents reporting to medical device vigilance system, who is a medical doctor, pharmacist or a healthcare professional (10-12). Eventhough many medical devices and drug-device combination products such as medical monitors, pacemakers, cochlear implants, micropumps, antimicrobial central venous catheters, and orthopedic device-based drug delivery systems gain significant recognition in improving the quality of patient’s life, it has to be noted that they may

increase the risk of errors related to health care devices (13).

PV the monitoring of safety after drugs' marketing approval, can be determined highly by the proper reporting of ADRs. Studies indicated that approximately "5% of all acute hospitalizations" were originated from ADRs (14-16). "Healthcare professionals" and "marketing authorization holders" (MAHs) are the two vital sources for ADR reports submitted to TUFAM nationwide. The "Regulation on the Safety of Medicinal Products" defines the "healthcare professionals responsible for ADR reporting" as "a physician, pharmacist, dental practitioner, nurse or midwife" in Turkey (4,6). The literature related to PV is scarce in Turkey. A current study analyzing the ADR reports reached to TUFAM from 2005 to 2014 determined the gradually increasing reporting rates since 2005. It was found that 59.8% of the reporters were healthcare practitioners, 28.7% were other healthcare professionals and 9.1% were pharmacists (6). According to a study among nurses conducted in a state hospital in Turkey, it was determined that only 8% of nurses knew about TUFAM (17). Another study among practitioners and nurses, in particular, conducted in Turkey showed that the term "pharmacovigilance" was heard for the first time by 35.5% of the participants (9). Another study conducted among pharmacists showed that only 17.2% of the pharmacists had any knowledge about "pharmacovigilance" (18). In another study aiming to evaluate the awareness of TUFAM among physicians and nurses, conducted in a university hospital in Turkey showed that it was as low as 30% (19). In another survey aiming to evaluate the awareness of PV among nurse and midwives determined that only 23.3% of the participants could correctly define it (20). Underreporting is a global problem which creates health and ethical burden and our reporting rates are low compared to those in developed countries (9, 21).

In September 2010, the European Parliament adopted the amendments to existing PV legislation that serve to extend the realm of conventional pharmacovigilance to encompass the environmental concerns (22,23). We also agree that conventional PV may be extended to include the environmental concerns such as active pharmaceutical ingredients (APIs) in medications and their residues as environmental pollutants originated from the afterlife of drugs and the environmental footprints of healthcare industry (24). "The International Society of Pharmacovigilance (ISoP)" communicated "the Environment Committee of the European

Parliament" and " the Working Party on Pharmaceuticals and Medical Devices" in order to "to have ecopharmacovigilance as an integral part of pharmacovigilance" (25). The term ecopharmacovigilance, first coined by Velo, has been defined as "the science and activities concerning detection, assessment, understanding and prevention of adverse effects or other problems related to the presence of pharmaceuticals in the environment, which affect both human and the other animal species" (25, 26). Pharmacovigilance works in the field of adverse effects of pharmaceuticals on patients and ecopharmacovigilance, which can be interpreted as a form of pharmacovigilance focusing on the environmental concerns, aims to monitor the adverse effects of pharmaceuticals both on the environment and on humans through indirect non-therapeutic exposure (26). Accumulated unused medications, ultimately becoming chemical waste, serve as indicators of an avoidable burden to the environment. They represent wasted health-care resources and lost opportunities for achieving rational therapeutic medication. They are also primary targets in the growing public health crises of drug diversion, antibiotic resistance and non-therapeutic use and accidental or self-inflicted poisonings (27, 28). Because of these reasons, we should raise the awareness of PV and ecopharmacovigilance among the healthcare professionals (not only health practitioners, pharmacist, dentist, nurses, midwives but also veterinary doctors) and teach them proper reporting of ADRs and safe disposal of pharmaceuticals and personal care products (PPCPs).

As of 2018, there are 92 registered active medical schools in Turkey (29). The important first step toward bringing standardization of undergraduate medical education began with the decision taken by "Medical/Health Sciences Education Council" in 2001 and a national core education program developed in 2002 by the Council of Higher Education. At the meeting of the "Council of Medical Deans" in 2014, a new national framework was named as "National Core Curriculum-2014 (NCC-2014)" for undergraduate medical education which had been extensively revised as an outcome/competency-based curriculum (30,31). The NCC-2014 was reconstructed in the framework of four fundamental components: "The Aim of Medical Education" and The Frame of National Competencies" (competencies of a medical graduate) with the lists of the "Symptoms/Situations", "Core Diseases/Clinical Problems" and "Basic Medical Practices" and was approved by the Turkish Interuniversity Council

