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Editorial:

DRUG SELECTION AND ADVERSE DRUG REACTIONS: BALANCING OUTCOMES AND COSTS

Enrique Seoane-Vazquez, Ph.D.

Assistant Professor, College of Pharmacy and College of Public Health, The Ohio State University, Columbus, Ohio, USA

pharmacoeconomics @ osu.edu

Version española

Regulatory agencies approve drugs for marketing when the ratio of risk to benefit of the drugs is positive, i.e. the potential benefit of using the drug justifies the risk of drug related adverse reactions (ADR). At the point of approval of a drug there is not adequate information about all possible negative outcomes arising from its use in clinical practice. The information is even more limited for patient subgroups, diseases and treatment combinations that were not evaluated in the clinical trials required for approval. Therefore, performing post-marketing pharmacoepidemiological studies is necessary for a better understanding of drug use in usual clinical practice conditions and the effect of the drugs on the general patient population.

The incidence of ADRs has been considered high. A study pooling the incidence of ADR related hospital admissions of multiple studies derived a median of 4.1% ADR related hospital admissions in the USA[1]. Higher ADR related hospital admissions were reported among specific subpopulations at risk, e.g. cardiovascular patients[1]. Another study found that 6.5% of all hospitalizations in the UK were related to ADR[2]. Severe ADRs may lead to hospital intensive care unit admission[3]. The intensive care units also have a higher rate of ADRs than other hospital units[4]. A high incidence of ADRs was also identified in the ambulatory setting with an estimated 180.000 life threatening or fatal adverse drug effects per year in the USA[5].

The article by Alfonso Orta et al[6] is a pharmacoepidemilogic study that presents a series of case reports of ADRs identified in the intensive care unit of a Cuban hospital. The study identifies streptokinase, a thrombolytic drug used for dissolving blood clots, as the drug involved in 61% of the ADRs reported. Problems associated with the safety of streptokinase have been known to be caused by its potential antigenicity, short half-life, and lack of fibrin specificity[7,8]. These problems motivated a drastic reduction of streptokinase use in the USA.

Streptokinase is available as a generic drug and its therapeutic alternatives have higher cost[9]. Drug cost is the main reason why streptokinase continues to be used around the world in spite of its potential risks, especially in health care systems with fewer resources available for health care.

Rational drug utilization requires consideration of drug cost as a factor in the therapy selection decision-making process. But other costs should also be considered in the process. Health care costs such as physician visits or hospital care, and not health care costs such as informal caregiver time and patient time for treatment should also be considered. Consideration of health care costs is especially important when a drug of lower cost may generate a higher rate of ADRs that could require expensive hospital care or intensive care.

While ADRs generate negative health outcomes, costs are also associated with the prevention, identification and treatment of these reactions. Hospital care represents an important part of the costs of ADRs due to an increase in admissions and in the length of stay[1,10,11].

Rational drug utilization requires an evaluation of the risk/benefit ratio and the cost of pharmaceuticals. Pharmacoepidemiologic studies of ADRs allow for the identification of potential drugs and therapeutic classes where prevention efforts could best improve clinical outcomes and/or reduce the costs of those events. The fact that the majority of the ADR identified by Alfonso Orta et al[6] are related to the use of streptokinase suggests that prevention efforts in Cuba should first focus on this drug. Additionally, the cost-benefit of streptokinase from the perspective of the Cuban health care system should be assessed.

Several strategies have been proposed to reduce the incidence of ADRs[1,10]. These strategies include educational activities, risk group identification programs, implementation of clinical guidelines, clinical and laboratory monitoring of ADR, and drug safety monitoring. Special mention should be given to the need of more pharmacoepidemiologic research, such as the one conducted by Alfonso Orta et al[6], and more organized pharmacoepidemiologic studies (e.g. case-control studies).

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