

The Evaluation of CYP2D6, CYP2C9 and CYP2C19 Polymorphisms for Personalized Medicine in Psychiatry Patients

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Introduction

The cytochrome P450 proteins are drug-metabolizing enzymes that involves in many catalytic reactions (1). Interindividual variability in drug response is a majör problem in clinical practice. Interindividual variability in drug response is a major clinical problem (2). In this study we aimed to investigate the role of CYP2D6, CYP2C9, CYP2C19 polymorphisms of shizophrenic and bipolar patients to evaluate the therapeutic response may allow the treatment to be individualized.

Material and Method

This study was carried out on patients who attended to the Çukurova University Psychiatric Unit with a diagnosis of schizophrenia and bipolar disorder involved in our study. DNA was automatically extracted by MagnaPure Compact instrument (Roche). Melting curve analysis by real-time PCR (Roche LightCycler 480) was performed by LightMix Kit® (TIB MOLBIOL) after DNA isolation to determine the genotype for CYP2D6 (*3/*4), CYP2C9 (*2/*3) and CYP2C19 (*2/*3) variants (3).

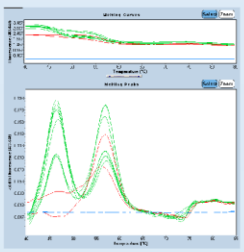


Figure 1. CYP2C9 *2 and *3 genotyping

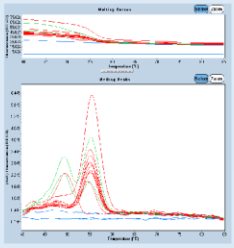


Figure 2. CYP2C19 *2 and *3 genotyping

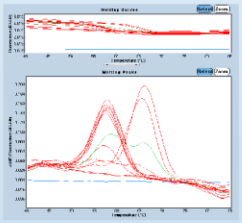


Figure 3. CYP2D6 *3 and *4 genotyping

Results

One hundered and one patients involved in our study. The genotypes and the melting curve results are are shown in Table 1 and Figure 1-3.

Table 1. Genotype frequencies of study population

	Genotype	Number of Subjects	Observed Frequency %
Psychosis			
CYP2C9	CYP2C9 *1/*1	19	35.2
	CYP2C9 *1/*2	5	9.3
	CYP2C9 *1/*3	28	51.9
	CYP2C9 *2/*2	0	
	CYP2C9 *3/*3	0	
	CYP2C9 *2/*3	2	3.7
CYP2C19	CYP2C19 *1/*1	44	81.5
	CYP2C19 *1/*2	8	14.8
	CYP2C19 *1/*3	0	
	CYP2C19 *2/*2	3	3.8
	CYP2C19 *3/*3	0	
	CYP2C19 *2/*3	0	
CYP2D6	CYP2D6 *1/*1, *1/*5	43	79.6
	CYP2D6 *1/*3	2	3.7
	CYP2D6 *1/*4	7	13.0
	CYP2D6 *3/*3, *3/*5	0	
	CYP2D6 *4/*4, *4/*5	1	1.9
	CYP2D6 *3/*4	1	1.9
	Genotype	**Number of Subjects**	**Observed Frequency %**
Bipolar Disease			
CYP2C9	CYP2C9 *1/*1	9	10.6
	CYP2C9 *1/*2	1	2.1
	CYP2C9 *1/*3	28	51.9
	CYP2C9 *2/*2	0	
	CYP2C9 *3/*3	0	
	CYP2C9 *2/*3	2	3.7
CYP2C19	CYP2C19 *1/*1	44	81.5
	CYP2C19 *1/*2	8	14.8
	CYP2C19 *1/*3	0	
	CYP2C19 *2/*2	2	3.7
	CYP2C19 *3/*3	0	
	CYP2C19 *2/*3	0	
CYP2D6	CYP2D6 *1/*1, *1/*5	43	79.6
	CYP2D6 *1/*3	2	3.7
	CYP2D6 *1/*4	7	13.0
	CYP2D6 *3/*3, *3/*5	0	
	CYP2D6 *4/*4, *4/*5	1	1.9
	CYP2D6 *3/*4	1	1.9

Conclusion

Genetic polymorphism of human P450 enzymes enzymes and receptors known in the treatment process, may be important to maintain the availability of the treatment. This information may allow the prediction of therapeutic response or treatment to be individualized. Inter-individual variation in CYP expression can lead to marked variability in drug response, drug activity and therefore it is important to understand the genetic factors that influence CYP levels and activities.

The genetic variants are well established of CYP2C9, CYP2C19 and CYP2D6 have different frequencies for populations. We detected aproximately 20-30 % of pateints that have a mutation of CYP gene. This findings confirm the ethnic diffrernces of these polymorphisms. The drug response of the patients will be discussed at the end of the project. Pharmacogenetics will be used in clinical practice only if precise and specific treatment options and guidelines based on genetic tests can be provided (5).

Acknowledgements

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References

1. **Ingelman-Sundberg M.** Pharmacogenetics of cytochrome P450 and its applications in drug therapy: the past, present and future. TRENDS in Pharmacological Sciences, 2004; 25: 193-200.
2. **Samer CF, Lorenzini KI, Rollason V et al.** Applications of CYP450 Testing in the Clinical Setting. Mol Diagn Ther. 2013; 17: 165–184.
3. **Sistonen J, Sajantila A, Lao O et al**. CYP2D6 Worldwide genetic variation shows high frequency of altered activity variants and no continental structure. Pharmacogennetics and Genomics. 2007; 17: 93-101.
4. **Scordo MG, Caputi A, D'Arrigo C et al**. Allele and genotype frequencies of CYP2C9, CYP2C19 and CYP2D6 in an Italian population. Pharmacological Research 2004 ;50: 195–200.
5. **Porcelli S, Fabbri C, Spina E et al**. Genetic polymorphisms of cytochrom P450 enzymes and antidepressant metabolism. Expert Opin. Drug Metab. Toxicol. 2011; 7(9): 1101-1115.