(TUC 2014) (31). According to the NCC-2014, pharmacovigilance and medical device vigilance related competencies of a graduated medical student can be listed as follows: To plan, administer and monitor a rational medical treatment and to act according to the principles of treatment in special populations; pregnant and lactating women, pediatric, geriatric individuals and patients with renal and hepatic diseases (32). “Adverse effects of drugs and drug interactions” is listed in “symptoms/clinical situations” part of NCC-2014. We propose adding “medical device safety” to the same part. We also introduce a proposal to discuss adding the term on which a general consensus will be reached (as it is a newly emerging science) to “D.Environmental / global conditions section” in the “symptoms/clinical situations” part (26). The terms are ecopharmacology (33), environmental pharmacology (34), pharmacoenvironmentology (35), pharmacoecovigilance (23), ecopharmacostewardship (36) and finally ecopharmacovigilance. This latter term ecopharmacovigilance reflects the approach communicated at the “ISoP annual meeting in Ghana in November 2010” and that endorsed by Velo and Moretti (37, 25). In NCC-2014, “drug side effects” are classified as multisystem problem and “the skill objectives” are defined as follows: “to diagnose and treat”, “to define and treat the emergency condition”, “to refer to a specialist in case of need”, “to apply the prevention methods and to monitor and control for long term under primary health care conditions”. In this review we propose that “medical device incident” should be added to “drug side effects” in “core disease/clinical problems” part with the same skill objectives. The reporting of adverse drug reaction and medical device incident is a critical element of collecting post-marketing safety data, these practices are also regulated by national pharmacovigilance and medical device regulations. We determined that activity of ADR and medical device incidents reporting and pharmacovigilance related other activities at least causality and severity assessment of the ADR and communication skills are not included to the “record keeping, reporting and communication” section of “the basic medical practices list” defined by NCC-2014 (30). We propose adding “adverse drug reaction reporting and medical device incident reporting” to the “record keeping, reporting and communication section” of the list. We also suggest adding “Safe disposal of pharmaceuticals and personal care products (PPCPs)” to “invasive and noninvasive procedures section” in “basic medical practices list” of NCC-2014.

“A stakeholder’s meeting was initiated on behalf of the WHO”. It was organized by LAREB in 2016. The “LAREB WHO Collaborating Centre for Pharmacovigilance in Education and Patient Reporting” indicated and agreed on the “competencies in the field of pharmacovigilance” for undergraduate students that should be developed and “the key aspects that should be taught”. We also agree that “the WHO PV core curriculum” can be integrated into the education of healthcare professionals both in undergraduate and postgraduate levels in accordance with the national needs as no relevant international standard exists on teaching pharmacovigilance at universities for undergraduate and postgraduate students (38). This may result in updating the key aspects of their pharmacology curricula for medicine educators in higher education. The pharmacology academics who are tasked with teaching pharmacovigilance may seek for the materials that may provide the appropriate topics they should cover in their courses. A platform of sharing educational materials can be considered in a web-portal developed by “The Netherlands Pharmacovigilance Centre LAREB the WHO Collaborating Centre for Pharmacovigilance in Education and Patient Reporting” (39). The EMA publications of “Good pharmacovigilance practice” and also new guideline in paediatric populations “Guideline on good pharmacovigilance practices: Product- or Population-Specific Considerations IV: Paediatric population” can also be referred (40).

Conclusion

In line with the needs of professional training, we also want to suggest that pharmacology educators in medicine should pay particular attention to errors with medication, good prescription practices, “rational drug use” and “drug use in special populations” in their curricula. These are topics that are also relevant to aforementioned concepts and should be continuously updated. Academic world, societies of pharmacology, pharmaceutical industry and regulatory authority should join forces and provide contribution to raise the awareness of the necessity and legal importance of pharmacovigilance and medical device incidents reporting in undergraduate medical education for high quality healthcare delivery. Seeking curricular interventions yielding the greatest benefit is critical for making progress toward raising the awareness of pharmacovigilance, ecopharmacovigilance, safe medication disposal practice in order to reduce antibiotic resistance and environmental footprint of healthcare professionals for maintaining or improving the collective health and well-being.

