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DETERMINATION OF VORICONAZOLE METABOLISER PHENOTYPE IN THE ABSENCE OF GENETIC TESTING

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BACKGROUND AND IMPORTANCE

It is metabolized mainly by CYP2C19 → enzyme with a considerable genetic polymorphism → variable metabolism in the population

Its genotyping is expensive and inaccessible → Development of alternative methods to determine the patient's metaboliser phenotype

AIM AND OBJECTIVES

To determine the metaboliser phenotype according to plasma concentrations (Cp) of voriconazole using a population pharmacokinetic model

MATERIALS AND METHODS

Observational, descriptive, retrospective study of patients treated with intravenous and oral voriconazole in a second level hospital from 01/2016 to 06/2024.

1. Clinical data collection: medical history number, weight, posology, route and rate of administration, Cp and concomitant treatments with prednisone, methylprednisolone, dexamethasone, carbamazepine, phenytoin, ritonavir and St. John's wort.

2. Application the Dolton pharmacokinetic model to each patient using NONMEM software through Pirana

Patient X
- CYP2C19=1 → Patients with one or more loss-of-function alleles (**Poor metaboliser**)
- CYP2C19=0 → Patients not meeting the previous criteria (**Normal/rapid metaboliser**)

→ Cp CYP2C19=0 (CppCYP2C19=0)
→ Cp observed (Cpo)
→ Cp CYP2C19=1 (CppCYP2C19=1)

3. Deduction of metaboliser phenotype

Cpo value closest to CppCYP2C19=1	→	**Poor metaboliser**
Cpo value closest to CppCYP2C19=0	→	**Normal/rapid metaboliser**
Values very different or very similar to each other	→	**Not possible to determine the metaboliser phenotype**

RESULTS

Patients= 47 → Cp voriconazole= 85

Metaboliser phenotype	Number of patients (%)
Normal/rapid	30 (63.9%)
Poor	3 (6,4%)
Not determined	14 (29,7%)

CONCLUSION AND RELEVANCE

The metaboliser phenotype could be estimated in 70,3% of patients.

The application of the Dolton pharmacokinetic model to the Cp of voriconazole obtained could be a useful tool, in the absence of genetic studies, to determine the metaboliser phenotype of our patient.