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Review Article

Risk undermined in the bilateral pharmaceutical regulatory system in Taiwan

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ABSTRACT

The concept of Pharmacovigilance Planning and Risk Minimization Planning (PVP/RMP), initiated by the International Conference on Harmonization (ICH), addressed an important conceptual change from monitoring the safety of individual medicine to proactively conducting risk prevention for the minimization of medication error. However, the implementation of PVP/RMP is a challenge in societies like Taiwan where irrational medication and co-medication is prevalent. It is even more difficult in Taiwan where two regulatory bodies are governing pharmaceutical affairs, namely Taiwan Food and Drug Administration (TFDA) in charge of Western Medicine (WM) and the Department of Chinese Medicine and Pharmacy (DCMP) in charge of Traditional Chinese Medicine (TCM). There are thus dual-tract drug approval panels, two GMP controls and two independent adverse drug event reporting systems. This rendered irrational co-medication of WM and TCM undetectable and the standard tools for monitoring pharmacovigilance inapplicable. The bilateral regulatory system is conceptually unscientific in accordance with PVP/RMP and unethical from humanity point of view. The first part of this review delivers (1) social aspects of polypharmacy in Taiwan; (2) regulatory aspects of pharmaceutical administration; (3) risks undermined in the bilateral regulatory system and (4) pharmacoepidemiology in relation to the risk of polypharmacy. As evidence-based medicine (EBM) forms the fundamental risk-benefit assessment on medication, the second part of this review delivers (1) the scientific aspects of the beauty and the odds of biological system that governs host–xenobiotics interaction; (2) conceptual evolution from product management (pharmacovigilance) to risk management (PVP/RMP); (3) non-biased due process is essential for risk-benefit assessment on medicinal products and (4) the opinion of the authors on system building for safe medication.

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1. Introduction

Pharmacovigilance Planning and Risk Minimization Planning (PVP/RMP), a theme of proactive system building on safe medication, represents important conceptual evolution from monitoring the safety of individual medicine (pharmacovigilance) to conducting risk prevention for the minimization of medication error (use of medicine). It was initiated by the International Conference on Harmonization (ICH) and becomes a global trend [1,2].

However, the implementation of PVP/RMP is a challenge in societies like Taiwan where irrational medication and co-medication is prevalent. It is even more difficult in Taiwan where the dual-track regulatory bodies are governing pharmaceutical affairs of western medicine (WM) and traditional Chinese medicine (TCM). Attempts in integrating WM and TCM into a sound uni-track regulatory body under Taiwan Food and Drug Administration (TFDA) failed when the Governmental Reformation Plan took place in year 2005.

Potential risk of irrational medication in Taiwan will first be described in this report from social and pharmaco-epidemiological aspects. Risk generated due to the complexity of product-oriented bilateral regulation and administration will be analyzed. How to implement a sound risk management on pharmaceuticals based on evidence-based risk-benefit assessment will be discussed.

To be specific, quality, safety and efficacy (QSE) are three criteria in drug approval for IND (investigational drugs) and NDA (new drug application) no matter they are synthetic, natural, biological or biotech generated origin. In practice, the approval panel is an integrative evaluation process of which the review committee is composed of a pool of QSE experts. As the products are different by nature, standards are set in different categories for products of different origin. In other words, pharmaceuticals are subjected to a uni-track review scheme while the review is executed based on different standards according to their nature.

TCM, as licensed drug, is logically subjected to the same approval panel. There is no point to single out TCM from other pharmaceuticals. However, sponsors in Taiwan can choose, at their own will, either administration body to apply for IND and NDA, as QSE criteria are different in the bilateral drug approval systems. Moreover, with two administration bodies independently in charge of TCM and drugs other than TCM, there are two quality assurance schemes, two post-marketing monitoring systems and two adverse drug reporting systems in Taiwan. Unknown risks are thus undermined both for consumers (health risk) and for the society (pharmaco-epidemiology), as there is no mechanism to exercise an integrative risk analysis. It is government's responsibility to establish a due process in order to exercise integrative risk analysis along the life cycle of all pharmaceuticals.

This report will then describe the humanity-based risk-benefit assessment on pharmaceuticals. The conceptual change initiated by ICH and the publication of PVP/RMP guidance thereof for system building of safe medication indicates that product management need to be transformed to humanity-based risk management in modern era. With two independent pharmaceutical administration bodies it is impossible to exercise such risk management. It is the responsibility of lawmakers to seriously review current situation and take into consideration of system building for safe medication in order to keep abreast of the global trend on PVP/RMP.

1.1. *Polypharmacy*

Polypharmacy is widespread in the general public. Besides registered medicine, the population of complementary/alternative medicine (CAM) and TCM users is growing, especially in the aged and in patients with chronic disease [3,4]. As a considerable large portion of patients take CAM (including TCM) with registered medicines without notification to professionals, standard tools for monitoring of pharmacovigilance have its limitation. Safety threat thus emerges from various scientific and pharmacoepidemiological reports. Evaluation of clinical efficacy and adverse reactions caused by interactions of herbal remedy with conventional therapy becomes a critical issue [5,6].

1.2. *Social aspects of irrational medication and co-medication in Taiwan*

Taiwan is known for its outstanding national health insurance program which benefits 99% of the population. The welfare-like program rendered Taiwanese overusing the healthcare resources, indicated by the high physician's visit per person and the large number of drug items (both WM and TCM) per prescription [7,8]. Other than prescription drugs, patients took TCM in retail shop without notifying medical professionals. The imbalanced distribution of pharmacy service between hospitals, clinics and community pharmacies further reflects the lack of mechanisms for professional pharmacists to conduct pharmacovigilance monitoring on polypharmacy [9].

1.3. *Regulatory aspects of pharmaceutical administration in Taiwan*

CAM, including TCM, are marketed without license in most of the developed countries. Claims for therapeutic efficacy are thus prohibited or limited to authorized indications. TCM however are classified as licensed drugs in Taiwan. There are two regulatory bodies governing pharmaceutical affairs, namely Taiwan Food and Drug Administration (TFDA) in charge of WM and the Department of Chinese Medicine and Pharmacy (DCMP) in charge of TCM. There are thus two parallel drug approval panels in regulating clinical trials of investigational new drugs (IND) and new drug application (NDA), two GMP regulations and two adverse drug event reporting systems within the government [10].

The bilateral regulating system rendered standard tools for pharmacovigilance monitoring inapplicable, which is conceptually unscientific in accordance with evidence-based risk-benefit assessment for PVP/RMP in modern era. It led to the irrational co-medication undetectable and considered unethical from humanity point of view [11].