References

1. WHO. The Importance of Pharmacovigilance - Safety Monitoring of Medicinal Products, 2002; 1-52.
2. WHO. Pharmacovigilance: ensuring the safe use of medicines. WHO Policy Perspectives on Medicines, 2004; 1-5.
3. UMC, cited 12.03.2019, <https://www.who-umc.org/about-us/our-story>.
4. TMMDA, Turkish Medicines and Medical Devices Agency, Turkish Pharmacovigilance Center, cited 14.02.2019 <https://www.titck.gov.tr/faaliyetalanlari/ilac/farmakovijilans>.
5. Republic of Turkey Official Gazette. Regulation on the monitoring and assessment of the safety of medicinal products for human use, 2005, cited 12.03.2019 <http://www.resmigazete.gov.tr/eskiler/2005/03/20050322-7.htm>.
6. Ozcan G, Aykac E, Kasap Y, Nemutlu NT, Sen E, Aydinkarahaliloglu ND. Adverse Drug Reaction Reporting Pattern in Turkey: Analysis of the National Database in the Context of the First Pharmacovigilance Legislation. *Drugs Real World Outcomes*, 2016; 3(1):33-43.
7. Republic of Turkey Official Gazette. Regulation On The Safety Of Medicinal Products By Turkish Medicines and Medical Devices Agency Legislation on Drug Safety, 2014; Official Gazette No: 28973 2014.
8. TMMDA Turkish Drug and Medical Device Agency. Guideline on Good Pharmacovigilance Practices: Module I - Management and reporting of adverse drug reactions Guideline on Good Pharmacovigilance Practices: Appendix I – Definitions, 2014.
9. Guner MD, Ekmekci PE. Healthcare professionals' pharmacovigilance knowledge and adverse drug reaction reporting behavior and factors determining the reporting rates. *J Drug Assess*. 2019; 8(1):13-20
10. TMMDA. T.C. Sağlık Bakanlığı Türkiye Tıbbi Cihaz Sektörü Strateji Belgesi Ve Eylem Planı 2016-2020; 1-19
11. Mashaki Ceyhan E, Gürsöz H, Alkan A, Coşkun H, Koyuncu O, Walker S. The Turkish Medicines and Medical Devices Agency: Comparison of Its Registration Process with Australia, Canada, Saudi Arabia, and Singapore. *Front Pharmacol*. 2018; 25;9,9.
12. TMMDA. Notification on the principles and procedures related to the warning system of medical devices 2010, cited 12.03.2019 http://www.farmakovijilansdernegi.org/files/2010.07.14_Notification_on_the_principles_and_procedures_related_to_the_warning_system_of_medical_devices
13. Fitzpatrick D. *Implantable Electronic Medical Devices*, 1st ed. ISBN: 9780124165779; 2014.
14. Pirmohamed M, James S, Meakin S, Green C, Scott AK, Walley T, Farrar K, Park BK, Breckenridge AM. Adverse drug reactions as cause of admission to hospital: prospective analysis of 18820 patients. *BM J* 2004.;329(7456):15-9.
15. Angamo MT, Chalmers L, Curtain CM, Bereznicki LRE. Adverse drug reaction related hospitalisations in developed and developing countries: a review of prevalence and contributing factors. *Drug Saf*. 2016;39(9):847-57.
16. Leendertse AJ, Egberts ACG, Stoker LJ, van den Bemt PM, HARM Study group. Frequency of and risk factors for preventable medication related hospital admissions in The Netherlands. *Arch Intern Med*. 2008;168(17):1890-6.
17. Vural F, Ciftci S, Vural B. The knowledge, attitude and behaviours of nurses about pharmacovigilance, adverse drug reaction and adverse event reporting in a state hospital. *Northern Clinics of İstanb*. 2015;1(3):147-152
18. Toklu HZ, Uysal MK. The knowledge and attitude of the Turkish community pharmacists toward pharmacovigilance in the Kadikoy district of Istanbul. *Pharm World Sci*. 2008;30(5):556-62
19. Ergün Y, Ergün TB, Toker E, Ünal E, Akben M. Knowledge attitude and practice of Turkish health professionals towards pharmacovigilance in a university hospital. *Int. health*. 2018. DOI: 10.1093/inthealth/ihy073
20. Alan S, Ozturk M, Gokyildiz S, Avcibay B, Karataş Y. An evaluation of knowledge of

pharmacovigilance among nurses and midwives in Turkey. *Indian J Pharmacol.* 2013;45(6):616-8

21. Aydınkarahaliolu N.D., Aykaç E, Atalan Ö, Demir N, Hayran M. Spontaneous Reporting of Adverse Drug Reactions by Consumers in Comparison with Healthcare Professionals in Turkey from 2014 to 2016. *Pharmaceutical Medicine* 2018;32:353–364

