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GENOTYPING ANALYSIS OF POLYMORPHISMS IN THE DIAHYDROPYRHYDROMIDINE DEHYDROGENASE (DPYD) GENE PRIOR TO ADMINISTRATION OF FLUOROPIRMIDINES

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BACKGROUND AND IMPORTANCE

It is highly recommended to genotype DPYD gene polymorphisms before administration. Complete deficiency of DPD activity is very rare, estimated at 0.01% to 0.5% of individuals, partial deficiency has been estimated at 3% to 8%.

AIM AND OBJECTIVE

The aims of the study included the description and frequency of DPYD gene polymorphisms prior to fluoropyrimidine administration in all tumour types and the measures taken.

MATERIALS AND METHODS

Retrospective, multidisciplinary study in a tertiary hospital, with the participation of pharmacy, clinical analysis and oncology departments, by reviewing the genotyping of DPYD gene polymorphisms. Oncology patients who were genotyped in the period from June 2020 to December 2021 were included.

DPYD variants

- DPYD*2A
- c.2846A>T
- c.1679T>G
- c.1236G>A(HapB3)

Variables

- Sex
- Age
- Tumour location
- Variant found
- Degree of enzime activity

Enzime activity

- Poor metaboliser (0-0.5)
- Intermediate metaboliser (1-1.5)
- Normal metaboliser (2)

RESULTS

Tumour location

- Colorectal 48,7%
- Breast 22,7%
- Gastric 8,7%
- Pancreatic 8,7%
- Cholangiocarcinoma 6%
- Head and neck 2,7%
- Others 2,5%

Enzyme activity level deficiency

- Activity level 1,5 → 5 (30%)
- Activity level 1 → 8 (53%)
- Activity level 0,5 → 1 (6%)
- Activity level 0 → 1 (6%)

Variants found

- 6 (40%) c.2846A>T
- 3(20%) c.1129-5923C>G
- 7(46.7%) c.1156G>T(*12)
- 1 (6.7%)c.1777 G>A
- 1(6.7%) c.1905+1G>A
- 1(6.7%) c.483+18G>A
- 1(6.7%) c.1236G>A.

150 patients, 56.7% female, median age of 68.9 years (53.2-84.6)

15 patients (10%) had some degree of enzyme deficiency

CONCLUSION AND RELEVANCE

The main diagnoses were colon and breast cancer. 10% of patients studied had some degree of enzyme deficiency according to the variants analysed, 8.6% with partial deficiency and 1.3% with complete deficiency. Our population showed a high prevalence of deficiencies in relation to the literature described. This determination allowed dose adjustment of these drugs, which represents an advance in terms of safety, allowing personalised treatments, individualising doses and avoiding toxicities.

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