DETERMINATION OF GENETIC POLYMORPHISMS OF THE DIHYDROPYRIMIDINE DEHYDROGENASE GENE IN REAL CLINICAL PRACTICE: POSOLOGICAL INDIVIDUALISATION

Alvarado Fernández, MD.; Murillo Izquierdo, M.; Cordero Ramos, J.; Rendon de Lope, L; Donoso Rengifo, C.; Moya Martin, M.
UGC Farmacia. Hospital Universitario Virgen Macarena. Sevilla.

BACKGROUND

Fluoropyrimidines are antineoplastic drugs used for the treatment of many types of solid tumors. Approximately 80-90% administered is metabolized by the enzyme dihydropyrimidine dehydrogenase(DPYD).

The partial or total deficiency of this enzyme is related to severe toxicity and in some cases it can cause the death of the patient.

PURPOSE

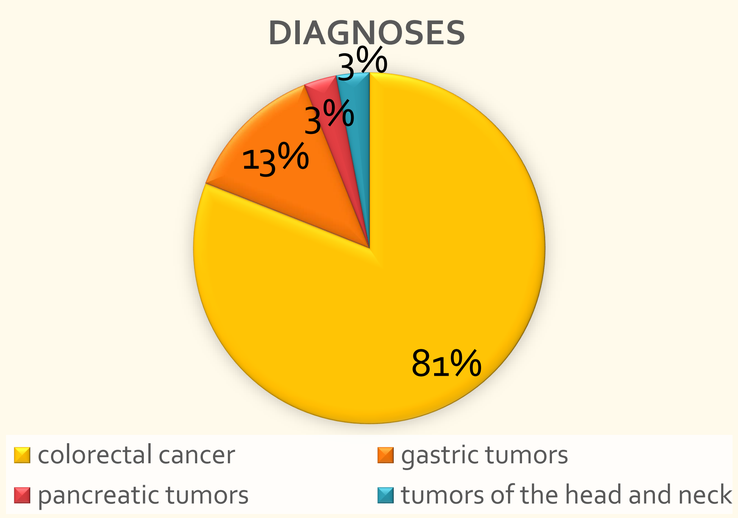
The aim of our study is to determine the frequency of these polymorphisms in the DPYD gene in patients treated in our hospital and identify those patients with predisposition to excessive toxicity if they are exposed to fluoropyrimidines.

MATERIAL AND METHODS

The genetic analysis of the DPYD gene was performed on all patients who started treatment with fluoropyrimidines between September 2017 and June 2018. The variables collected were: sex, age, type of tumor diagnosed and toxicity presented in the first five treatment cycles according to the CTCAE (Common Terminology Criteria for Adverse Events) classification. Data was obtained by the electronic medical record (Diraya®) and the electronic prescription program (Farmis®).

The polymorphisms studied were rs3918290, rs55886062, rs67376798, rs56038477(evidence 1A).

RESULTS



The genetic analysis was performed on 89 patients, 76% men and 24% women. The median age was 70 years.

Most of the diagnoses correspond to colorectal cancer (81%). 13%gastric tumors, 3%pancreatic tumors and 3%tumors of the head and neck. The patients presented the following adverse events: digestive toxicity in 57% of patients (CTCAE:1,2,3), haematological toxicity 15% (CTCAE:2), hepatotoxicity 6%(CTCAE:2, 3), neuropathy 16% (CTCAE:1,2) and erythrodysaesthesia 10% (CTCAE:1,2,3).

37% of patients required drug withdrawal or dose reduction due to the toxicity presented.
Regarding the results of the polymorphisms studied, 97% presented a wild-type genotype for the analyzed variants. 3% patients presented some mutated allele (heterozygote): one patient for rs3918290 and two patients for rs67376798 coinciding with the patients who presented greater toxicity.

CONCLUSIONS

The heterozygous patients detected are at risk of developing severe toxicity when they are treated with fluoropyrimidines and they required a dose adjustment of these drugs.

The use of these pharmacogenetic tools for the determination of polymorphisms of the DPYD gene in routine practice allows us to predict the potentially serious toxicity favoring the individualized use of these drugs.

Servicio Andaluz de Salud
CONSEJERÍA DE SALUD Y FAMILIAS

ATC code:
L01 - Cytostatics

http://www.eahp.eu/24-5PSQ-061

5PSQ-061

Hospital Universitario Virgen Macarena