Farmacia HOSPITALARIA
Órgano oficial de expresión científica de la Sociedad Española de Farmacia Hospitalaria

EDITORIAL
Bilingual edition English/Spanish

Personalized drug therapy: A new challenge for hospital pharmacy departments

Farmacoterapia personalizada: Un nuevo reto para los servicios de farmacia

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Received 22 October 2021;
Accepted 29 October 2021.
DOI: 10.7399/fh.13044

How to cite this paper
Bermejo-Vicedo T, Gorgas MQ. Personalized drug therapy: A new challenge for hospital pharmacy departments. Farm Hosp. 2021;45(Suppl 1):S3-4

In the last few decades personalized medicine and pharmacogenomics have experienced great advances due to their impact on improving therapeutic individualization. This helps to identify the most effective treatment for the patient, avoiding potential damage.

Pharmacogenetics/pharmacogenomics uses genetic information to predict response to drug therapy (identification of responding and non-responding patients), determine the probability of adverse events, and establish the optimal dose for each patient. It identifies individual differences in response to the treatments, which is key to therapeutic optimization[1]. It is a well-known fact that differences with respect to response to treatment are related to genetic factors, age, nutrition, health status and environmental conditions, among others. Pharmacogenetics/pharmacogenomics may also contribute to selecting the most effective therapy for subpopulations of patients sharing the same disease but with different genetic profiles[2].

On the other hand, we know that individual variability in the response to drug therapy depends on the drug 's pharmacokinetics and pharmacodynamic profile.

There are many genetic variations (polymorphisms) in metabolizing and transporting enzymes that affect the response of drugs, by affecting the pharmacokinetic process. Therefore, pharmacogenomics impacts the pharmacokinetics and pharmacodynamics of the drug[3]. Therefore, pharmacogenetics/pharmacogenomics will play a significant role in future drug development and decision-making in clinical practice[1].

The pharmacist's role in clinical pharmacogenetics as part of the multidisciplinary team (physicians, laboratory staff and geneticists) in charge of following up on the patient has recently been defined by the American Society of Health-System Pharmacists (ASHP)[4].

According to the ASHP, clinical pharmacogenomics, using genetic information, is a tool that allows pharmacists to guide decisions on therapeutic individualization in relation to the optimal selection of the drug and dose for the patient, maximizing the therapeutic effect and minimizing toxicity. Pharmacogenetic data should therefore be included in the patients' electronic medical record, just like potential allergies, adverse events, interactions, adherence and other therapeutic monitoring parameters to be taken into account by the pharmacist.

In Spain, at this time, not many hospitals pharmacy services (HPS) engage in pharmacogenetics. According to a survey conducted by the Spanish Society of Hospital Pharmacists (SEFH) in 2019[5], intended to gain a better understanding of the clinical activities of HPS, only 4.3% of HPS make pharmacogenetic reports. The percentage rises to 23% in the larger hospitals. These figures are significantly lower than those related to determination of drug plasma levels (carried out by 12% of HPSs) and pharmacokinetic reports (performed by 34.1% of all HPSs and by 76% of those in hospitals with over 1,000 beds).

Pharmacokinetic and pharmacogenomic principles are relevant to a wide number of drugs, including cardiovascular, anti-infectious, antineoplastic, antipsychotic and immunosuppressant agents. For that reason, and to encourage a better understanding of this discipline, *Farmacia Hospitalaria* journal has prepared this special issue titled "Personalized drug therapy in clinical practice".

This publication includes review articles and originals dealing with the pharmacokinetic and pharmacodynamic criteria needed to monitor plasma concentrations of drugs such as antineoplastic and anti-infectious agents to personalizing a patient's treatment. This could result in a decrease in the toxicity and an increase in the effectiveness of antineoplastics. Likewise, pharmacokinetic models for anti-infectious agents have been shown to be an invaluable tool to optimize the drugs' plasma levels and prevent the development of resistance to the drugs, improving their safety profile.

This issue also provides information on how to optimize the pharmacokinetic adjustment of sirolimus plasma concentrations using a population-based pharmacokinetic model to achieve a higher clinical benefit. This drug's high pharmacokinetic variability means that dose individualization and monitorization of plasma levels in patients with a renal transplant are crucial to boost the treatment's effectiveness.

Another study included in this issue shows that monitorization of plasma concentrations of vedolizumab during the induction phase in patients with

ulcerative colitis is extremely useful in individualizing treatment and increasing its effectiveness.

It is also shown how proactive pharmacogenetic analyses of biologic drugs in patients with inflammatory bowel disease may achieve benefits in terms of clinical remission.

In the area of neuropsychiatry, the use of drugs with wide interindividual pharmacokinetic variability and metabolized by highly polymorphic enzymes such as CYP2D6 and CYP2C19 is common. Application of pharmacokinetics and pharmacogenetics to the dosing of the drugs to be employed is likely to become a useful tool in personalizing a patient's treatment adjustments in psychotropic drug therapy.

The complexities inherent in the surgical management of hemophilic patients require an appropriate titration of clotting factors to prevent hemorrhagic complications and avoid an excessive consumption of these products. We include a systematic review of a series of pharmacokinetic studies on hemophilic patients, analyzing the methods used, the main pharmacokinetic covariants used and the recommendation made by clinical guidelines.

In the field of oncology, one of the studies in this special issue discusses the relatively high prevalence of loss of function variants in the dihydropyrimidine dehydrogenase (DPYD) gene in patients with digestive tumors, as well as the importance of genotyping such variants before starting treatment with fluoropyrimidines as a way of preventing their toxicity.

Furthermore, use of genetic identification in clinical practice requires a new generation of sequencing panels. These have been shown to be an extremely effective and high-quality tool to determine the prevalence of new pharmacogenetic variants and identify the treatments that may potentially be affected by them.

At the same time, it is essential to systematize the evidence available on the different computer tools that can be used for pharmacokinetic drug monitoring to make it easier for users to identify, evaluate and select them.

Lastly, one of the studies reports on the results of a recent survey on the clinical and educational activities of the pharmacokinetics and pharmacodynamics units of HPSs. According to the survey, such units are experiencing a steady development in our country.

All of us should, as hospital pharmacists, take advantages the opportunities made available by pharmacogenetics and pharmacokinetics to make a significant contribution to the multidisciplinary teams we participate in thus enhance the effectiveness and safety of patients' treatments.

We would like to thank all contributing authors for their great work. This issue would not have been possible without their invaluable collaboration.

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