22. Directive 2001/83/EC European Parliament. Draft European Parliament Legislative Resolution: proposal for a directive of the European Parliament and of the Council amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to medicinal products for human use (COM(2008)0665 – C6 0514/2008-2008/0260(COD)). Committee on the Environment, Public Health and Food Safety, European Parliament, Strasbourg, Session Document A7–0159/2010, 2010 www.europarl.europa.eu/sides/getDoc.do?pubRef=//EP//NONSGML+REPORT+A7-2010-0159+0+DOC+WORD+V0//EN

23. Daughton CG, Ruhoy IS. Green pharmacy and pharmecovigilance: prescribing and the planet. *Expert Rev Clin Pharmacol.* 2011; 2:211-32

24. Daughton CG, Ruhoy IS. The afterlife of drugs and the role of pharmecovigilance. *Drug Saf.* 2008; 31(12):1069-82.

25. Velo G, Moretti U. Ecopharmacovigilance for better health. *Drug Saf.* 2010; 33(11):963-8

26. Holm G, Snape JR, Murray-Smith R, Talbot J, Taylor D, Sörme P. Implementing ecopharmacovigilance in practice: challenges and potential opportunities. *Drug Saf.* 2013;36(7):533-46

27. Daughton CG. Eco-directed sustainable prescribing: feasibility for reducing water contamination by drugs. *Sci Total Environ.* 2014; 493:392-404.

28. Daughton CG, Ruhoy IS. Lower-dose prescribing: minimizing "side effects" of pharmaceuticals on society and the environment. *Sci Total Environ.* 2013;443:324-37.

29. YÖK Tıp eğitiminde intörlük çalıştay 10.01.2018, cited 12.03.2019, https://www.yok.gov.tr/Documents/Yayinlar/Yayinlarimiz/Tip_egitiminde_intornluk_calistayi.pdf

30. Gulpinar M, Gürpınar E, Vitrinel A. Evaluation of the undergraduate medical education national core curriculum-2014: National frame of medical education in Turkey. *KMJ* 2018; 50(1): 43-53

31. Turkish Interuniversity Council. National Core Curriculum 2014. Cited 12.03.19 https://www.yok.gov.tr/Documents/Kurumsal/egitim_ogretim_dairesi/Ulusal-cekirdek-egitimi-programlari/tip_fakultesi_cep.pdf

32. Guner MD. Incentives to Increase Pharmacovigilance Practices from an Educational and Ethical Point of View. *J of Pharmacol & Clin Res.* 2017;3 (5)

33. Kummerer K, Velo G. Ecopharmacology: a new topic of importance in pharmacovigilance. *Drug Saf.* 2006;29(5):371–3.

34. Rahman SZ, Khan RA. Environmental pharmacology: a new discipline. *Indian J Pharmacol.* 2006;38:229–30.

35. Rahman SZ, Khan RA, Gupta V, Uddin M. Pharmacoenvironmentology: a component of pharmacovigilance. *Environ Health* 2007.;6:20.

36. Taylor D. Chapter 7 - Ecopharmacostewardship – A Pharmaceutical Industry Perspective, In: K. Kümmerer, M. Hempel (eds.), *Green and Sustainable Pharmacy*, DOI 10.1007/978-3-642-05199-9_7, C Springer-Verlag Berlin Heidelberg, 2010

37. Murray-Smith R. Ecopharmacovigilance: a drug company perspective. 10th Annual Meeting of the International Society of Pharmacovigilance, Accra, Ghana. 2010. Cited 04.04.13 http://isop2010.isoponline.org/uploads/prog/Programme_-3rd_-_7th_November-.pdf

38. Van Eekeren R, Rolfes L, Koster AS, Magro L, Parthasarathi G, Al Ramimmy H, Schutte T, Tanaka D, van Puijenbroek E, Härmark L. What Future Healthcare Professionals Need to Know About Pharmacovigilance: Introduction of the WHO PV Core Curriculum for University Teaching with Focus on Clinical Aspects. *Drug Saf.* 2018;41(11):1003-1011

39. LAREB, Netherlands Pharmacovigilance Centre Lareb, cited 03.01.17 <https://www.pv-education.org/>

40. GVP Guideline on good pharmacovigilance practices (GVP): Product- or Population-Specific

Considerations IV: Paediatric population,2008,
cited:19.03.2019[https://www.ema.europa.eu/en/doc
uments/scientific-guideline/guideline-good-
pharmacovigilance-practices-gvp-product-
population-specific-considerations-iv_en-0.pdf](https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-good-pharmacovigilance-practices-gvp-product-population-specific-considerations-iv_en-0.pdf)