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Pharmacovigilance in the Long-Term use of Medications and the Alternative Based on the Combination of Drugs to Reduce Adverse Effects

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Abstract

Some demographic changes such as increased life expectancy and increased chronic degenerative diseases make pharmacovigilance is an important opportunity to clarify aspects of drug safety in patients with long-term treatment. A pharmacological alternative which seeks to improve these aspects of safety of using drugs, it is the combination of drugs with different mechanisms of action are analyzed through mathematical models to reduce the therapeutic doses but maintaining and even improving the therapeutic effect and thus reducing the adverse effects to avoid toxicity.

Keywords: Pharmacovigilance; Drug combinations; Adverse effects; Drug interaction

Introduction

Evolution is something inherent to the human being and can be noticed in the changes in the population pyramid, the increase in life expectancy, hygienic-dietary habits, and advances in research for the development of treatment strategies for various diseases. This general public health problems because chronic degenerative diseases are the main causes of morbidity and mortality in the world.

These changes impact on the pharmacovigilance process, defined by World Health Organisation as the science and activities relating to the detection, assessment, understanding, and prevention of the adverse effects or any other drug-related problem [1], due to the increased prevalence of chronic degenerative diseases, patients ingest several drugs for life.

This implies that there are new questions such as: How long can a drug maintain effective? What about adverse effects? What about polypharmacy in patients with chronic diseases? How important drug interactions in these patients?.

At first drug design was focused on efficacy and not security, but due to some major events such as chloroform death cases in 1848, cases of malformation using thalidomide in pregnant patients in 1961 [1]. Emerge strategies to ensure both the effectiveness and safety of medicines and toxicity tests in animals, controlled clinical trials and today with the help of technology was implement bioinformatics tools to predict some mutagenic toxicological, teratogenic or used based on the chemical structure before moving to the biological tests, improving the selection process of new molecules on security issues [2].

Despite the use of these strategies are used to establish a security profile, there is currently no preclinical or clinical study that might clarify the questions above however, this information could be obtained by an adequate system of pharmacovigilance with systematic and detailed collection of data on the harmful effects associated with drugs in patients with chronic treatments or polypharmacy. Clarifying that this is only a small contribution which carries this branch of pharmacology, the pharmacovigilance.

Beyond the analysis of the information obtained through routine actions of Pharmacovigilance is also important to consider the molecular aspects that may help explain some questions as How long can a drug maintain effective? This is of special interest because for instance, patients who present with chronic pain must use two or more medicines for pain, plus there is a significant percentage of detachment to treatment by the presence of adverse effects or decreased efficacy.

The pharmacodynamics tolerance, refers to the diminished by repeated administration of a drug response, that is that over time higher dose is required to have the desired effect. It is given by defensive actions of the organism against the presence of the drug, changing the number or receptor expression, or changes in signaling pathways [3]. This explains why some drugs cannot remain effective in prolonged treatment because the body can activate other ways to counteract the effects of drugs, leading to a need to ingest more than one drug or even having to replace it.

A pharmacological alternative which seeks to improve these aspects of safety of using drugs, it is the combination of drugs with different mechanisms of action are analyzed through mathematical models to reduce the usual doses but maintaining and even improving the therapeutic effect and thus reducing the adverse effects to avoid toxicity [4].

By combining drugs pharmacological interaction that is when the activity or effect of a drug undergoes quantitative or qualitative modification by the presence or by the action of another occurs, drug interactions mainly occur by two different mechanisms, and based on this are classified into pharmacokinetic and pharmacodynamic interactions, but there are occasions where can perform the two types of interactions [5].

Pharmacokinetic interaction occurs when a drug combination influences the cycle of the other drug in the body, altering any of

pharmacokinetic processes such as absorption, distribution, metabolism and elimination.

The pharmacodynamic interaction occurs when a drug influences the action mechanism of generating another drug synergy, potentiation, antagonism, or hypersensitization receptor desensitization by modification in subsequent molecular processes activation.

To administer two or more drugs can alter its individual effect generating three effects, when the observed effect is higher than expected have as a supra-additive effect or potentiation, when the observed effect is less than expected have infra-additivity or antagonism, and when the observed effect is like that expected that is no interaction will be called additive effect [4,6-8]. What defines either a drug combination, the deviation of the observed effect relative to expected.

As science and technology advances, drug combinations have been defined and continues to expand its scope however because biological systems and mathematical analysis of dose-response curves are complex, there are several models, approaches, assumptions and theories analysis drug combination [6,7,9,10].

A method which provides the mathematical basis for assessing synergy to determine dose combination is the isobolographic analysis is based on the concept demonstration of dose equivalence applied to an experimental design [8]. After knowing the type of interaction by combining two drugs in equi-effective dose is important to an assessment of adverse effects to verify that it complies with the aim of decreasing the dose also decreases the probability of adverse characteristics of each drug combination.

Conflict of Interest

None of the authors has any conflict of interest to disclose.

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